International Journal of Advances in Medicine
Oak M et al. Int J Adv Med. 2025 May;12(3):333-339
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933

DOI: https://dx.doi.org/10.18203/2349-3933.ijam20251086

Review Article

High altitude marathon physiology changes

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Received: 30 January 2025
Accepted: 10 March 2025

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ABSTRACT

High-altitude marathons present unique physiological challenges due to environmental factors such as reduced oxygen availability, decreased atmospheric pressure, and extreme temperature fluctuations. These conditions impose significant stress on the human body, requiring acute and chronic physiological adaptations to maintain performance. Acute responses include increased ventilation, elevated heart rate, and enhanced oxygen delivery mechanisms, while chronic adaptations involve hematological changes such as elevated erythropoiesis, cardiovascular remodeling, and skeletal muscle adaptations. Despite these adaptations, high-altitude conditions can substantially impact athletic performance, reducing aerobic capacity and increasing the risk of hypoxia-induced fatigue. Effective training and acclimatization strategies, such as altitude training camps and pre-acclimatization protocols, are critical for optimizing performance and minimizing the risks of high-altitude illnesses, including acute mountain sickness (AMS), high-altitude pulmonary edema (HAPE), and high-altitude cerebral edema (HACE). Furthermore, genetic predispositions, as observed in high-altitude native populations, may influence an athlete's ability to adapt to these environments. This review explores the interplay between environmental challenges, physiological adaptations, and athletic performance in high-altitude marathons. It highlights current strategies for preparation, potential medical risks, and future research opportunities in understanding the unique demands of high-altitude endurance events. Insights from this study aim to guide athletes, coaches, and medical professionals in optimizing training, performance, and safety during high-altitude marathons.

Kaywords: High altitude marathon, Hypoxia, Vo2 Mx, Genetics, Training

INTRODUCTION

High-altitude marathons, such as those held in the Himalayas or the Andes, pose unique physiological challenges to athletes due to environmental conditions characterized by low oxygen availability, reduced atmospheric pressure, and extreme temperatures. These challenges are compounded by the physical demands of endurance running, necessitating a comprehensive understanding of physiological adaptations for optimizing performance and ensuring athlete safety.

At higher altitudes, the reduced partial pressure of oxygen decreases arterial oxygen saturation, impairing oxygen delivery to tissues.[1] To counteract this hypoxia, the body initiates acute compensatory mechanisms, including increased ventilation and elevated heart rate, to enhance oxygen uptake and transport.[2] Prolonged exposure results in chronic adaptations, such as increased red blood cell mass and hemoglobin concentration, driven by hypoxia-induced erythropoiesis, which enhances the oxygen-carrying capacity of the blood.[3] However, even with these adaptations, endurance performance is compromised at high altitudes.

Maximal oxygen uptake (VO_2 max), a critical determinant of aerobic performance, declines with increasing altitude, leading to reduced endurance capacity.[4] Additionally, high-altitude conditions heighten the risk of altitude-related illnesses, such as acute mountain sickness (AMS), high-altitude pulmonary edema (HAPE), and high-altitude cerebral edema (HACE), which can severely affect athletic performance and health.[5] Training and acclimatization strategies have been developed to address these challenges. The "live high, train low" approach, which involves living at high altitudes to stimulate erythropoiesis and training at lower altitudes to maintain high-intensity workouts, has shown promise in improving sea-level and high-altitude performance.[6] Nonetheless, the effectiveness of this method for high-altitude marathon preparation requires further exploration.

This review aims to examine the physiological changes associated with high-altitude marathon running, emphasizing the interplay between environmental stressors, acute and chronic physiological responses, and their impact on athletic performance. By integrating current research findings, the article seeks to provide actionable insights into training, acclimatization, and medical management strategies for high-altitude endurance events.

ENVIRONMENTAL CHALLENGES OF HIGH-ALTITUDE MARATHONS

High-altitude marathons expose athletes to extreme environmental conditions that significantly influence physiological function and athletic performance. These challenges stem primarily from reduced oxygen availability, decreased atmospheric pressure, temperature fluctuations, dehydration risks, and increased solar radiation.

