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REVIEW ARTICLE

ALTITUDE AND ITS IMPACT ON OCULAR PHYSIOLOGY AND PATHOLOGY

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Abstract: Altitude is an environmental factor that induces systemic physiological adaptations, many of which extend to the visual system. These changes are multifactorial and stem from fluctuations in atmospheric pressure, varying rates of oxygen deficiency (hypoxia), reduced gravitational forces, and increased exposure to ultraviolet radiation. Notably, environmental pressure differentials below sea level also bear clinical significance. For instance, divers—particularly those engaged in frequent and deep-sea diving—are subject to a unique set of environmental stressors that may predispose them to physiological alterations. Similarly, individuals residing in high-altitude regions exhibit numerous long-term adaptive mechanisms, which have their downsides. Aviation, especially at high altitudes and during high-speed flight, imposes additional visual health risks on pilots and aircrew. Furthermore, spaceflight represents an extreme environmental condition; prolonged exposure to microgravity has been associated with the development of spaceflight-associated neuro-ocular syndrome, a constellation of neuro-ophthalmic changes that are still under active investigation. In all these contexts, the composition of ambient air, including its humidity, temperature, and pollutant content, can significantly impact the ocular surface.

Keywords: high-altitude retinopathy, acute mountain sickness, space-associated neuro-ocular syndrome, aviation medicine, military pilots

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INTRODUCTION

At high altitudes, the partial pressure of oxygen declines, leading to ocular tissue hypoxia, which may impair the function of photoreceptors and the optic nerve [17]. Chronic hypoxia has also been implicated in the pathogenesis of age-related macular degeneration [7] and optic neuropathy [32]. Above 2,000 meters above sea level, the thinner atmosphere permits increased ultraviolet (UV) radiation to reach the Earth's surface. Prolonged exposure to ultraviolet light has been linked to a higher risk of cataract formation, macular degeneration, and corneal damage, including photokeratin [40]. Epidemiological studies confirm a significantly elevated risk of such conditions in populations living or working at high altitudes, particularly in the absence of adequate ocular protection [16]. Additionally, environmental stressors such as strong winds, cold temperatures, and low humidity can lead to conjunctival and corneal irritation, predisposing individuals to ocular infections and inflammatory conditions [28]. The presence of airborne dust and pollutants at high elevations may further exacerbate these effects, particularly in individuals with pre-existing ocular or systemic comorbidities [23].

METHODS

This review was conducted using a systematic approach to identify and synthesize current evidence on the impact of high altitude on ocular health. A comprehensive literature search was performed across databases, including PubMed, Scopus, and Web of Science, for articles published in the last 20 years: between April 2005 and April 2025. Keywords and Medical Subject Headings terms such as "high altitude," "hypoxia," "ocular physiology," "retina," "optic nerve," "intraocular pressure," and "visual function" were used in various combinations. Peer-reviewed original research articles, clinical trials, case reports, and relevant review articles were included, provided they discussed altitude-related ocular changes in human subjects. Articles not available in English, lacking full-text access, or focused solely on animal models were excluded. Reference lists of key articles were also reviewed to identify additional relevant studies. The selected publications were critically appraised for methodological quality and relevance to the research question.

DISCUSSION

Individuals ascending to altitudes between approximately 2,500 and 3,500 meters above sea level are at risk of developing acute mountain sickness, a condition primarily attributed to the reduced partial pressure of oxygen in the thinner atmosphere [3]. Visual disturbances may occur, most commonly in the form of blurred vision, and less frequently as visual field defects or vitreous floaters. These ocular symptoms are largely associated with retinal vascular dilation in response to systemic hypoxemia. The resultant increase in capillary hydrostatic pressure can compromise the integrity of the retinal vascular endothelium, potentially leading to retinal or vitreous hemorrhages [18]. As the condition progresses, ischemic phenomena may develop, manifesting as cotton wool spots or non-arteritic ischemic optic neuropathy [10]. In some cases, optic disc edema may be observed, which can serve as an early warning sign of high-altitude cerebral edema, a life-threatening condition requiring urgent intervention [45]. Corneal edema may also occur at high altitudes, causing transient changes in the refractive power of the ocular system [20]. However, this phenomenon is not typically associated with clinically significant visual impairment. Early signs of acute mountain sickness often include dizziness, nausea, and fatigue. In these instances, carbonic anhydrase inhibitors commonly used by climbers can be effective in mitigating symptoms [2], as they promote metabolic acidosis, which stimulates hyperventilation, thereby enhancing oxygen uptake. Additionally, these agents reduce cerebrospinal fluid (CSF) production by inhibiting secretion from arachnoid granulations, leading to a decrease in intracranial pressure and reducing the risk of cerebral edema. On the other hand, the influence of hypobaric hypoxia on inducing acidosis generates in turn a higher need for bicarbonate ions to equalize systemic pH, which cannot be used in aqueous humor production, being the probable cause of intraocular pressure lowering observed as a result [45].

