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REVIEW ARTICLE

Physiological Changes and Recovery After Short-Term High-Altitude Hypoxia: A Narrative Review

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ABSTRACT

Introduction Exposure to high altitude induces substantial physiological changes across various systems, enabling humans to withstand hypoxic environments. These physiological changes have been frequently explored and described in the existing literature. In contrast, the process of readjusting to lower altitudes, known as high-altitude de-acclimatisation, remains understudied, especially for individuals who spend brief periods at high altitudes. This narrative review aims to consolidate existing research on the physiological alterations and recovery patterns experienced by individuals returning from short-term stays at high altitudes, highlighting the acclimatisation and de-acclimatisation processes..

Methods A total of 29 articles were reviewed to extract insights from current evidence.

Results The findings reveal that de-acclimatisation is a complex process influenced by various factors. Cardiovascular adaptations, such as increased heart rate, cardiac output, and pulmonary artery pressure, begin to reverse upon descent but demonstrate varying recovery timelines. While heart rate typically normalises within days, stroke volume and pulmonary pressures may take weeks to months to recover fully. Similarly, respiratory adaptations, including ventilatory drive and oxygen saturation, show gradual improvement, although symptoms such as nocturnal hypoxemia and periodic breathing may persist for several days' post-descent. Haematological parameters, such as haemoglobin and haematocrit levels, decline rapidly, yet full recovery of molecular and systemic markers may extend beyond three months. Metabolic and immune system changes, including increased oxidative stress and immune suppression persist, highlighting the long-term impact of high-altitude exposure. Hormonal fluctuations affecting reproductive health in both sexes further underscore the systemic effects of high-altitude environments. This review also highlights the need for comprehensive public health strategies, including medical consultations prior to travel to high altitude, plans for structured acclimatisation and de-acclimatisation protocols, and extended monitoring for vulnerable populations such as frequent high-altitude workers or hikers with pre-existing medical conditions.

Conclusions Although progress has been made in understanding the physiological challenges of de-acclimatisation, substantial gaps remain, particularly in the long-term implications and recovery trajectories. Addressing these gaps through targeted research will enhance guidelines for managing high-altitude transitions and safeguarding the health of diverse populations.

Keywords High altitude de-acclimatisation , High altitude acclimatisation, Hypoxia

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INTRODUCTION

Medically, hypoxia begins at high-altitude environments at elevations 1,500 m and above.[1] This occurs due to a decrease in barometric pressure with a corresponding reduction in the partial pressure of oxygen (PO2). For every 100-metre increase above 1,500 metres, both healthy and compromised cardiovascular systems typically experience 1% reduction in maximal oxygen uptake.[2] These changes become more pronounced as altitude increases. At around 1,600 m, central sleep apnoea may begin. By 1,860 m, median nocturnal oxygen saturation (SpO_2) drops to 96%. The risk of asthma rises at elevations between 2,000 and 3,500 metres. Above 3,500 m, arterial oxygen saturation (SaO_2) decreases to 75–85% while arterial partial pressure of oxygen (PaO_2) drops to 40–60 mmHg.

Given these challenges, the process of acclimatisation has been widely studied, particularly among native populations, workers, and outdoor enthusiasts who engage in "green exercise" in high-altitude regions. The reverse process, high-altitude de-acclimatisation, has been relatively overlooked in scientific studies. This gap is especially important given the growing number of people experiencing short-term high-altitude exposure for tourism, work and athletic training. Recent data illustrate this trend: approximately 1,200 individuals attempted to ascend the Death Zone of Mount Everest in spring 2023,[3] while Mount Kinabalu in Malaysia (4,095 m) recorded 47,212 registered climbers in the same year.[4]

Upon descent, the human body undergoes a series of physiological adaptations across multiple organ systems. It ranges from subtle metabolic changes to more pronounced symptoms, collectively termed High-Altitude De-Acclimatisation Syndrome (HADAS).[5,6] The severity of de-acclimatisation is more pronounced in long-term high-altitude residents. Approximately 84.36% of individuals who lived in Tibet for 10 to 20 years experienced significant symptoms upon return to lower altitudes, ranging from fatigue and sleep disturbances to multi-system symptoms, alongside measurable physiological changes.[6] In contrast, the effects of short-term high-altitude exposure, typically lasting days to weeks, remain comparatively understudied. They may have different physiological adaptation patterns compared to long-term residents at high altitude and may vary based on factors such as duration of stay, altitude level, individual physiology and descent characteristics.[7]

This narrative review, therefore, aims to synthesise the current knowledge of physiological changes during de-acclimatisation following short-term high-altitude exposure. It summarises changes in various bodily systems by describing both the acclimatisation and de-acclimatisation processes. This information is valuable for researchers, clinicians, and individuals involved in high-altitude activities, as it can inform strategies for optimising performance and health after high-altitude exposure.