Hypoxia and reduced oxygen availability

The defining characteristic of high-altitude environments is hypoxia, resulting from reduced barometric pressure and partial pressure of oxygen (PO_2). At 3,000 meters above sea level, arterial oxygen saturation decreases by approximately 10–15%, impairing oxygen delivery to working muscles and reducing exercise capacity.[7] This hypoxia also triggers immediate physiological compensations, such as hyperventilation and increased heart rate, to enhance oxygen uptake and delivery.[4]

The defining feature of high-altitude environments is hypoxia, stemming from reduced barometric pressure and partial pressure of oxygen (PaO_2). This hypoxia not only impairs oxygen delivery to tissues but also causes a measurable decline in maximal oxygen uptake (VO_2 max), which decreases by approximately 10% per 1,000 meters above 1,200 meters. Such reductions significantly affect endurance performance.

The 1968 Olympics in Mexico City, held at 2,240 meters, marked the first major athletic event to expose athletes to these challenges, providing a historic lens to evaluate altitude's impact on performance.[8] Edward Weiss later defined the "death zone" as altitudes above 8,000 meters, where oxygen levels are critically low for sustained human function.

Training models such as "live high, train high" and "live high, train low" have since been developed to address these challenges. While LHTH can impair training quality due to hypoxia, LHTL combines altitude acclimatization with high-intensity workouts at sea level, yielding superior outcomes.[9,10]

Atmospheric pressure reduction

Decreased atmospheric pressure at high altitudes reduces the driving force for oxygen diffusion into the blood, limiting maximal oxygen uptake (VO_2 max).[2] This reduction has direct implications for endurance performance, as VO_2 max is a critical determinant of aerobic capacity.

Temperature fluctuations

High-altitude environments are characterized by significant diurnal temperature variations, with daytime heat and nighttime cold. These fluctuations impose additional thermal stress on athletes, requiring efficient thermoregulation. The low ambient temperatures also increase the risk of hypothermia during pre-race and post-race recovery periods.[11]

Dehydration risks

Altitude-related dehydration is exacerbated by increased respiratory water loss due to hyperventilation and reduced thirst response in hypoxic conditions.[12] This fluid imbalance can impair thermoregulation, reduce plasma volume, and negatively affect cardiovascular function and endurance performance.

Increased solar radiation

The thinner atmosphere and lower oxygen levels at high altitudes result in greater exposure to ultraviolet (UV) radiation. This heightened UV exposure increases the risk of sunburn, oxidative stress, and eye damage.[7] Athletes require appropriate protective measures, including sunscreen and UV-protective eyewear, to mitigate these risks.

Combined stressors

The simultaneous exposure to hypoxia, thermal stress, dehydration, and UV radiation creates a complex environment that challenges the physiological homeostasis of marathon runners. Athletes must adapt not only to the individual stressors but also to their combined effects, which may exacerbate fatigue and impair performance.[4]

PHYSIOLOGICAL ADAPTATIONS TO HIGH-ALTITUDE MARATHONS

High-altitude marathons demand significant physiological adaptations due to the hypoxic environment, where oxygen availability is markedly reduced. Athletes undergo acute and chronic changes to optimize oxygen delivery and utilization, enhancing their ability to perform in these challenging conditions.

Acute adaptations

Increased ventilation

Hypoxia at high altitudes stimulates peripheral chemoreceptors, leading to hyperventilation. This response increases alveolar oxygen pressure and compensates for reduced oxygen availability.[13] Hyperventilation also facilitates the removal of carbon dioxide, improving blood pH and promoting oxygen unloading at tissues. Increased ventilation at high altitudes not only enhances oxygen uptake but also plays a critical role in maintaining blood pH and optimizing gas exchange. The Halden Bohr effect further supports this adaptive mechanism by facilitating efficient oxygen delivery and carbon dioxide removal. The Bohr effect ensures enhanced oxygen unloading at the tissue level, driven by the elevated carbon dioxide and hydrogen ion concentrations resulting from hypoxic exercise.

