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# Ignoble Gas: The Questionable Role of Xenon in Rapid Ascents of Mount Everest

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#### **Abstract**

Manferdelli, Giorgio, Marc M Berger, and Andrew M Luks. Ignoble Gas: The Questionable Role of Xenon in Rapid Ascents of Mount Everest. *High Alt Med Biol.* 00:00–00, 2025.—Beyond the logistical, technical, and physiological challenges associated with climbing extremely high mountains such as Mount Everest, an important feature of such expeditions is their long duration. Among the strategies used in recent years to reduce expedition duration, one particularly novel approach was implemented during Everest expeditions in 2024 and 2025—inhalation of the noble gas xenon prior to the expeditions. Despite the tremendous attention this approach received in the media, significant questions remain as to whether it is truly effective at improving acclimatization and shortening the duration of expeditions. This review examines this issue in greater detail. After providing background information on xenon, the review examines potential rationales for xenon's use in the mountains, assesses the risks of xenon administration, and considers other aspects of the expedition protocol that likely affected the odds of summit success. Based on this analysis, there is no basis for widespread implementation of xenon inhalation at this time. Evidence of benefit is lacking, and there are strong reasons to believe other aspects of the expedition protocol contributed significantly to the expeditions' outcomes. Much further research on these questions is warranted before any more climbers should engage in this potentially risky practice.

**Keywords:** acclimatization; Everest; hypobaric hypoxia; xenon

#### Introduction

Everest (8,849 m) in the early 20th century, a consistent feature of climbing expeditions on the mountain has been their long duration. While the ability to fly to the village of Lukla at the start of south side expeditions or drive to base camp for north side climbs has shortened expedition length to some extent, many modern expeditions still require around 6-8 weeks for the endeavor, including time spent getting to and from base camp, acclimatizing to hypobaric hypoxia, and climbing the mountain itself. Recent years have been marked by attempts to limit the time spent acclimatizing on Mount Everest with an eye toward reducing risk and/or shortening the duration of the expedition. Some South Col expeditions, for example, now use climbs on other mountains in the region, such as Lobuje East (6,119 m), to facilitate acclimatization and reduce the number of trips through the everdangerous Khumbu Icefall. In addition, many climbers on

north and south side routes are using hypoxic training systems at home for many weeks leading up to their expedition to speed along acclimatization prior to the expedition and reduce the time spent acclimatizing and climbing the mountain itself.

In the past two years, another strategy for shortening the duration of expeditions to Everest and other very high mountains has garnered significant attention—inhalation of the anesthetic gas xenon prior to departure. Based on a theory that the intervention stimulates acclimatization to hypoxic conditions, this approach first gained wide attention in the spring of 2024 when a professional guide, who had been experimenting with the gas for several years, used it to facilitate a climb of Mount Everest from the north side of the mountain. A significantly greater degree of attention was directed at the intervention in the spring of 2025 when four paying clients overseen by this guide underwent xenon inhalation during their expedition preparation and subsequently traveled from London to the summit of the mountain and back in only seven days (Wolfe and Sharma, 2025).

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While this novel intervention has gained widespread attention as a result of this and the prior year's expeditions, it remains unclear whether xenon inhalation is actually of benefit or whether other aspects of preparation for or conduct of the expedition are the primary contributors to the climbers' success in reaching the summit. This review article is intended to examine these issues in greater detail to inform future approaches to this intervention. After examining background information on xenon, we discuss how xenon might be useful for climbing expeditions at extremely high altitudes. Specifically, we address whether xenon improves acclimatization to and exercise performance in hypobaric hypoxia and whether xenon plays any role in preventing acute altitude illness. After considering the risks of xenon administration, we examine the impact of other aspects of the protocol used by climbers who underwent xenon inhalation on the likelihood of reaching the summit. We conclude with recommendations on how to approach future use of this intervention. The focus throughout will be on the evidence for or against this intervention rather than the ethical issues surrounding its use.