METHODS

This narrative review was conducted to answer the research question: "What is known about the physiological recovery and adaptations in humans after returning from high-altitude exposure?" We focused on short-term travellers and visitors experiencing high-altitude exposure while selecting a small number of long-term studies solely for contextual comparison. A comprehensive literature search was conducted across three databases: PubMed, Scopus, and Web of Science in December 2024 using a combination of selected terms that encompassed three main concepts: high-altitude exposure, de-acclimatisation and physiological responses. The initial search yielded a total of 1,099 articles, with 29 articles ultimately selected for inclusion in this review, as shown in Figure 1.

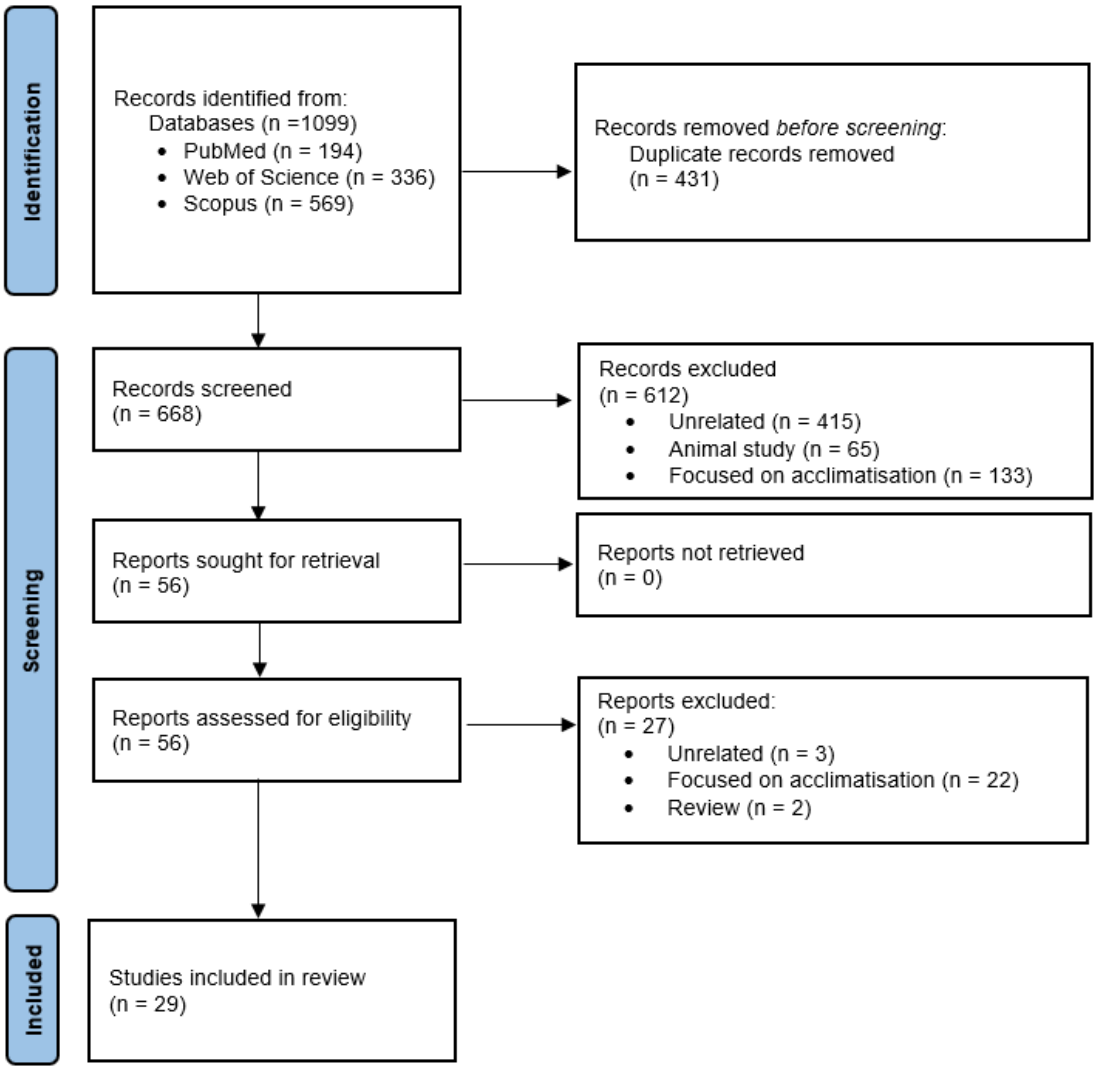

Figure 1 Flowchart of literature selection process

RESULTS

A Brief Overview of High-Altitude Acclimatisation

With increasing altitude, there is a decrease in barometric pressure, accompanied by a corresponding reduction in the partial pressure of oxygen (PO_2). The barometric pressure at sea level is measured at 759.6 mmHg, while at an approximate height of 4,000 m, the barometric pressure is only around 60% of that at sea level, at approximately 475.4 mmHg.[7] At a higher altitude of approximately 5,800m, the barometric pressure is one-half of sea level. Additionally, barometric pressure is influenced by weather, humidity and temperature. The barometric pressure is usually lower during winter than during summer.[7]