Simultaneously, the Halden effect complements this by improving carbon dioxide transport in oxygen-rich conditions, ensuring metabolic byproducts are efficiently cleared. Together, these mechanisms enhance the body's ability to cope with the dual challenges of oxygen deficit and metabolic stress in high-altitude environments. These processes underscore the intricate physiological interplay critical for sustaining endurance performance in marathon runners exposed to severe hypoxia.[14]

Elevated heart rate

The immediate cardiovascular response to hypoxia includes an increase in heart rate, which augments cardiac output to improve oxygen delivery to muscles and vital organs.[2]

Redistribution of blood flow

Blood flow is preferentially redirected to vital organs and active muscle groups. This compensatory mechanism helps prioritize oxygen delivery to regions most critical for performance and survival.[11]

Chronic adaptations

Erythropoiesis and haemoglobin concentration

Chronic exposure to high altitudes stimulates erythropoiesis through hypoxia-inducible factor-1 (HIF-1), which upregulates erythropoietin (EPO) production. This leads to an increase in red blood cell mass and hemoglobin concentration, enhancing the blood's oxygen-carrying capacity.[3] Additionally, the dynamic regulation of the oxygen dissociation curve plays a vital role in optimizing oxygen transport. During acute hypoxia, the curve shifts leftward, increasing hemoglobin's oxygen affinity to improve pulmonary uptake. In contrast, prolonged exposure induces a rightward shift, mediated by elevated 2,3-diphosphoglycerate (2,3-DPG) levels, to enhance oxygen unloading at the tissues. These adjustments are essential for meeting the oxygen demands of working muscles during high-altitude endurance activities, were hypoxia limits oxygen availability.[13]

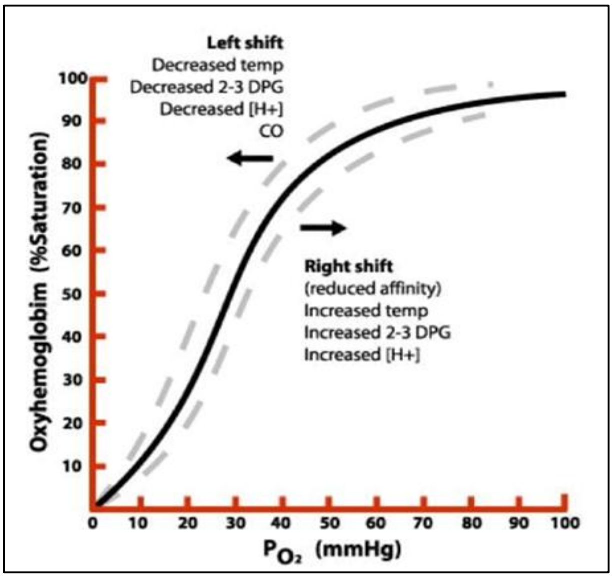

Figure 1: Oxygen hemoglobin saturation curve.

Capillary density and angiogenesis

Chronic hypoxia promotes angiogenesis and increases capillary density in skeletal muscles, facilitating more efficient oxygen diffusion from the blood to tissues.[15]

Mitochondrial efficiency

Muscle mitochondria adapt to hypoxia by optimizing oxidative phosphorylation pathways, enabling more efficient ATP production despite reduced oxygen availability.[16]

Enhanced oxygen utilization

Improved oxygen extraction at the tissue level is achieved through upregulation of myoglobin and other oxygen-binding proteins, enhancing muscle oxygen storage and delivery.[17]

Limitations of adaptations

Despite these adaptations, high-altitude conditions significantly impair maximal oxygen uptake (VO_2 max), leading to reduced endurance capacity. The adaptations also vary among individuals, influenced by genetic factors and the duration of acclimatization.[4]

Impact on athletic performance

High-altitude environments significantly impair athletic performance, particularly in endurance activities such as marathons.

Decline in VO_2 max

VO_2 max decreases by approximately 6–8% per 1,000 meters of altitude due to reduced arterial oxygen content, limiting high-intensity efforts and aerobic capacity.[2,4]

Aerobic and metabolic challenges

Endurance performance suffers as submaximal exercise demands a higher proportion of VO_2 max, leading to early fatigue. Hypoxia also shifts metabolism toward anaerobic pathways, increasing lactate production and muscle fatigue.[17,18]

Slower race times

Marathon runners often experience slower race times due to decreased oxygen delivery, altered energy metabolism, and environmental stressors like cold temperatures and steep terrain.[11]

Training and acclimatization

Acclimatization, particularly "live high, train low" strategies, mitigates some declines by improving oxygen transport and metabolic efficiency, though responses vary among individuals.[3]

Training and acclimatization strategies

Effective preparation for high-altitude marathons involves tailored training and acclimatization strategies, including pre-acclimatization protocols, altitude training camps, and nutritional interventions.