In populations permanently residing at high altitudes, the human body undergoes physiological adaptations to cope with environmental hypoxia. One of the principal mechanisms is an increase in red blood cell production, which enhances oxygen-carrying capacity. While this adaptation improves tissue oxygenation, the resulting elevated hematocrit can impair microvascular perfusion, including that of the ocular circulation, due to increased blood viscosity [25]. At elevations exceeding 2,500 meters above sea level, the body must adapt to increasingly harsh conditions. It is generally recommended that individuals do not ascend more than 300–500 meters per day beyond this altitude without allowing for 24–48 hours of acclimatization, although this interval may vary depending on individual susceptibility. Despite preventive measures, certain individuals may still experience adverse outcomes, such as optic disc edema or an increased risk of glaucoma development [29]. Acclimatization, a gradual ascent tailored to the altitude of residence during the prior 2–3 weeks, is crucial to permit adaptive physiological responses [44]. This principle also applies to individuals who have lived most of their lives in high-altitude regions and travel to lower altitudes for short periods. These environmental transitions challenge the cardiovascular system, which must sustain increased cardiac output and heart rate to maintain adequate tissue perfusion. This is contingent on vascular health, including endothelial integrity, venous competence, and the presence or absence of atherosclerotic plaques. Emerging evidence suggests that chronic high-altitude exposure may induce corneal structural changes. A study reported transient corneal edema in high-altitude residents, potentially affecting visual acuity [38]. Furthermore, UV radiation exposure, being significantly higher at elevated altitudes, is a recognized risk factor for cataract formation. Chronic hypobaric hypoxia may also lead to retinal changes, including retinal edema and vascular remodeling [47], which can compromise both central and peripheral vision. Adaptation to hypoxia at high altitudes may involve angiogenesis within the retinal vasculature to enhance oxygen delivery, ultimately increasing the risk of vascular proliferation [5].

Aircraft crew members are also subject to physiological challenges resulting from changes in environmental conditions during flight. Although ascent and descent typically occur gradually and predictably, they can cause transient sensations such as ear barotrauma, commonly experienced as ear “clogging.” However, supersonic jet pilots are exposed to additional physiological stressors due to rapid changes in acceleration and body orientation relative to the gravitational axis during flight maneuvers [34]. These shifts subject the body to gravitational forces (G-forces), resulting in blood pooling in the distal extremities and diminished cerebral perfusion. A common visual manifestation is peripheral vision constriction, known as “grey-out”, progressing to potential syncope in severe cases, an event called G-LOC [26,19]. To counteract central nervous system hypoxia and associated symptoms, supersonic pilots are trained to perform anti-G straining maneuvers. These involve voluntary contraction of the lower limb and abdominal muscles to augment venous return via the muscle pump mechanism, thereby enhancing cardiac output and sustaining cerebral oxygenation. In the long run, no evident structural changes have been observed in the retinal parameters of these pilots [33]. Night flying introduces additional visual challenges due to low ambient light levels, affecting both civilian and military pilots. Dark adaptation, a process that can physiologically take up to 40 minutes, happens faster when preceded by dim environmental conditions. Night vision primarily depends on rod photoreceptors, which are absent in the fovea, the central area of the retina responsible for high-resolution vision, thus impairing scotopic and mesopic visual acuity. A phenomenon occurring during nighttime operations is night myopia, typically approximating −1.0 diopters [12]. Supposedly, hypoxia may also be a confounding factor in this myopic shift, since it causes the edema of corneal stroma, particularly in eyes previously subjected to keratorefractive surgery, where corneal tectonic stability is weakened [31]. Proper correction involves prescribing the full refractive correction identified under standard clinical conditions, without intentional overcorrection. Additionally, due to iridocilliary relaxation, depth perception becomes compromised in low-light environments, posing increased risks during landing or while navigating near elevated terrain, such as in mountainous regions. In cases of low visibility due to dense cloud cover or fog, even optimal visual acuity is insufficient. Therefore, reliance on aeronautical navigation systems becomes essential to maintain flight safety.

