

Central Sleep Apnea at High Altitude

From Pathophysiology to Treatment



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KEYWORDS

- Central sleep apnea • High altitude • Periodic breathing • Loop gain • Hypobaric hypoxia
- Nocturnal hypoxemia • Chronic mountain sickness. • Sleep quality

KEY POINTS

- High-altitude central sleep apnea (CSA) is characterized by non-rapid eye movement (NREM)-predominant periodic breathing (PB) with central apneas/hypopneas occurring after recent ascent; prevalence and severity increases with altitude.
- Mechanism: altitude-related hypobaric hypoxia → hyperventilation → hypocapnia; when P_{aCO_2} falls below the apnea threshold during NREM sleep, central apneas/hypopneas recur, producing PB.
- Acclimatization modulates expression: renal bicarbonate loss alters pH, ventilatory responses increase, and plant-controller interactions evolve over days to weeks.
- Lowlanders versus high-altitude populations (eg, Sherpa) differ in ventilatory control and expression of PB at altitude.
- Descent or supplemental oxygen promptly suppresses CSA; acetazolamide reduces instability via metabolic acidosis. Temazepam and related hypnotics improve sleep continuity in some contexts without worsening oxygenation.

INTRODUCTION

More than 500 million individuals live at altitudes above 1500 m, and over 80 million reside above 2500 m.¹ In addition, an increasing number of people travel or commute to high-altitude regions for occupational, scientific, or recreational purposes. An elevation exceeding 2500 m in the context of rapid ascent is widely accepted as high altitude.^{2,3} Exposure to high altitude has direct effects on respiratory physiology. Additionally, disruptions in both sleep architecture and continuity often occur, beginning as early as the initial night. Research on sleep at high altitude has important implications for improving sleep health and quality of life in individuals living in, or traveling to, high-altitude environments.

The effects of high altitude on sleep and breathing are primarily driven by reduced atmospheric pressure, which proportionally decreases oxygen availability and results in a lower partial pressure of inspired oxygen (PiO_2). Interestingly, hypobaric hypoxia has been shown to exert a greater impact on nocturnal breathing and sleep structure than normobaric hypoxia.⁴ Regarding sleep, hypobaric hypoxic exposure is associated with reductions in total sleep time, sleep efficiency, slow-wave sleep, and rapid eye movement (REM) sleep, as well as increases in arousal duration and frequency.^{5–7} Notably, a substantial proportion of individuals (32%–74%) report poor sleep quality or insomnia at high altitude, particularly during the initial days of exposure.^{6,8} Exposure to hypobaric hypoxia also triggers an immediate ventilatory response,

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Abbreviations	
AMS	acute mountain sickness
ASV	adaptive servo-ventilation
CBF	cerebral blood flow
CMS	chronic mountain sickness
EE	excessive erythrocytosis
HA-CSA	high-altitude central sleep apnea
HCVR	hypercapnic ventilatory response
HVR	hypoxic ventilatory response
NREM	non-rapid eye movement
OSA	obstructive sleep apnea
Paco ₂	partial pressure in CO ₂
PB	periodic breathing
REM	rapid eye movement

followed by gradual physiologic adaptation over days to weeks. These processes specifically alter nocturnal breathing patterns, including the development of apneas and hypopneas, often leading to nocturnal periodic breathing (PB).⁵ Historical descriptions of altitude-related PB are commonly attributed to Angelo Mosso, who in 1898 published observations including a tracing from his brother.⁹ PB is thought to arise from instability in respiratory control mechanisms caused by hypobaric hypoxia and altered carbon dioxide sensitivity.⁷

In susceptible individuals, and even from first night of exposure to elevations above 2500 m, central sleep apnea related to high-altitude PB (high-altitude central sleep apnea [HA-CSA]) may develop, with increasing prevalence and severity at higher altitudes. At very high altitude (≥5000 m), HA-CSA is common among most sojourners.