The resulting decrease in PO_2, known as hypoxia, is then observed throughout each stage of the oxygen transport cascade, from inspired air to the alveolar space, arterial blood, tissues and finally venous blood.[8] Comparing the inspired partial pressure of oxygen (PiO_2) of 149.6 mmHg at sea level, there is almost a 40% reduction. This decrease in PO_2 and PiO_2 leads to a reduction in the diffusion of oxygen across all these points, ultimately resulting in a decrease in the available oxygen at the cellular level.

The human body responds physiologically to a decrease in oxygen tension through a complex series of physiological adaptations occurring across multiple organ systems, which is called acclimatisation. This helps individuals adapt to hypoxic conditions at high altitudes. In the pulmonary system, the reduction of oxygen level in the blood (hypoxaemia) causes an increase in minute ventilation and respiratory alkalosis, which limits the initial ventilatory response.[9] However, as continuous time is spent at high altitudes, the kidney or renal compensates for the respiratory alkalosis, thus allowing minute ventilation to increase further. Additionally, reduced oxygen in the alveoli leads to

increased pulmonary vascular resistance and pressure. This response occurs immediately upon exposure, with maximum effect after four to seven days.

Due to respiratory alkalosis, the kidneys (renal) respond by expelling bicarbonate through diuresis. Detecting the low oxygen level in the blood, renal production of erythropoietin is increased.[10] In cardiac response, an increase in heart rate (HR) leads to an increase in cardiac output (CO). Conversely, stroke volume decreases due to a decline in plasma volume. Furthermore, blood pressure increases to varying extents. Due to the reduction in stroke volume, there is a corresponding increase in haematocrit. Subsequently, there is an increase in red blood cell mass due to increased erythropoietin. The brain also receives more cerebral blood flow. Understanding these complex acclimatisation processes is essential for contextualising the physiological reversals that occur during the subsequent de-acclimatisation phase upon descent to a lower altitude.

De-Acclimatisation Process

High-altitude de-acclimatisation is a process in which physiological readjustment occurs in individuals who return to sea level or a lower altitude from high altitude. De-acclimatisation follows a varied and unpredictable pattern, with changes and patterns occurring across multiple organ systems.[6] The period for de-acclimatisation also varies among individuals with different physiological parameters and duration of high-altitude exposure. Furthermore, recovery patterns may vary by system as well.

Cardiovascular system

Humans undergo physiological adaptations in response to these conditions in the hypobaric hypoxic environment present at high altitude. Immediate cardiovascular and circulation responses occur, including increased cardiac output, heart rate, and raised pulmonary artery pressure (PAP), as sympathetic activity increases.[7,11] Systemic blood pressure (BP) also increases as a result. Stroke volume (SV) may not initially be affected but will eventually be reduced due to a reduction in plasma volume. HR and CO eventually return to normal values following acclimatisation. Ventricular function is typically maintained, though initially increased, then preserved or slightly diminished systolic function indices, accompanied by an altered diastolic filling pattern. Upon returning to lower elevations, high-altitude adaptations start to reverse. The duration and completeness of this readjustment depend on factors like the time spent at high altitude, the maximum elevation reached and individual physiological traits.

CO is observed to recover over two to five days from a 5-day exposure at high altitude.[12] However, SV recovery lags behind cardiac output normalisation and can take weeks to normalise.[12,13] Full normalisations of both parameters require additional time, depending on the individual's prior exposure and baseline health. It has been noted that alterations in left ventricular filling patterns, with increased reliance on atrial contraction due to reduced SV and raised pulmonary pressures, persisted above baseline for weeks post a simulated climb of Mount Everest.[14] Repeated or prolonged hypoxia, which are frequently seen among workers with daily migration to high-altitude regions or training athletes, exacerbates pulmonary hypertension and imposes a significant strain on the right ventricle, with recovery often extending over months to years.[15] In a 50-day exposure to an altitude of 3,700 m, while PAP and left ventricular function partially normalise over a couple of weeks, indicators of heart efficiency, such as the Tei index, remains impaired for weeks, reflecting delayed diastolic and systolic recovery.[16]