## Xenon: History, Properties, and Applications

Xenon (empirical formula Xe) was first discovered in 1898. (Ramsay and Travers, 1898) It is a colorless, odorless, tasteless, mono-atomic noble gas with a relative molecular weight of 131.3. Xenon is an extremely rare gas that represents no more than 0.0875 ppm in the atmosphere. (Maze and Laitio, 2020) Its commercial use has been limited to high-priced industrial applications, including flash lamps and thrusters for space travel, and to medical applications, notably anesthesia, critical care, and medical imaging (Jin et al., 2019; Maze and Laitio, 2020; McGuigan et al., 2023). Xenon is purified from the atmosphere as a byproduct of the separation of air into oxygen and nitrogen. Because this involves high capital costs and consumes large amounts of energy, its production is expensive.

Xenon was first used for human anesthesia by Cullen and Gross in 1951 (Cullen and Gross, 1951). As an anesthetic, xenon is nonflammable, nontoxic, and not transformed into potentially toxic metabolites. The blood-gas (0.115) and brain-blood (0.23) coefficients are the lowest among all inhalational anesthetics, ensuring that xenon floods in and out quickly, making anesthesia easy to control (Coburn et al., 2007). With its minimum alveolar concentration (MAC) of 71% (Cullen et al., 1969), narcotic effects are seen at concentrations of around 50%, while full anesthesia is achieved at approximately 80%.

The anesthetic effect is mainly caused by noncompetitive inhibition of the *N*-methyl-D-aspartate receptor through binding at a specific glycine site. Xenon also exerts potent effects on neuronal background potassium channels, including two-pore domain potassium channels such as TREK and TASK, which modulate neuronal excitability (Gruss et al., 2004), and on ATP-sensitive potassium channels (Bantel et al., 2010). It also has a significant inhibitory effect on nicotinic acetylcholine receptors as well as a stimulatory effect on gamma-aminobutyric acid receptors (de Sousa et al., 2000; Jin et al., 2019). Xenon upregulates the transcription factor hypoxia inducible factor-1-alpha (HIF- $1\alpha$ ) and its downstream cytoprotective effectors, including erythropoietin (EPO) (Ma et al., 2009; Stoppe et al., 2016). In addition, xenon is an ATP-sensitive potassium channel opener that crosses the

blood-brain barrier, which may contribute to neuroprotective properties.

Although its high cost and need for a specialized delivery and monitoring system remain a barrier to use, xenon has potential benefits compared to other inhalational or intravenous anesthetics. Perhaps its biggest advantage is the cardiovascular stability observed during anesthesia. Because it preserves cardiac output and vascular resistance, use of xenon is associated with significantly less hypotension and reduced need for intraoperative vasopressors (Al Tmimi et al., 2015; Schaefer et al., 2011; Wappler et al., 2007). Other advantages include faster recovery of consciousness and reduced environmental impact (McGuigan et al., 2023). For example, patients undergoing xenon anesthesia opened eyes, were extubated, oriented spatially, counted down, and reacted on demand faster than those who underwent sevoflurane, isoflurane, desflurane, or propofol anesthesia (Law et al., 2016). Xenon has also been reported to exert neuroprotective effects against a range of neurotoxic insults when used pre-, during, or post-injury (Van Hese et al., 2018). However, these findings have not, to date, translated to improved cognitive outcomes (Nair et al., 2021). The primary side effects associated with use as a general anesthetic include increased intracranial pressure (Plougmann et al., 1994), bradycardia (Law et al., 2016), and nausea and vomiting (Law et al., 2016; Lo et al., 2016).

Beyond its role in anesthesia, xenon has other applications in medicine. Various isotopes, for example, are used as part of magnetic resonance, computed tomography (CT), and single-photon emission CT imaging and have been employed in studies of human physiology (Pain et al., 1967; Zardini and West, 1966).

## How Might Xenon Be Useful in the Mountains?

To assess whether xenon has use outside the medical setting and, in particular, a role in mountaineering, it is necessary to examine the different ways in which xenon inhalation might be of benefit to climbers and the state of the evidence for such potential benefits.