HA-CSA typically presents as clusters of 2 to 4 hyperpneas separated by an apnea/hypopnea before the next burst.^{10,11} This differs from the crescendo–decrescendo waxing and waning respiratory pattern of Cheyne–Stokes breathing in heart failure and from the irregular, often chaotic central events seen with opioid exposure.^{10,12}

Acclimatization, the so-called systemic physiologic and molecular responses to prolonged exposure to high altitude, introduces countervailing forces,^{5,13,14} leading to reductions in the prevalence of HA-CSA.¹⁵ Renal bicarbonate excretion gradually offsets the acute hypocapnic alkalosis, permitting ventilation to rise further and Pao₂ to increase. Sympathetic activity and cardiac output are initially elevated, and cerebral blood flow (CBF) is high soon after ascent; over ~2 weeks at ~5000 m, CBF tends to return toward sea-level values despite sustained sympathetic tone.¹⁶ Across this time course, hypoxic and hypercapnic ventilatory responses augment, which can raise loop gain even as Pao₂ improves.¹⁷

This article integrates the description of HA-CSA mechanisms, clinical expression, ethnic and chronic-exposure perspectives, and management strategies.

PATHOPHYSIOLOGY OF HIGH-ALTITUDE CEREBRAL BLOOD FLOW

Altitude is characterized by hypobaric hypoxia, the severity of which increases proportionally with elevation.¹⁸ Upon arrival at high altitude, hypoxic stimulation of peripheral chemoreceptors in the carotid and aortic bodies increases minute ventilation, a response known as the hypoxic ventilatory response (HVR).^{19,20} HVR sensitivity progressively rises over several days of exposure. Contemporary mechanistic models describe respiratory control as a closed-loop negative-feedback system that maintains arterial blood gases within narrow limits, with arterial carbon dioxide tension (Paco₂) representing the dominant regulated variable during non-REM (NREM) sleep. At altitude, hypobaric hypoxic-induced hyperventilation lowers Paco₂ below the apneic threshold generating a central apnea.⁵ Whether isolated apneas evolve into sustained PB depends on the stability of ventilatory control, commonly expressed as *loop gain*.^{21–23} Loop gain reflects the product of controller gain (chemosensitivity), plant gain (the efficiency of CO₂/O₂ exchange relative to ventilation), and feedback delay (circulatory and neural latencies). Elevated chemosensitivity combined with delayed and efficient gas-exchange dynamics favors ventilatory oscillations.²² Thus, for a given ventilatory stimulus, longer subsequent apneas indicate higher loop gain.^{22,23} A long-standing view links the severity of HA-CSA to heightened HVR. Additionally, imbalance between hypoxic and hypercapnic chemoreflex gains may independently predispose to PB.¹¹ Pathophysiology of HA-CSA is summarized in Fig. 1.

Maximal ventilatory acclimatization is typically achieved after 4 to 7 days at a constant altitude, coinciding with renal compensation for respiratory alkalosis. HVR is genetically determined, varies widely between individuals and is unaffected by physical training.³ Classic human studies demonstrate that individuals with greater chemosensitivity develop more pronounced HA-CSA and PB, and that early acclimatization may paradoxically increase PB while improving subjective sleep quality.^{16,24} Field observations in trekkers ascending to approximately 5000 m show increasing arousals and central respiratory events during the first days at altitude, followed by partial sleep consolidation despite persistent PB.^{16,25} However, it can