Significant sympathetic overdrive during a short-term duration of acute hypoxia normalises rapidly upon descent but varies by individual exposure duration and fitness.[17] Continued sympathetic nervous system activation is also noted after returning from an elevation of 4,300 m.[18] While young, healthy individuals typically handle this well, it may contribute to an elevated risk of high BP in those who have a higher baseline cardiovascular risk. Older studies have looked at electrocardiography (ECG) changes during high-altitude exposure (lasting from 16 to 30 days), which typically disappear within a couple of weeks after descent, though they may persist for up to four weeks.[19] In a previous study examining the effects of high altitude during a 5-day simulation in a compression chamber, ventricular ejection time indices remain unstable for up to a year, suggesting long-term cardiovascular adaptation to hypoxic stress.[20] At molecular level, persistent molecular alterations in the plasma proteome post-altitude were observed.[5] The acute phase and coagulation systems remained perturbed even 180 days post-descent, indicating prolonged subclinical cardiovascular strain. These molecular disturbances provide a mechanistic basis for why functional parameters like SV and PAP recover more slowly than HR or BP.

In addition to systemic markers, cerebral blood flow (CBF) also undergoes significant changes that mirror cardiovascular recovery patterns. In response to low oxygen levels at high elevations, CBF increases despite reduced carbon dioxide levels in the blood.[21] This phenomenon is attributed to compensatory vasodilation. These changes occur consistently, whether during rapid

ascent, following successful acclimatisation, or in individuals native to high-altitude regions.[7] The raised CBF resolves as oxygen levels normalise post-descent.

These findings, as summarised in Table 1, show that metrics like HR often recover within days, but PAP, SV, and autonomic balance may take weeks to months. Long-term effects, such as ventricular instability and prolonged pulmonary hypertension, highlight the need for extended monitoring in individuals with repeated or prolonged altitude exposure. These insights emphasise the need for targeted interventions to mitigate risks, particularly in high-risk populations, including those with pre-existing cardiovascular conditions or repeated high-altitude exposure.

Table 1 Summary of cardiovascular changes after descent or de-acclimatisation.

Parameters	Changes on descent or de-acclimatisation	References
Heart rate and systemic blood pressure	In general, heart rate normalises within 2-8 days (often shorter in brief exposures). BP normalises by the first (1) week.	
	HR back to sea-level values by day 4-8 after descent.	Penaloza et al. 1958[19]
	Elevated sympathetic tone with mean HR and BP still elevated on day 1 of descent but settling over first week.	Ponchia et al. 1994[13]
	HR back to baseline in 24-48 hours.	Hoon et al. 1977[12]
	In a hypobaric chamber study, HR spike resolves quickly on exit.	Ma et al. 2022[17]
Cardiac output and stroke volume	At high altitude, CO usually rises despite decrease in SV. After descent, CO normalises in 2-5 days with SV lagging in recovery (still reduced at 48 hours). SV generally back to baseline after 1-3 weeks	Hoon et al. 1977[12] Boussuges et al. 2000[14]
Pulmonary arterial pressure	PAP elevates promptly at high altitude. After descent, it remains elevated after more than 48 hours.	Boussuges et al. 2000[14]
Autonomic balance, heart rate variability	Raised sympathetic drive resolves within hours to days, vagal tone recover follows within 2 weeks.	
	Raised Low Frequency (LF)/High Frequency (HF) ratio and reduced vagal tone persist through first few days.	Ponchia et al. 1994[13]
	Enhanced baroreflex sensitivity normalises rapidly and up to less than 48 hours after hypoxia exposure.	Roche et al. 2002[22]
	Muscle sympathetic nerve activity still raises at 24h post-descent but BP and orthostatic responses normal.	Mitchell et al. 2018[18]
	HRV metrics recovered rapidly on leaving barometric chamber.	Ma et al. 2022[17]
Electrocardiographic changes	Most ECG changes resolve within 8-14 days of return (after 16 to 30 days high-altitude exposure)	Penaloza et al. 1958[19]
Molecular/proteomic signals	At high altitude, more than 100 plasma protein dysregulated (related to inflammation, coagulation, cardiac stress). Proteome still perturbes at 30 days despite normal HR and BP.	Paul et al. 2023[5]

Notes:
HR = heart rate, BP = blood pressure, CO = Cardiac output, SV = stroke volume, PAP = pulmonary arterial pressure, ECG = electrocardiogram, HRV = heart rate variability

Respiratory system

When the body detects a decrease in PO_2, it triggers signals to the medulla's central respiratory centre, prompting an increase in ventilation. This phenomenon, known as the hypoxic ventilatory response (HVR), which results in enhanced ventilation, underpins acclimatisation to a hypoxic environment. Similar to changes in the

cardiovascular system, as the cardiovascular and respiratory systems are intricately connected, the recovery of respiratory function may vary in its timeline. It has been noted that hyperventilation may take up to 1–3 days to resolve partially, and in some cases, elevated ventilatory drive can linger for several weeks, theorised due to sustained carotid chemoreceptor sensitivity and central nervous system (CNS) plasticity.[23]

Nocturnal breathing instability, including periodic breathing and central apnoea, is a common feature of high-altitude exposure.[7] In a study looking at repeated exposures to high altitude, where participants were subjected to two cycles of 7 nights at altitude of 2,900 m combined with daytime sojourns at 5,050 m, with a 7-day recovery period near sea level in between, it has been observed that nocturnal hypoxaemia (reduced nocturnal SpO_2) and periodic breathing were less pronounced in the second cycle. This could be due to the observation that at the end of the recovery period, after 6 days of descent from high altitude, higher nocturnal SpO_2 and a lower HR are observed compared to the baseline. This may provide a ceiling or floor effect for subsequent exposure.