# Acclimatization to high altitude and exercise performance

Exposure to hypobaric hypoxia triggers a series of physiological responses in multiple organ systems over varying time frames, the majority of which are beneficial and help the body adjust to the low oxygen conditions (Luks, 2015). At the molecular level, many of these responses are mediated by HIF-1 $\alpha$  and HIF-2 $\alpha$ , transcription factors that regulate gene expression and provoke many downstream responses. One of the most important responses for acclimatizing to high altitude and maintaining exercise capacity is an increase in serum EPO concentration and the subsequent increase in hemoglobin concentration, which helps maintain tissue oxygen delivery in the face of low arterial partial pressures of oxygen.

One of the reasons xenon has been thought to be of benefit in preparation for climbing at high altitude is via its effect on EPO production. Findings in mice and *in vitro* human kidney cells demonstrated that short-term ( $\leq 2$  hours) xenon inhalation (fraction of inspired xenon [F<sub>I</sub>Xe] 0.7, fraction of inspired oxygen [F<sub>I</sub>O<sub>2</sub>] 0.3) transiently (Ma et al., 2009) upregulated both HIF-1 $\alpha$  and HIF-2 $\alpha$  (Goetzenich et al., 2014; Jin et al., 2019; Limatola et al., 2010; Zhao et al., 2014), and, as a result,

increased EPO concentrations (Ma et al., 2009). Plasma EPO concentration has also been shown to be elevated 192 hours following a single episode of xenon inhalation ( $F_1Xe~0.3-0.7$ ,  $F_1O_2~0.21-0.6$ , balance nitrogen) in healthy humans (Dias et al., 2019; Stoppe et al., 2018).

Although it is well-established that EPO improves both submaximal and maximal exercise capacity (Lundby et al., 2008; Thomsen et al., 2007), the evidence regarding xenon's effect on hemoglobin mass, oxygen delivery, and exercise performance is limited to a single comprehensive study (Dias et al., 2019). The authors investigated the effects of acute (1 session), prolonged (7 days), and chronic (4 weeks) xenon inhalation on erythropoiesis, blood biomarkers, and exercise capacity. For the acute exposure, subjects inhaled three subanesthetic concentrations of xenon: F<sub>I</sub>Xe 0.3 for 20 minutes, F<sub>I</sub>Xe 0.5 for 5 minutes, and F<sub>I</sub>Xe 0.7 for 2 minutes, with measurement of EPO concentration before, during, and after xenon inhalation. For the prolonged exposure, subjects breathed F<sub>1</sub>Xe 0.7 for 2 minutes on seven consecutive days with assessment of EPO concentration and total blood and plasma volume. In the chronic exposure, subjects were randomly assigned to a 4-week protocol of either xenon (F<sub>I</sub>Xe 0.7 for 2 minutes) or sham gas inhalation with assessment of EPO concentration, total blood volume, VO<sub>2max</sub> and 3-km time trial performance before and after the exposure. Although acute and prolonged xenon exposure increased EPO concentration, chronic xenon inhalation did not result in significant increases in EPO concentration, hemoglobin mass,  $\dot{V}O_{2max}$ , or 3-km time trial performance (Dias et al., 2019). Importantly, changes in EPO concentration following xenon inhalation demonstrated high interindividual variability and did not translate into increased red cell volume, hemoglobin mass, or reticulocyte volume. Altogether, these results demonstrate that the physiological changes elicited by xenon inhalation are dosedependent and transient and may not elicit the necessary changes to enhance exercise performance or acclimatization by improving oxygen-carrying capacity (Dias et al., 2019).

## Prevention of acute altitude illnesses

Another question is whether xenon is specifically useful for preventing the main forms of acute altitude illness—acute mountain sickness (AMS), high altitude cerebral edema (HACE), and high altitude pulmonary edema (HAPE). Because no studies have directly addressed this question, the only way to evaluate it is to extrapolate from what is known about the pathophysiology of these diseases and then consider whether xenon affects such processes.