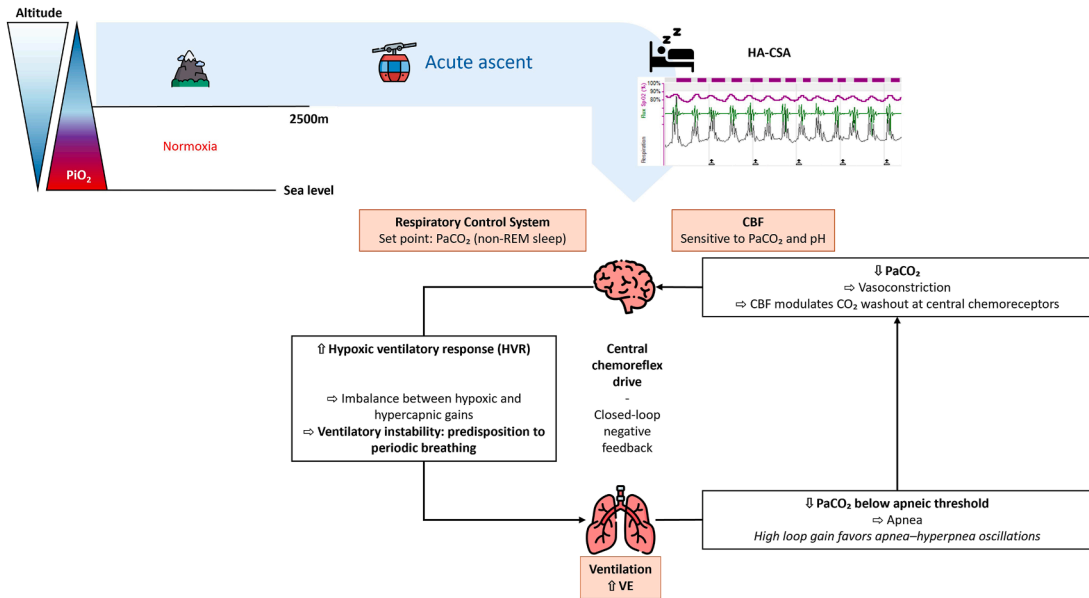


Fig. 1. Pathophysiological mechanisms of acute high-altitude central sleep apnea (HA-CSA): the coupled cerebrovascular-ventilatory model. CBF, cerebral blood flow; HCVR, hypercapnic ventilatory response; HVR, hypoxic ventilatory response; $PaCO_2$, partial pressure in CO_2 ; VE, Minute Ventilation Loop gain = controller gain (chemosensitivity) $\times$ plant gain (the efficiency of CO_2/O_2 exchange relative to ventilation) $\times$ feedback delay (circulatory and neural latencies).

be modulated by external factors: respiratory depressants (eg, alcohol and sedative-hypnotics) and sleep fragmentation attenuate HVR, whereas respiratory stimulants (eg, progesterone) and sympathomimetics (eg, caffeine and coca) enhance it.²⁶ As ventilation increases in response to hypoxia, $PaCO_2$ decreases and blood pH rises. The resulting alkalosis of the cerebrospinal fluid suppresses central chemoreceptor drive, promoting HA-CSA and attenuating the overall ventilatory response.²⁷

Respiratory instability with HA-CSA and PB is most pronounced during NREM sleep, when ventilatory control is dominated by metabolic rather than behavioral mechanisms. At high altitude, sleep architecture is characteristically altered, with a shift toward lighter stages of NREM sleep (stages N1 and N2) and a relative reduction in slow-wave sleep.⁶ These architectural changes are not merely epiphenomena but appear to be integrally involved in the pathophysiology of HA-CSA. Light NREM sleep is associated with increased susceptibility to arousals and greater variability in ventilatory drive. Cortical arousals, frequently accompanied by sighs or transient hyperventilation, can acutely lower $PaCO_2$. In the context of altitude-induced hypocapnia, such transient reductions are more likely to push $PaCO_2$ below the apneic threshold, precipitating CSA. The ensuing apnea promotes CO_2

accumulation, triggering a compensatory hyper-ventilatory response that may culminate in further arousal, thereby sustaining a self-perpetuating cycle of ventilatory instability and sleep fragmentation.

Moreover, the predominance of lighter NREM sleep reduces the stabilizing influence of deeper sleep stages on respiratory control, further amplifying loop gain and facilitating PB. Rather than being passive markers of disturbed sleep, recurrent arousals play an active role in destabilizing ventilatory control, perpetuating cycles of hyperventilation, apnea, and re-arousal. As a result, sleep instability and arousal propensity emerge as key clinical determinants of altitude-related CSA, linking altered sleep structure directly to the expression and severity of central breathing disturbances.^{10,25} Thus, alterations in sleep architecture at altitude both reflect and exacerbate disordered breathing, creating a bidirectional interaction in which sleep fragmentation promotes CSA and PB, while respiratory instability further disrupts sleep structure. This interplay highlights sleep architecture as a fundamental component of the mechanistic framework underlying HA-CSA, rather than a secondary consequence of hypoxia alone.