SpO_2 also has a slight delay in recovery after descent. Nocturnal hypoxaemia and increased oxygen desaturation index (ODI) are prominent during the first few nights post-altitude but show gradual improvement within 6 to 7 days.[24] However, it has also been found that arterial blood gases, including partial pressure of oxygen in arterial blood (PaO_2) and oxygen saturation in arterial blood (SaO_2), can take between 50 to 100 days to return fully to baseline levels, particularly in individuals experiencing HADAS.[6] There were also respiratory symptoms, including coughing, expectoration, and chest tightness, which are prevalent during the initial days post-altitude. These symptoms peak around the third day following descent and show marked improvements by 50 days, with complete resolution typically occurring within 100 days.[6] The de-acclimatisation or recovery timeline is summarised in Table 2.

Table 2 Summary of respiratory changes after descent or de-acclimatisation.

Parameters	High-altitude physiological changes	Changes on descent or de-acclimatisation	References
Oxygen saturation	Can fall to 86% at 2,900m but subsequently improve by day 6.	Baseline level of SpO_2 restored within 7 days, subsequent re-ascent produces a smaller drop, showing retained adaptation	Furian et al. 2022[24]
Oxygen desaturation index	ODI surges on night 1, then falls by night 6.	Returns to baseline after 7 days at sea level and on re-ascent the peak ODI is around 40 % lower	Furian et al. 2022[24]
Full vital capacity	Decreases at high altitude and plateaus after day 6	Fully returns within the 7-day low-altitude interval	Furian et al. 2022[24]
Forced Expiratory Volume in 1 second / Full vital capacity	Declines over months at altitude	Limited rebound 15 weeks after descent, suggesting some persistent obstruction	Kamat et al. 1972[25]
Peak Expiratory Flow	Reduces with longer stays at high altitude	Recover within 15 weeks with larger recovery after longer stays	Kamat et al. 1972[25]
Respiratory symptoms (cough, chest tightness)	Not prominent at altitude but peak after descent	Some improve by day 50 and few by day 100 (near-complete resolution) after descent	He et al. 2013[6]

Notes:
SpO_2 = Oxygen saturation, ODI = oxygen desaturation index, FVC = full vital capacity, FEV1 = forced expiratory volume in 1 second, FVC = full vital capacity, PEF = peak expiratory flow

Haematological system

Adaptations to high-altitude hypoxia involve significant haematological changes, including increased erythropoietin (EPO) production, enhanced erythropoiesis, and elevated haemoglobin (Hb) concentration.[7,26] Upon descent to sea level, these adaptations are gradually reversed. In a study measuring haemoglobin mass (Hbmass) after 16 days of exposure at an altitude of 5,260 m, there was a 6% loss of Hbmass within 7 days of descent, correlating with an increase in serum ferritin, suggesting accelerated red blood cell (RBC) destruction. Although women typically have lower absolute Hbmass, studies observe no significant sex difference in the relative percentage changes of Hbmass. In another study with longer exposure of 6

months at high altitude, by the third day after the descent, the level of Hb, Hct, RBC, creatine kinase (CK), and lactate dehydrogenase (LDH) is significantly lower than at altitude and normalised by the 50th day. However, only LDH takes longer and only normalises on the 100th day after descent.

RBC destruction during re-oxygenation after descent has been linked to oxidative stress, which increases RBC lysis, elevates ferritin levels, and is counteracted by upregulation of the pentose phosphate pathway (PPP), facilitating RBC recovery.[27] Targeting PPP upregulation or antioxidant pathways might improve recovery outcomes in individuals experiencing oxidative damage post-high-altitude exposure. Upon initial exposure to hypoxia, EPO concentrations increase rapidly, reaching their highest levels within a few days to promote erythropoiesis. As oxygen tension returns to normal, EPO levels quickly decrease. This reduction in EPO leads to a decline in erythropoietic activity, resulting in lower haemoglobin and RBC counts within several days.[28,29]

Exposure to high altitudes induces a rapid reduction in plasma volume (PV) during the first 1 to 3 days, primarily due to diuresis caused by hypoxic conditions. A study has shown that after spending a week at an elevation of 4,350 m, individuals experience a significant PV decline of about 13.6%.[28] Upon returning to sea level, plasma volume (PV) quickly returns to normal. This restoration occurs within 2 days, primarily due to decreased urine production and hormonal shifts, including elevated levels of renin and aldosterone. These increased levels of hormones contribute to increased water retention following descent. A concise timeline of these processes is presented in Table 3.