Acute mountain sickness and high altitude cerebral edema. While it is well-established that hypoxemia is an indispensable requirement for the development of AMS and HACE, the pathophysiology of these diseases has not been fully elucidated despite considerable research on this issue (Luks et al., 2021a, 2021b). One factor that is thought to play a role is the hypoxemia-mediated increase in cerebral blood flow (CBF) (Wilson et al., 2011). Higher CBF helps maintain cerebral oxygen delivery in the face of a low arterial PO<sub>2</sub> but may also increase hydrostatic vascular pressure in the cerebral circulation. This can activate the trigeminovascular system and predispose to the headache typically seen in AMS, cause edema formation in HACE, and decrease systemic and cerebral oxygenation (Manferdelli et al., 2021). Whether

xenon affects CBF is unclear, as there are no data on this question in humans, and the results of animal studies are conflicting; some studies show an increase (Gur et al., 1985; Hartmann et al., 1991; Laitio et al., 2007; Luttropp et al., 1993; Yao et al., 1992a; Yonas et al., 1985), while others show a decrease (Laitio et al., 2007; Yao et al., 1992b) or no effect at all (Fink et al., 2000; Frietsch et al., 2001).

Another consequence of hypoxemia, which may contribute to the pathophysiology of AMS and HACE, is the increase in vascular permeability of the brain due to increased oxidative stress, inflammation, and/or upregulation of vascular endothelial growth factor (VEGF) (Bailey et al., 2009; Tissot van Patot et al., 2005). Data directly assessing xenon's effect on cerebral vascular permeability during hypoxia in humans are lacking. However, xenon is known to upregulate VEGF (Goetzenich et al., 2014; Tassel et al., 2016), which would, theoretically, increase vascular permeability and, therefore, the likelihood of developing HACE. On the contrary, various animal models have shown that xenon reduces oxidative stress (Zhang et al., 2022; Zhao et al., 2015) as well as inflammatory responses to ischemiareperfusion injury (Yang et al., 2020; Zhao et al., 2015). However, neither of these findings has been validated in human studies (Breuer et al., 2015).

High altitude pulmonary edema. HAPE is a non-cardiogenic form of pulmonary edema caused by excessive hypoxic pulmonary vasoconstriction (Dehnert et al., 2007; Swenson and Bartsch, 2012). The exaggerated pulmonary vascular response to hypoxia results from reduced nitric oxide (NO) availability and increased endothelin production, as demonstrated in studies measuring plasma endothelin-1 and NO in exhaled air, bronchoalveolar lavage fluid, and the systemic circulation (Berger et al., 2020). Other factors, such as impaired alveolar fluid clearance, may also play a role (Sartori et al., 2007; Swenson and Bartsch, 2012).

Whether xenon interferes with these pathophysiologic processes is unclear. Human data on the effect of xenon on pulmonary vascular responses to hypoxia are lacking. Studies in pigs reveal conflicting results, with one study showing xenon increases pulmonary artery pressure and right ventricular afterload (Hein et al., 2008), and another showing it reduces pulmonary artery pressure (Baumert et al., 2005). Data on the effect of xenon on NO and endothelin-1 are also scarce. In isolated guinea pig hearts, xenon had no, or very minimal, physiologically important effects on NO-dependent vascular responses (Pagliaro et al., 2024). In anesthetized dogs, the hemodynamic effects of xenon are independent of the endothelin system (Francis et al., 2006; Francis et al., 2008). No studies have examined the effect of xenon on alveolar fluid clearance. Thus, as with AMS and HACE, there is no strong evidence to suggest that xenon is useful for preventing HAPE.

Beyond the fact that there are no plausible mechanisms by which xenon prevents acute altitude illness, another factor that warrants attention is the time span between xenon administration and when climbers are at high altitude and face a risk of acute altitude illness. Even if xenon could interrupt the pathophysiology of these diseases, given the gas' short half-life of about 2.7 hours (Schaefer et al., 2017), it is unlikely that xenon administration days or weeks ahead of a planned climb would have any effects on CBF, pulmonary

vascular resistance, and other variables of sufficient duration to yield any benefit during the actual ascent.