More recently, cerebrovascular regulation has emerged as an additional contributor to HA-CSA. Larger reductions in CBF at sleep onset are associated with more severe CSA.^{28,29} Experimental

evidence supports a coupled cerebrovascular-ventilatory model. During ascent, hypoxic vasodilation increases CBF, partially compensating for reduced arterial oxygen content (CaO₂). With acclimatization, hemoconcentration and subsequent erythropoiesis, together with increased ventilation, improve CaO₂, allowing CBF to return toward sea-level values.³⁰ Throughout this process, CBF remains highly sensitive to PaCO₂ and pH. Hypocapnia induces cerebral vasoconstriction, which may counteract hypoxic vasodilation and reduce perfusion in specific brain regions.³⁰ Because CBF determines washout of CO₂ near medullary chemoreceptors, changes in perfusion directly influence the central chemostimulus, establishing bidirectional coupling between cerebral perfusion and ventilatory stability.^{30,31}

Acclimatization mitigates HA-CSA by modifying all 3 components of the loop gain. Initially, respiratory alkalosis exerts a “hypocapnic braking” effect on the central chemoreflex drive.³² With continued exposure, both HVR and the hypercapnic ventilatory response increase, shifting the ventilation–PaCO₂ relationship leftward and steepening its slope. This adaptation supports sustained hyperventilation despite alkalosis and preserves chemosensitivity at low PaCO₂.³⁰ Progressive bicarbonate excretion restores arterial and brain pH toward neutrality, permitting further increases in ventilation, reductions in PaCO₂, and improvements in PaO₂ via the alveolar gas equation. Early after

ascent, elevated CBF may enhance CO₂ washout near central chemoreceptors, blunting ventilatory responsiveness. As CBF gradually normalizes over approximately 2 weeks at 5000 m,³³ CO₂ clearance from the chemoreceptor environment diminishes, potentially increasing local CO₂ relative to arterial PaCO₂ (Fig. 2).

CLINICAL IMPLICATIONS OF HIGH-ALTITUDE CENTRAL SLEEP APNEA AND SLEEP ARCHITECTURE: INSIGHTS FROM POLYSOMNOGRAPHIC STUDIES

The symptomatic presentation of HA-CSA includes sleep-onset or maintenance insomnia, frequent awakenings (often with air hunger), morning headache, nonrestorative sleep, and daytime fatigue or sleepiness.^{6,10} The burden of PB does not always impact sleep quality and fragmentation, underscoring the primary role of hypoxemia and other causes related to high altitude in sleep disruption.^{10,11}

Polysomnography or portable monitoring typically reveals central events clustered in NREM with cycle times less than 40 s and event durations of ~10 to 12 s in adults, accompanied by oxygen desaturation of variable depth depending on altitude and physiology.¹⁰ Apnea duration can be shorter than 10 s, which is out of the definition of the respiratory events according to the American Academy of Sleep Medicine (AASM) (at least 10