Table 3 Timeline of haematological changes after descent or de-acclimatisation.

Time Frame	Key Processes
0 to 7 days	• Rapid decline in EPO levels • Expansion of plasma volume (haemodilution) • Initial drop in Hb and Hct
7 to 50 days	• Gradual stabilisation of RBC mass • Decrease in oxidative stress • Continued activation of the PPP
50 to 100+ days	• Full normalisation of Hb and Hct levels • Ongoing resolution of molecular changes (e.g., inflammation, lipid metabolism)

Notes:
EPO = erythropoietin, Hb = haemoglobin. Hct = haematocrit, RBC = red blood cell, PPP = pentose phosphate pathway

Metabolic system

Studies specifically looking at metabolic changes after short-term exposure to high altitude are scarce. However, in a study looking at the effects of chronic intermittent hypoxia among army men at 3,550 m altitude, high-altitude exposure disrupts lipid metabolism, as evidenced by elevated triglycerides and changes in cholesterol levels during exposure and recovery phases. Even after descent, triglyceride levels were observed to stay high for prolonged durations, indicating a delayed return to normal metabolic function.[15] More recently, proteo-metabolomic profiling of low-landers who have spent 120 days at 4,500 m, demonstrate that lipid-handling proteins (liver X receptor/retinoid X receptor, high-density lipoprotein/very low-density lipoprotein remodelling, acute-phase complement) remain up-regulated 180 days after descent, despite normal vital signs.[5]

In a longitudinal metabolomic analysis, during hypoxic exposure at an altitude of 3,650 m, 13 metabolites have significant changes, including lipid and lipid derivatives, adenosine, inosine, and melatonin, compared to those at normal altitude.[30] These metabolites recover when return to low altitude, but a small portion of metabolites continue to be affected by high-altitude exposure even after two weeks of returning to lower elevations, suggesting that the metabolic impact of high-altitude conditions persists for an extended period. Metabolic de-acclimatisation is dominated by extended lipid and redox remodelling, begins within hours of descent and may persist for weeks, even when overt physiology appears normal. Prolonged hypertriglyceridaemia and altered HDL/VLDL trafficking may increase atherosclerotic risk in frequent high-altitude commuters.

Immune function

Current evidence on changes to immune function after descent is limited. Existing reviews and studies on this particular topic highlight that the majority of studies end while participants are still hypoxic or at high altitude.[31,32] Here, we summarise the changes that occur during high-altitude exposure and then

note what the existing literature cautiously infers about their reversal on re-oxygenation.

T-cell Lymphocytes

Hypoxia disrupts the typical immune and haemostatic equilibrium. It appears that T lymphocyte function is impaired, as their overall numbers are decreased.[33] Total CD3+ counts fall, CD4+ proliferation, interleukin-2 (IL-2) secretion and mixed-lymphocyte reactivity are blunted. This suppression is reversible once normoxia is restored, though specific data on timelines have not been explored.[32]

B-cell Lymphocytes and Humoral Immunity

Conversely, B-cell lymphocytes do not seem to be affected. Because of this, there is an increased susceptibility to bacterial infections. To illustrate, a suppurative hand wound would fail to respond to antibiotic treatment at a high altitude and would only show improvement upon descending to a lower altitude. An individual suffering from a severe infection while at a high altitude may require oxygen therapy or descent for effective treatment.[34]

Natural-Killer (NK) cells and Dendritic cells

However, NK cell cytotoxicity is similarly affected, where NK cell cytotoxicity was reduced, which may compromise the body's ability to combat viral infections during this period despite B lymphocytes seeming to be unaffected.[31] Dendritic cell populations are also similarly suppressed.

Cytokines

At high altitudes, certain pro-inflammatory cytokines, specifically interleukin-6 (IL-6) and interleukin-7 (IL-7), show increased levels and have been linked to acute mountain sickness.[31]

Gut-Immune Axis

The condition of hypoxia leads to changes in the gut microbiome and decreases the production of secretory immunoglobulin A (sIgA), thereby compromising mucosal immunity. This weakened immune response results in a higher risk of gastrointestinal infections and widespread inflammation.

When individuals descend to lower altitudes and experience re-oxygenation, the restoration of immune function typically begins. However, timelines for recovery remain undefined; thus, longitudinal studies are needed to quantify recovery and to test whether acute mountain sickness delays it.