The influence of altitude must also be considered in the context of individuals residing below sea level. The lowest inhabited regions on Earth, such as areas surrounding the Dead Sea (Israel/Jordan), exhibit atmospheric pressure approximately 5% higher than at sea level [27]. This modest increase in pressure is unlikely to have a clinically significant impact on ocular physiology. However, the topographical positioning of cities within basins or depressions, such as Kraków (Poland), Jakarta (Indonesia), Delhi (India), Lima (Peru), and Bogotá (Colombia), poses environmental health risks. The limited air circulation in these regions, especially post-industrialization, promotes air pollution accumulation, which has been linked to ocular surface irritation, contributing to dry eye syndrome, conjunctivitis, and subclinical toxicity through systemic absorption of pollutants. Atmospheric conditions such as wind, low temperatures, and reduced humidity may lead to irritation of the conjunctiva and cornea, thereby increasing susceptibility to ocular infections and inflammatory conditions. Additionally, the accumulation of dust and airborne pollutants in topographically enclosed areas, such as the city of Jericho in Jordan, may further elevate the risk of ocular surface disease in these environments [1]. UV radiation, despite its shorter wavelength and higher energy relative to visible light, has a well-established role in the pathogenesis of cutaneous melanoma and ocular surface neoplasia, particularly pterygium, which occurs significantly more often in regions with year-round high solar exposure [39]. Although the ocular lens serves a protective function by absorbing part of this radiation, thereby contributing to cataract formation, this feature also highlights the increased cataract prevalence in equatorial regions. When it comes to the posterior segment of the eye, current scientific evidence remains insufficient to confirm a direct relationship between UV exposure and increased susceptibility to age-related macular degeneration or uveal melanoma [35]. However, these posterior segment pathologies are notably more prevalent among individuals of Caucasian descent. This observation suggests a potential association with decreased melanin content in their tissues, indicating a possible deficiency in intrinsic UV protection. The influence of blue light, however, which lies on the spectrum close to UV, remains a subject of ongoing debate. While the natural crystalline lens offers partial protection by absorbing short-wavelength light, contributing over time to cataract formation, modern ophthalmic strategies now propose integrating blue-light filters into intraocular lens IOL implants used during cataract surgery [24]. This recommendation gains relevance in the context of increasing exposure to artificial blue light emitted by digital devices. To mitigate the detrimental ocular effects of solar radiation, stronger at greater heights due to a thinner composition of the atmosphere, precautions such as UV-filtering sunglasses are of utmost importance. Also, lubricating eye drops containing riboflavin can offer additional UV filtration [6]. However, such drops should not be viewed as substitutes for mechanical UV protection provided by eyewear. This precaution is particularly critical in mountainous regions, due to the impact of UV radiation intensified by high summer solar irradiance and the strong reflectance of nearly the full visible spectrum from snow-covered surfaces during winter.

In contrast, diving introduces a broader range of ocular risk factors related to altitude. Exposure to contaminated or unfiltered water can serve as a vector for infectious conjunctivitis or keratitis. While bacterial and viral etiologies are common, divers are also at risk for protozoal (e.g., Acanthamoeba) or fungal infections, which may result in significant ocular morbidity if not promptly diagnosed and treated [8]. Additionally, allergic reactions or irritative responses to chemicals, algae, or suspended particulates can trigger ocular redness, pruritus, epiphora, and general discomfort [15]. During submersion, particularly at greater depths, the ambient pressure increases markedly due to the weight of water molecules above the body altogether. Recreational SCUBA diving typically occurs at depths of up to 40–50 meters, whereas professional deep-sea divers and researchers, following rigorous training, may descend to 300–400 meters. These pressure changes can lead to transient alterations in ocular blood flow dynamics and intraocular pressure, occasionally resulting in blurred vision, foggy perception, or ocular discomfort [11]. Upon resurfacing, divers may experience decompression sickness, a condition that in severe cases can lead to neurological and ophthalmic complications. Reported manifestations include optic disc edema, headache, and, in extreme cases, vision loss.