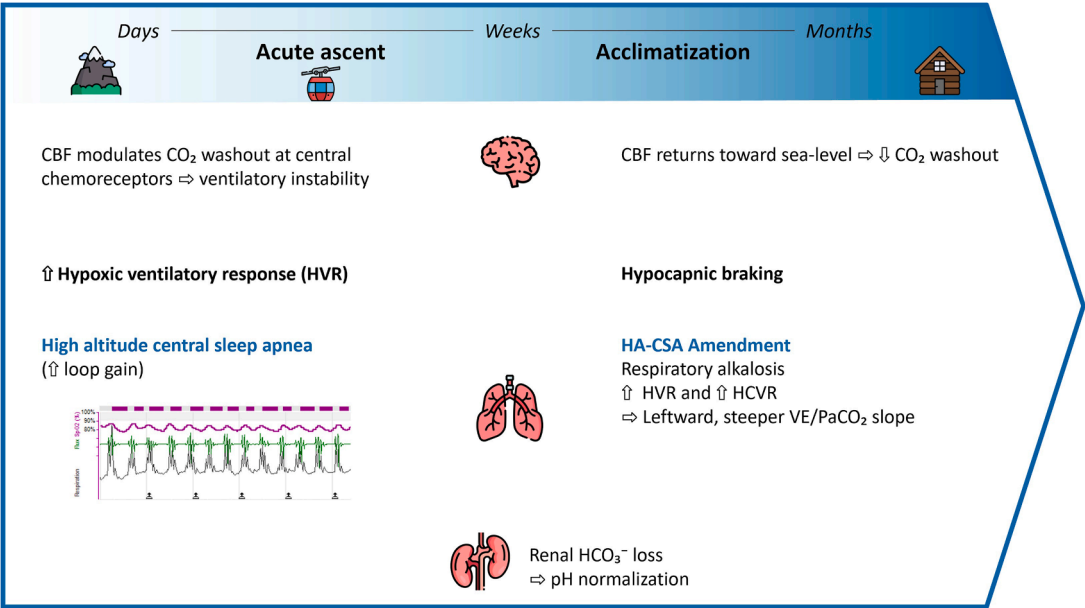


Fig. 2. High altitude CSA: from acute exposure to acclimatization. CBF, cerebral blood flow; HCVR, hypercapnic ventilatory response; HVR, hypoxic ventilatory response; PaCO₂, partial pressure in CO₂; VE, Minute Ventilation; Loop gain = controller gain (chemosensitivity) x plant gain (the efficiency of CO₂/O₂ exchange relative to ventilation) x feedback delay (circulatory and neural latencies).

s of durations), but adds to the hypoxic and ventilatory burden experienced by subjects at high altitude.¹⁰ Fig. 3 represent a sample of CSA with PB recorded at HA.

As previously described, at high altitude, HA-CSA and PB occur predominantly during light NREM sleep, where arousals and altitude-induced hypocapnia facilitate P_{aCO_2} drops below the apneic threshold. Sleep fragmentation and reduced slow-wave sleep actively destabilize ventilatory control, perpetuating cycles of apnea, hyperventilation, and re-arousal, whereas REM sleep is relatively less affected by cyclic CSA patterns.^{6,10}

Coexisting sleep-disordered breathing phenotypes are common. In susceptible subjects with established obstructive sleep apnea (OSA), simulated altitude (eg, normobaric hypoxia at ~15% O_2) can worsen the sleep respiratory disturbance converting the main type of apnea to sustained CSA.^{34,35} These effects are explained by hypobaric hypoxia increasing ventilatory controller gain, narrowing the CO_2 reserve, and elevating loop gain, thereby rendering the system more unstable to arousal-related perturbations.³⁶ Interestingly, altitude exposure in untreated patients with OSA, beyond the increase in sleep-related breathing disturbances due to frequent central apnoeas/hypopnoeas aggravates nocturnal hypoxemia, impairs driving simulator performance and induces cardiovascular stress, including significant increase in mean nocturnal heart rate.³⁵ These findings highlight the susceptibility of untreated OSA lowlanders to HA-CSA, with implications for

counseling and care of OSA patients planning to travel to HA.

Impact of Periodic Breathing on Mean SpO_2

Recent studies converge on the finding that HA-CSA is not responsible for the reduction of mean nocturnal oxygen saturation despite frequent desaturations.³⁷ When comparing within subjects at a simulated altitude of 3500 m, the average SpO_2 did not differ between periods of regular breathing and PB, if sleep stage and body position were controlled. Additionally, at higher altitudes, increasing HA-CSA severity was not linked to lower mean sleeping SpO_2 across various ascent profiles.³⁷ Rather, PB increased SpO_2 variability without affecting average oxygenation, consistent with alternating phases of hypoventilation and compensatory hyperventilation that result in a neutral net effect.³⁸ Importantly, baseline (awake) SpO_2 emerged as the strongest predictor of mean nocturnal SpO_2 in hypoxia, pointing to individual ventilatory acclimatization and chemoresponsiveness as the main drivers of nocturnal oxygenation, rather than CSA burden per se.³⁷ With ascent, apnea-hypopnea index (AHI)/oxygen desaturation index (ODI) rise and mean/nadir SpO_2 fall as expected, but higher CSA severity does not translate into worse mean nocturnal oxygenation at altitude.³⁸ This concept provides a physiologic bridge to acute mountain sickness (AMS), the most common form of high-altitude illness, defined as a symptom complex—including headache, nausea, dizziness, fatigue, and sleep