Reproductive system

For the reproductive system, a hypoxic environment at high altitude has its own significant but reversible effects. This is mainly due to its effects on hormonal regulation through the suppression of the hypothalamic-pituitary-gonadal (HPG) axis and disruption in hormonal regulation. In females, oestrogen and progesterone levels decline significantly with increasing altitude.[35] Acclimatisation reverses some of the suppression seen in the gonadal axis, with luteinising hormone (LH) and follicle stimulating hormone (FSH) levels returning to near baseline. The oestrogen level also normalises in a couple of days after descent; however, progesterone remains lower than its baseline level at normal altitude, which suggests the possibility of long-lasting changes in the HPG axes.[36] These hormonal fluctuations can disrupt the menstrual cycle, particularly ovulation.

In males, significant reductions in sperm concentration and seminal volume in participants after trekking through high-altitude environments were observed. Sperm concentration showed a reduction 10 days after descent, but declined even further during follow-up at 70 days post-descent.[37] Seminal volume showed a similar trend after descent but had partial recovery during the follow-up. This could be due to the fact that sperm concentration depends on the health and functionality of spermatogenic cells, which are more sensitive to prolonged hypoxic damage and oxidative stress. Due to the lengthy spermatogenesis cycle (approximately 70 days), the restoration of sperm concentration occurs more gradually or may not be complete. In contrast, seminal volume is affected by fluid production from accessory glands, including the prostate and seminal vesicles. These structures are less susceptible to long-term hypoxic effects, enabling some degree of recovery.

However, these findings are derived from studies that had very small cohorts (n = 5 – 7 in semen studies and less than 25 per sex in the endocrine profiling) of recreational trekkers with heterogeneous baseline fitness and hormonal status. Therefore, generalisation to other populations should be made with caution. Larger longitudinal studies are needed to confirm both the magnitude and the reversibility of reproductive changes.

Endocrine responses

The thyroid axis is generally activated by exposure to high altitudes, with hormonal patterns varying according to the length of exposure. Rapid elevations in thyroxine (T4) and triiodothyronine (T3) concentrations are observed within the first 24 hours of being at an altitude of 3,700 m.[38] However, thyroid-stimulating hormone (TSH) remains stable, suggesting a peripheral adaptation rather than direct hypothalamic-pituitary activation. A study involving approximately 14 days of high-altitude trekking observed an elevation in T4 level and less pronounced alterations in T3 level.[35] Upon return to lower altitudes, T4 level remains elevated longer

than T3, indicating a delayed recovery of the thyroid axis.

The adrenal system exhibits a two-phase response, especially during extended periods of exposure. In a study conducted over a three-week expedition, researchers observe an initial reduction in cortisol levels at moderate elevations (4,844 m), following by a substantial increase at extreme heights (7,050 m). This observed pattern indicates that stress-induced activation occurs at higher altitudes.[35] Nevertheless, a different study reveals no significant alterations in cortisol levels among hikers and Nepalese porters, suggesting specific populations may have developed resilience and adaptations to stress.[39] Any changes in the cortisol levels normalise quickly after descent.

These hormonal fluctuations can have meaningful clinical consequences. Persistently elevated T4 may affect metabolic rate and thermoregulation, contributing to fatigue, changes in heart rate, weight changes, or cold intolerance during the recovery phase. For individuals with pre-existing endocrine conditions, such as hypo- or hyperthyroidism or adrenal insufficiency, these shifts may exacerbate symptoms or necessitate closer pre- and post-altitude monitoring and medication adjustment if needed.

High-Altitude De-Acclimatisation Syndrome (Hadas)

HADAS refers to a range of symptoms and physiological alterations that occur when individuals descend to lower elevations rapidly after spending time at high altitudes. Unlike Acute Mountain Sickness (AMS) and Chronic Mountain Sickness (CMS), which are associated with ascent to high altitudes, HADAS emerges during the process of readjusting to lower altitudes.[40] Diagnostic criteria used in current literature are proposed based on epidemiological and clinical data, as shown in Table 4.

Table 4 Diagnostic criteria of HADAS

Component	Criteria
Diagnosis of high-altitude de-acclimatization included essential conditions and one Auxiliary condition	
Essential Criteria	1. Adult aged ≤60 years 2. Recent return to low altitude from high altitude 3. ≥3 of the following symptoms: a. Fatigue b. Sleepiness or insomnia c. Unresponsiveness or memory loss d. Irritability e. Headache, throat pain f. Coughing or expectoration g. Chest tightness, palpitations h. Appetite changes i. Diarrhoea, abdominal pain or bloating j. Lumbago or joint pain 4. No significant relief after 3 days of simple treatment
Auxiliary Criteria	At least one of the following: a. Elevated RBC, Hb or Hct b. Elevated myocardial enzymes (CK–MB, LDH) c. Microalbuminuria d. Cardiac dysfunction on ultrasound (e.g., ↓values of left ventricular ejection fraction, ↓right ventricular fractional shortening, ↑Tei index) a. Impaired short-term memory b. Elevated liver enzymes (ALT, AST, bilirubin)
Exclusion Criteria	1. Known cardiovascular, respiratory, neurological, renal, or haematological disease 2. Malignancy 3. History of highland heart disease or HAPC 4. Recent infection (e.g., flu, diarrhoea)