Pre-acclimatization protocols

Pre-acclimatization involves gradual exposure to simulated or actual high-altitude environments to mitigate the adverse effects of hypoxia. Intermittent hypoxic training (IHT) has been shown to enhance hematological adaptations, including increased erythropoiesis and hemoglobin levels, improving oxygen-carrying capacity.[19]

Altitude training camps: live high, train low paradigm

The "live high, train low" strategy is a cornerstone of altitude training. Athletes live at moderate altitudes to stimulate erythropoiesis and enhance oxygen transport while training at lower altitudes to maintain exercise intensity. This approach improves VO_2 max and endurance performance, with optimal results achieved after 3–4 weeks of altitude exposure.[3]

Nutritional interventions

Proper nutrition is essential for high-altitude adaptation. Increased carbohydrate intake supports energy demands and reduces reliance on fat metabolism, which is oxygen-intensive. Iron supplementation is critical for athletes undergoing erythropoietic adaptation to prevent iron deficiency anemia.[20] Antioxidants such as vitamins C and E may mitigate oxidative stress induced by hypoxia.[21]

Role of genetics in high-altitude adaptation

Genetics plays a critical role in determining individual and population-level adaptations to high-altitude environments. Insights from elite athletes and native high-altitude populations highlight the influence of genetic predispositions on physiological responses to hypoxia.

Genetic predispositions in elite athletes

Elite athletes often possess genetic variations that enhance oxygen transport, energy metabolism, and resistance to oxidative stress. For example, polymorphisms in the EPAS1 gene, which regulates the hypoxia-inducible factor (HIF) pathway, are associated with improved oxygen utilization and endurance performance.[22] Additionally, variants in genes like EPO and VEGF are linked to enhanced erythropoiesis and angiogenesis, respectively, conferring advantages in hypoxic conditions.[23,24]

Insights from high-altitude native populations

High-altitude native populations, such as Sherpas from the Himalayas and Andeans from South America, exhibit unique genetic adaptations to chronic hypoxia. Sherpas have specific EPAS1 and EGLN1 gene variants that limit excessive erythropoiesis, reducing the risk of chronic mountain sickness while maintaining efficient oxygen transport.

In contrast, Andeans demonstrate increased hemoglobin concentrations and oxygen-carrying capacity due to distinct genetic variations.[25] Interestingly, Tibetan populations exhibit adaptations that prioritize increased oxygen diffusion and utilization without excessive hemoglobin production, offering a distinct contrast to the Andean response.[26,27] These genetic differences underscore the diversity of high-altitude adaptations driven by evolutionary pressures.

Medical challenges and risk management

High-altitude marathons expose participants to unique medical challenges, necessitating proactive strategies for prevention and management to ensure athlete safety and optimal performance.

High-altitude illnesses

Acute mountain sickness

AMS is the most common high-altitude illness, presenting with symptoms such as headache, nausea, fatigue, and dizziness. It results from rapid ascent and insufficient acclimatization.[5] AMS often precedes more severe conditions such as high-altitude pulmonary edema.

High-altitude pulmonary edema

HAPE occurs as a result of hypoxia-induced pulmonary vasoconstriction, leading to elevated pulmonary artery pressure and fluid leakage into the alveolar spaces. The uneven vasoconstriction and subsequent mechanical stress on the capillaries are compounded by endothelial dysfunction, which increases vascular permeability.

These factors collectively result in fluid accumulation in the lungs, impairing oxygen exchange and causing symptoms like severe breathlessness and reduced exercise tolerance. If left untreated, HAPE can progress to respiratory failure, necessitating immediate descent to lower altitudes and oxygen therapy for effective management.[28] HAPE is often accompanied by more severe conditions like high-altitude cerebral edema, a life-threatening emergency.

High-altitude cerebral edema

HACE occurs due to hypoxia-induced cerebral vasodilation and increased intracranial pressure, coupled with blood-brain barrier (BBB) dysfunction that allows fluid to leak into brain tissue. This swelling impairs normal neurological function, presenting with symptoms such as confusion, ataxia, and decreased consciousness.