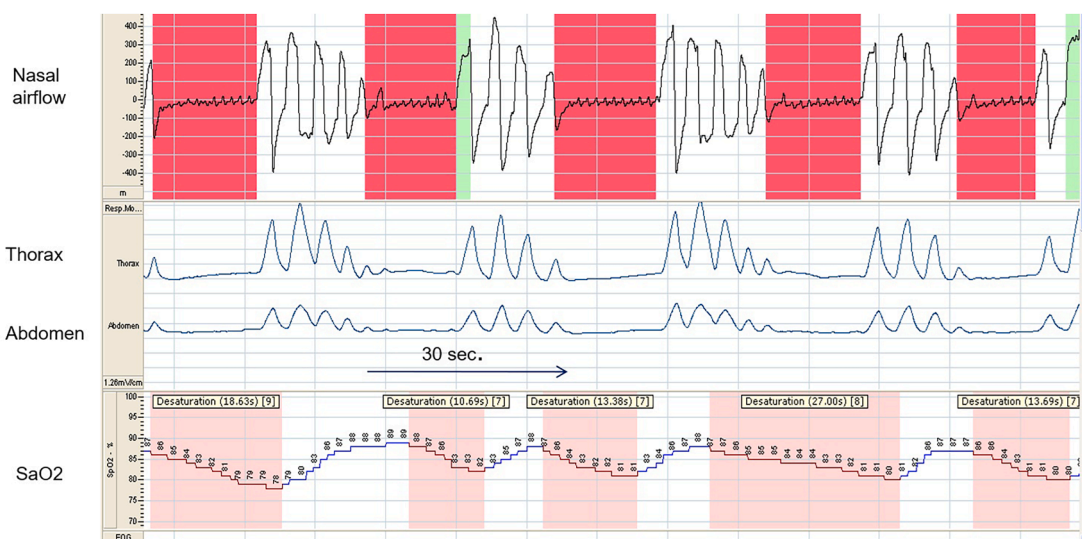


Fig. 3. Sample of CSA (red squares) with periodic breathing in a subject living at sea level ascending at 5000 m. First-line represent nasal cannula signal, second and third thorax and abdomen belts, fourth signal oxygen desaturation.

disturbance—that develops within hours to days after ascent and reflects inadequate acclimatization to hypoxia. In this context, the work by Nespolet and colleagues adds a critical mechanistic layer, showing that individuals susceptible to AMS exhibit reduced peripheral hypoxic chemosensitivity, lower mean nocturnal SpO₂, and fewer central respiratory events during sleep compared with altitude-tolerant subjects.³⁹ Thus, HA-CSA appears not as a cause of impaired oxygenation, but rather as an epiphenomenon of a high ventilatory drive that may paradoxically preserve mean nocturnal SpO₂ and reduce AMS risk.

Clinically, these data suggest that HA-CSA should not automatically be considered harmful in healthy sojourners or residents, shifting the focus from treating apnoea-hypopnoea indices alone toward identifying individuals with blunted ventilatory responsiveness and clinically relevant symptoms, who may be the ones most likely to benefit from targeted interventions.^{38,39} However, the greater SpO₂ oscillations during PB may still have physiologic consequences such as intermittent hypoxia-related oxidative stress and inflammation, sleep fragmentation, and sympathetic activation, warranting context-specific judgment especially in vulnerable populations.³⁷

NOVEL PERSPECTIVES

Ethnic Determinants

Population-specific and environmental factors may shape physiologic and pathophysiological responses to HA exposure. High-altitude populations such as Sherpa exhibit distinct ventilatory control characteristics, including higher ventilation and smaller nocturnal reductions in end-tidal CO₂ compared with nearby lowland groups, consistent with a lower propensity for PB.⁴⁰ Ethnicity has been addressed as the dominant predictor of altitude-induced AHI change, ahead of age and BMI.⁴⁰ These data imply inherited differences in breathing control: plant dynamics can protect against CSA in populations that were exposed to altitude-related hypobaric hypoxia for longer time.

In a prospective comparison across a standardized trek from ~2030 to ~4380 m, Sherpa showed a markedly smaller increase in AHI than Tamang,⁴¹ a smaller rise in oxygen desaturation index, and less nocturnal PB. Sherpa exhibited higher resting ventilation at both altitudes and a smaller drop in mixed-expired CO₂, suggesting less hypocapnia for a given ventilatory response.

In contrast, residents of extreme-altitude cities (eg, La Rinconada, ~5100 m) experience profound nocturnal hypoxemia. In these populations, OSA is often the predominant phenotype and may

exacerbate altitude-related chronic hypoxemia during sleep. Among individuals with excessive erythrocytosis (EE) or chronic mountain sickness (CMS), mean nocturnal SpO₂ is lower and desaturation nadirs are more pronounced.^{42,43} (See also below.)