Notes:
HADAs = high-altitude de-acclimatisation syndrome, RBC = red blood cell, Hb = haemoglobin, Hct = haematocrit, CK-MB = creatine kinase-MB, LDH = lactate dehydrogenase, ALT = alanine transaminase, AST = aspartate transaminase, HAPC = high-altitude polycythaemia

Individuals experiencing HADAS often report symptoms such as persistent fatigue, insomnia, and chest tightness. Cognitive impairments, including memory lapses and reduced

responsiveness, are also common.[6,16] Rapid descent to lower elevations without allowing the body adequate time to adapt can result in de-acclimatisation. This sudden change in altitude hinders the body's capacity to manage the sudden shift in oxygen concentration, creating a disparity between the physiological adjustments made at high elevations and the oxygen-rich environment found at lower altitudes. Prolonged stay at high altitude, rapid descent to lower altitude, and individual susceptibility (genetic predisposition, age, and fitness levels) are the factors that affect the risk and severity of HADAS.[6,18,24,29,40] Due to its rather vague diagnostic definition, treatment options are limited and largely unexplored. The treatment given is mainly symptom-based and largely supportive. Hyperbaric oxygen and drugs used for acclimatisation, such as acetazolamide, have been used to treat HADAS.[41,42] However, Traditional Chinese Medicine, Shenqi Pollen Capsules, have been shown to help improve patients' symptoms.[42]

From The Public Health Perspective

Pre-Travel Preparation

The public health ramifications of high-altitude de-acclimatisation are becoming increasingly significant as more individuals participate in high-altitude pursuits like trekking, mountaineering and work-related travel. These activities subject people to temporary high-altitude environments, potentially leading to adaptation difficulties upon their descent to lower elevations. The bodily adjustments that occur during this process have substantial consequences for population health concerns.

Short-term visitors, including hikers, mountaineers, researchers, or recreational travellers, are advised to undergo pre-travel assessments to evaluate their fitness for high-altitude travel. Certain medical conditions place individuals at risk for severe hypoxaemia or impaired oxygen delivery, and others may hinder physiological responses to hypoxia.[10,43] Moreover, the effects of hypoxic environments may continue to adversely affect pre-existing health conditions even after individuals return to lower elevations. When creating a customised travel plan, it is essential to consider various factors, including the traveller's age, any pre-existing medical conditions (such as cardiovascular disease) and previous high-altitude experiences.

Furthermore, individuals planning to ascend to high altitudes should be aware of their own fitness level and limitations prior to travel. It is essential for each climber to engage in individualised training and physical fitness preparation that is specifically tailored to the challenges of the climb.

Occupational Health

A special focus should be given to workers frequently exposed to high altitude, such as miners, mountain guides, first responders and military personnel. A structured health surveillance is necessary, as they are at higher risk of developing cognitive dysfunction and cardiovascular diseases.[44,45] The health surveillance should be supervised by medical personnel familiar with wilderness medicine and well-versed with occupational health practice. Each worker should be allotted sufficient, individually tailored time both to acclimatise to high altitude and to de-acclimatise afterwards.

POLICY RECOMMENDATIONS

Not all agencies have proper policies in place to carry out health surveillance for miners, mountain guides, first responders, and military personnel for determining their functional fitness level. Nepal's new rule that would-be Everest climbers must first summit a peak of ≥7,000 m exemplifies prudent safety policy for both climbers and guides, reinforcing the need for rigorous preparation and training before the ascent.[46] However, recognising inter-individual variation in recovery trajectories permits more strategic allocation of resources for managing high-altitude illness and de-acclimatisation, thereby informing inclusive and adaptable guidance for diverse populations.

CONCLUSION

This review highlights the complex physiological changes that occur during de-acclimatisation following short-term exposure to high altitudes. The recovery process exhibits variability across systems, with cardiovascular, respiratory, haematological, and metabolic adaptations demonstrating distinct temporal patterns. While certain parameters, such as heart rate and oxygen saturation, normalise rapidly, others, including stroke volume and haematocrit, may require weeks to months for complete restoration. Despite the increasing prevalence of high-altitude activities, significant knowledge gaps persist in the understanding of the de-acclimatisation process. Future research endeavours should focus on exploring these mechanisms and informing public health strategies to mitigate the risks associated with high-altitude exposure and subsequent descent.

This review uniquely focuses on short-term high-altitude exposure, a relatively understudied domain with growing relevance for recreational and occupational travellers. To support clinical practice, specific post-descent monitoring guidelines should be developed to identify at-risk individuals and improve recovery outcomes.

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