Progression from AMS to HACE underscores the need for prompt recognition and intervention. Immediate descent to lower altitudes, along with oxygen therapy and dexamethasone administration, is critical to prevent fatal outcomes.[5]

Strategies for prevention and management

Gradual ascent remains the most effective preventive measure for high-altitude illnesses, allowing the body time to acclimatize. Pharmacological prophylaxis, such as acetazolamide, can reduce the incidence of AMS by improving oxygenation and reducing hypoxemia.[29] Dexamethasone is also effective in preventing severe AMS and HACE.[30]

In the event of HAPE or HACE, immediate descent to lower altitudes is the most critical intervention. Supplemental oxygen and medications such as nifedipine for HAPE and dexamethasone for HACE are vital for stabilization.[28]

I*mportance of monitoring hydration and electrolyte balance*

Dehydration is a common issue at high altitudes due to increased respiratory water loss and reduced fluid intake. Maintaining hydration helps optimize blood viscosity, circulation, and thermoregulation. Electrolyte imbalances, such as hypokalemia or hyponatremia, can exacerbate symptoms of fatigue and impair muscle function, highlighting the need for balanced fluid and electrolyte intake.[31]

Future directions and research opportunities

High-altitude marathon physiology presents numerous avenues for future research and innovation. Addressing existing knowledge gaps and exploring new technologies and pharmacological interventions can enhance athlete safety and performance in extreme environments.

Gaps in understanding high-altitude marathon physiology

Current research has provided foundational insights into the physiological effects of high-altitude exposure, yet significant gaps remain.

Interindividual variability

The genetic and phenotypic factors influencing individual susceptibility to high-altitude illnesses and performance remain poorly understood.[32]

Long-term adaptation

While acute and subacute acclimatization are well-documented, the effects of prolonged exposure to high-altitude environments on musculoskeletal health and metabolic pathways require further investigation.[33]

Female-specific adaptations

There is limited understanding of sex-specific responses to high-altitude hypoxia, particularly regarding hormonal influences on oxygen transport and endurance capacity.[34]

Potential technological and pharmacological advancements

Emerging technologies and pharmacological strategies offer promising solutions to mitigate the challenges of high-altitude marathons:

Wearable monitoring devices

Advanced wearables equipped with sensors to track oxygen saturation, heart rate variability, and core temperature can provide real-time data to optimize performance and monitor for early signs of altitude-related illnesses.[35]

Hypoxia-mimetic agents

Pharmacological agents such as prolyl hydroxylases (PHD) inhibitors, which stabilize hypoxia-inducible factors, show potential for enhancing erythropoiesis and improving oxygen delivery during high-altitude exposure.[36]

Personalized nutrition and hydration plans

Utilizing genetic and metabolic profiling to tailor nutrition and fluid strategies can enhance individual adaptation and recovery.[31]

CONCLUSION

High-altitude marathons present unique physiological and environmental challenges, requiring a multidisciplinary approach to mitigate their impact on athlete performance and health. This review highlights key findings with practical implications for athletes, trainers, and researchers. The environmental challenges of high-altitude marathons, including hypoxia, extreme temperatures, and rugged terrains, underscore the need for thorough preparation and monitoring. Physiological adaptations such as increased erythropoiesis, enhanced oxygen delivery, and metabolic shifts demonstrate the body's remarkable ability to acclimatize to hypoxic conditions, emphasizing the importance of tailored acclimatization strategies.

High-altitude conditions significantly influence aerobic capacity, muscle function, and endurance, necessitating altitude-specific training and recovery plans. Effective interventions like pre-acclimatization protocols, altitude training camps, and nutritional strategies have been shown to enhance performance under these conditions. Genetic insights, particularly from high-altitude native populations, provide valuable lessons in optimizing adaptation strategies for athletes. Furthermore, the early detection and management of altitude-related illnesses, coupled with maintaining hydration and electrolyte balance, are critical for ensuring athlete safety.

As interest in high-altitude endurance events grows, future research should focus on integrating advanced monitoring technologies, pharmacological innovations, and personalized strategies to enhance safety and performance. While significant progress has been made, much remains to be explored, particularly in understanding interindividual variability, long-term physiological adaptations, and novel interventions. High-altitude marathons not only test human limits but also offer profound insights into human resilience and adaptation, making them a compelling and important field of study for the future.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Oak M, Oak A, Oak B. High altitude marathon physiology changes. Int J Adv Med 2025;12:333-9.