Extreme Altitude Residency. From Adaptation to Maladaptation

Highlanders are known to develop unique adaptations to chronic hypoxic exposure but also, for some of them, to present a maladaptive syndrome called CMS related to EE and with consequent cardiorespiratory diseases.^{44–46} The Expedition 5300 investigations in La Rinconada (~5100–5300 m) document a striking physiology: daytime SpO₂ near ~80%, Pao₂ ~35 mm Hg and Paco₂ ~34 mm Hg in non-CMS adults, and exceptionally high hemoglobin concentrations and blood viscosity.^{47,48} Across lowland Lima (80 m), Puno (~3800 m), and La Rinconada (~5100 m), increasing altitude was associated with lower mean nocturnal SpO₂ (~79% at 5100 m vs ~84% at 3800 m). Within La Rinconada, CMS was associated with lower mean nocturnal SpO₂ (~74% vs ~79% in non-CMS), deeper nadir desaturations (~49% vs ~67%), and higher nocturnal blood pressure variability.⁴³ These findings link sleep-related hypoxemia with vascular and autonomic stress and EE/CMS progression at extreme altitude.^{41,43} In this context, the specific role of CSA beyond hypoxia itself still needs to be defined.

Gender Determinants

Gender differences have been observed in PB responsiveness to hypoxia, reinforcing that demographics and physiology modulate expression of altitude-related sleep apnea.⁴⁹ The ventilatory control response to hypoxia—conceptualized as loop gain—appears to differ between sexes, potentially contributing to a progressive worsening of CSA severity over time in men but not in women. This sex difference in acclimatization appears to protect females from high altitude-related CSA.⁵⁰ Ventilatory chemosensitivity in women remains stable across the menstrual cycle, with no significant variation in HVR, ventilation, or oxygenation despite physiologic hormonal fluctuations.⁵¹ Moreover, neither HVR nor ovarian hormone levels predicted AMS occurrence in women after ascent to 3375 m.⁵² Taken together, these findings support the concept that, at least in women studied under controlled conditions, ventilatory acclimatization to hypoxia appears relatively stable across hormonal phases. While sex-related differences in the expression of HA-CSA have been reported,

the underlying mechanisms remain incompletely understood and cannot be attributed solely to menstrual hormonal fluctuations. It should also be acknowledged that, similarly to the broader OSA literature—including randomized controlled trials—women remain underrepresented in many studies investigating sleep-disordered breathing. This underrepresentation limits the availability of sex-specific data and makes it difficult to draw definitive conclusions regarding the role of biological sex and hormonal status in the pathophysiology and clinical expression of HA-CSA. Further studies are required to precise the role of biological sex and hormones in HA-CSA pathophysiology.

TREATMENTS OF HIGH-ALTITUDE CENTRAL SLEEP APNEA

Prevalence and severity of HA-CSA increase with elevation. Accordingly, descent is the definitive remedy when feasible. If descent is impractical or temporarily impossible, supplemental oxygen reliably suppresses central events.⁵³ Correction of hypobaric hypoxemia with supplemental oxygen has been shown to improve sleep apnea at altitude, both in nonacclimatized persons and long-term dwellers.^{54,55} However, nocturnal supplemental oxygen may have limitations, particularly as certain circumstances might preclude its use, as it might not be widely available in lowlanders ascending to altitude. In hypobaric environments, achieving normal arterial oxygen tension (P_{aO_2}) necessitates the administration of higher inspired oxygen fractions (F_{iO_2}). When oxygen is delivered nasally, local mucosal irritation may occur, and even moderate over-supplementation can exert significant systemic physiologic effects. Moreover, supplemental oxygen may hinder acclimatization by attenuating exposure to hypoxemia. Although a single-night study has shown no alteration in either hypoxic or hypercapnic ventilatory responses, longer-term investigations may be required to fully elucidate potential effects.⁵⁶ Some high-altitude working environments, such as mines situated at high altitude, have implemented sleeping rooms enriched by oxygen to help workers adaptions during weekly shifts at high altitude.^{57,58} In a randomized, single-blinded, crossover design, 12 men underwent 2 3-day sojourns separated by 4 weeks in hypobaric hypoxia corresponding to 4000 m of altitude, Ibrahim and colleagues tested the impact of increasing inspiratory CO_2 to prevent nocturnal PB.⁵⁹ They showed that CO_2 enrichment led to marked stabilization of ventilation during sleep, effectively preventing hypoxia-induced nocturnal PB without affecting sleep macro-architecture, as assessed by polysomnography. Whether this

strategy could translate into therapeutic practice require further investigations.