Extraterrestrial environments, such as those encountered during manned missions to the International Space Station, currently the only active orbital platform, and beyond, present unique physiological challenges due to the absence of Earth-induced gravity. Adaptation to this altered gravitational vector leads to complex redistribution of bodily fluids and changes in cardiovascular dynamics [36]. On Earth, the heart is positioned in the upper third of the body, allowing it to pump blood effectively both against gravity toward the brain and with gravity toward the distal extremities. In microgravity, this gravitational assistance and resistance disappear, altering cardiac preload, heart rate, and cardiac output. Although perfusion of metabolically demanding organs like the brain remains preserved, venous return from the lower body diminishes, increasing cardiac workload and predisposing to cardiovascular deconditioning [21,14]. A notable consequence of microgravity is venous congestion in the head and neck, leading to facial puffiness [4]. More significantly, alterations in

CSF dynamics, which are relatively independent of cardiac output, result in progressive accumulation of CSF along the brain and optic nerves, which are ensheathed by the meningeal layers [37]. This buildup exerts pressure on the posterior globe, flattening it and inducing hyperopic refractive shift. Initially reversible, such changes may become persistent after prolonged exposure (e.g., one-year missions), with ocular axial length failing to fully revert post-return [30,41]. Additionally, venous stasis in small-caliber vessels, particularly in the choroid, can lead to choroidal thickening, the formation of retinal folds, and metamorphopsia [13,9]. Concurrent optic disc edema may arise, likely due to elevated pressure on the posterior lamina cribrosa [45]. These phenomena, part of Spaceflight-Associated Neuro-ocular Syndrome (SANS), are often accompanied by retinal ischemia, manifesting as cotton wool spots, yet do not typically present with headaches or tinnitus, as seen in traditional intracranial hypertension [42]. Upon return to Earth, astronauts frequently experience muscular hypotrophy, orthostatic intolerance, dizziness, and general weakness, as previously atrophied muscles must again counteract gravity [28]. The fluid redistribution toward the cephalic region, including ocular tissues, contributes to optic disc swelling and structural ocular changes. Microgravity also disrupts ocular and orbital vascular regulation, with reported alterations in retinal and orbital vasculature that can impair visual performance. In some astronauts, an increase in intraocular pressure has been documented, posing a potential risk for glaucoma development [44]. Moreover, these alterations may persist well beyond mission completion, necessitating long-term ophthalmic surveillance and intervention. The longer the exposure to microgravity, the higher the likelihood of developing SANS. However, not all astronauts are affected, implicating individual genetic and physiological predispositions [46]. Ongoing research is focused on risk mitigation strategies, including pressure-regulating garments, pharmacologic countermeasures, and spacecraft engineering solutions [33]. Recent advances in imaging modalities such as optical coherence tomography and orbital ultrasonography have enhanced the monitoring of optic nerve and retinal changes during missions, also performed in-flight. Emerging research underscores the central role of vascular and CSF flow disturbances in SANS pathophysiology, with some studies highlighting the prophylactic potential of intracranial pressure-lowering agents, but it remains controversial in terms of a long stay treatment [43]. Moreover, recent reports warn that structural ocular changes may result in permanent visual impairment, which could impact astronaut safety and operational performance during long-duration missions.

CONCLUSION

Ophthalmologists and other medical professionals should be aware of the pathologies related to altitude, since it poses a challenge for ocular health, among other medical implications due to the change of the usual environment of residence and new forces in action. This issue is particularly relevant because of an increasing tendency in recreational mountain climbing, diving, flying, and travelling. Precautions such as targeted protection from risk factors and gradual acclimatization to mitigate the risk of exposure to unavoidable circumstances should be carefully implemented. General health evaluation by a professional multidisciplinary crew beforehand can prove crucial to the challenge. In the futuristic context of space conquests intended to expand scientific knowledge, but also in the search for new exoplanets as an alternative for life to Earth, this topic will be a captivating field for researchers in the years to come. Colonization of the moon or Mars with a group of healthy volunteers seems to be the first logical step in order to longitudinally observe how to best prepare for a smooth transition to such a different environment. Efforts are underway to develop specialized devices and interventions, such as advanced pressure regulation systems and targeted pharmacotherapy, to mitigate SANS risk during future extended missions. While many of these innovations remain in the experimental phase, preliminary findings are encouraging. The human organism's balance is easy to unsettle with changing atmospheric conditions, while evolution is an effective adaptive mechanism, but relatively slow, and needs many generations to pass on the required changes to the offspring. Further investigations, preferably in facilities equipped with special tools in a controlled environment, are required to clarify changes in crucial aspects: retinal vessels, photoreceptors, visual fields associated with altitude exposure, along with the stability of the visual acuity, tear film parameters and corneal architecture.

AUTHORS' DECLARATION

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