Acetazolamide is effective when administered orally, with multiple studies demonstrating substantial reductions in HA-CSA severity at altitude.^{60–63} The predominant mechanism with repeated oral dosing was a mild metabolic acidosis that increases the CO_2 reserve, moving the P_{aCO_2} level away from the apnea threshold and stabilizing the loop gain,⁶⁴ rather than the rapid effect of intravenous infusion of acetazolamide. In fact, acute intravenous acetazolamide exerts minimal immediate effect on acid–base status or ventilatory responses, but increases CBF²⁸—likely by preventing CO_2 -mediated vasoconstriction in cerebral arteries—and raises P_{aCO_2} by ~ 3 mm Hg.³¹ These combined actions temporally reduce central events without the delayed metabolic component of oral therapy.

Noninvasive ventilation with bi-level positive airway pressure has also been reported to mitigate high-altitude CSA in selected individuals. However, the underlying mechanism remains unclear, as this approach appears less physiologic for stabilizing ventilatory control. Potential contributors include elevation of mean P_{aCO_2} above the apnea threshold via intentional rebreathing, altered plant dynamics, and arousal stabilization.⁶⁵ Further investigations comparing adaptive servo-ventilation (ASV) with supplemental oxygen demonstrated that ASV was not consistently effective in controlling HA-CSA and PB. Moreover, ASV did not yield significant improvements in oxygenation indices, sleep quality, or related symptoms, apart from a modest increase in mean nocturnal oxygen saturation.⁶⁶

Hypnotic strategies can improve sleep continuity independent of effects on central events. Temazepam and related agents have been associated with better subjective sleep and modest reductions in HA-CSA indices in some studies, with little or no change in average nocturnal SpO_2 .^{67–69} Non-benzodiazepine hypnotics have been shown to enhance sleep quality at high altitude without exacerbating oxygen desaturation events.⁷⁰ Their use may therefore be considered in selected individuals to improve sleep continuity and restorative rest. However, the administration of any hypnotic agent under hypobaric conditions should be carefully individualized and closely monitored, given the potential variability in physiologic responses and susceptibility to hypoxemia. Additionally, alpinists should be aware of the risk of hypnotics' residual effects in case of an early start for an ascension, with consequences on processing speed and balance control,⁷¹ which may be deleterious for safety and performances of climbers.

In patients with known OSA (treated or not), coexisting HA-CSA management should address both the obstructive and central components of the disorder. Supplemental oxygen or acetazolamide can help suppress central apneas and, in doing so, may reveal residual obstructive events. Once these are unmasked, conventional OSA treatments—such as continuous positive airway pressure can be appropriately titrated to achieve optimal control of both types of events.^{72–74}

SUMMARY

HA-CSA is frequent in lowlanders ascending to altitude greater than 2500 m of elevation gain. HA-CSA arises from the convergence of heightened chemosensitivity, sleep-related reductions in respiratory drive, and the gas-, all modulated by cerebrovascular physiology in the presence of hypobaric hypoxia. Acclimatization reshapes these elements over days to weeks, and both clinical manifestations and treatment responses follow from these dynamics. Pragmatic management prioritizes descent or oxygen when necessary. Emerging work linking CBF to ventilatory stability, together with population studies in high-altitude residents, continues to refine this integrated model.

CLINICS CARE POINTS

- Ascent triggers HA-CSA: after rapid ascent above ~2500 m, hypobaric hypoxia can induce hyperventilation, hypocapnia, and NREM-predominant central apneas/periodic breathing.
- Acclimatization reshapes CSA: over days to weeks, bicarbonate loss, rising HVR/HCVR, and changing loop gain can modify CSA severity and expression.
- Descent is definitive treatment: when feasible, descent is the most direct remedy; if not possible, oxygen or drugs may be used to suppress central events.

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DISCLOSURE

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