#### Neuroprotection

Another purported benefit of xenon is that it may protect the central nervous system against hypoxic injury at high altitude. This notion is incorrectly extrapolated from work done in animal studies that examined the neuroprotective effects of xenon when given either before or following various forms of ischemic brain injury, including cardiac arrest, cardiopulmonary bypass, stroke, and traumatic brain injury (Liang et al., 2022) For example, Fries et al. (2008) administered xenon (F<sub>I</sub>Xe 0.7) for 1 and 5 hours after resuscitation from an 8-minute cardiac arrest and noted reductions in neuronal necrosis and perivascular inflammation as well as improvements in neurocognitive and neurological function 1-3 days after resuscitation. Similarly, Limatola et al. (2010) used 2-hour xenon administration (F<sub>I</sub>Xe 0.7) 24 hours prior to 60 minutes of middle cerebral artery occlusion in mice and found improved functional outcomes based on focal neurological deficit scales and reductions in the volume of the cerebral infarcts.

Although a systematic review and meta-analysis of these and other studies (Liang et al., 2022) suggests xenon protects against various forms of neurological injury in animal models, these data cannot be extrapolated to the situation faced by climbers at high altitude. Not only have these protective effects not been demonstrated in humans, but the model of brain injury in these studies is also far different than the issue faced by climbers at high altitude. Most of the models in these studies involve either direct injury to neuronal tissue or complete cessation of blood flow, where there is a risk of ischemia-reperfusion injury. Climbers, on the other hand, experience significant degrees of hypoxemia but preserve brain oxygen delivery to some extent due to increases in both CBF (Ainslie and Subudhi, 2014) and increases in hemoglobin concentration and oxygen-carrying capacity. There are no data to suggest xenon protects against injury in humans in this situation, which is far different than the tissue ischemia and cellular injury seen in the animal models noted above.

#### **Risks of Xenon Use**

In addition to examining the potential benefits of xenon inhalation, it is also important to consider the risks of such an intervention. The most important of these is the fact that, as noted above, xenon acts as a general anesthetic when given at certain inhaled concentrations and must be given in a monitored setting by a trained anesthetist. Such an approach was used for the climbers who used xenon prior to their Everest climb this past spring. Concern persists, however, that in light of the extensive coverage of the xenon inhalation protocol in the lay press and on social media, non-medically trained individuals might try to obtain xenon and administer it to themselves or others in an unmonitored setting and be predisposed to respiratory depression, loss of consciousness, and even respiratory arrest.

Information about other risks can be gleaned from some of the few human studies to investigate the acute physiological responses to inhalation of xenon at inspired concentrations of 30–70% (Holl et al., 1987a; Holl et al., 1987b; Lawley et al., 2019; Yagi et al., 1995; Yonas et al., 1981). Low, sub-

anesthetic doses increase mean arterial pressure via increases in total peripheral resistance, while higher concentrations (FiXe 0.5–0.7) induce tachycardia and mild hypertension (Lawley et al., 2019). Xenon-induced hypertension seems not to be mediated by the sympathetic nervous system, as muscle sympathetic nerve activity is unchanged in healthy adults breathing 70% xenon (Neukirchen et al., 2012), but rather by inhibition of norepinephrine clearance or reuptake. Although xenon was tolerated in these studies (Holl et al., 1987a; Holl et al., 1987b; Lawley et al., 2019; Yagi et al., 1995), and participants' cardiorespiratory parameters returned to pre-xenon levels within 1-4 hours (Lawley et al., 2019; Yonas et al., 1981), all tested xenon doses caused prolonged drowsiness, a sense of euphoria, hypnosis, anxiety, dysesthesias, and sedation in all participants (Dias et al., 2019; Lawley et al., 2019; Yagi et al., 1995; Yonas et al., 1981). Importantly, dysesthesia was typically observed prior to a 5-second period of complete unresponsiveness (Yonas et al., 1981). At higher doses (FiXe 0.5-0.7), Lawley et al. (2019) also described a subconsciously restless and agitated state in a number of participants during xenon inhalation. Whether these acute physiological and perceptional changes induced by xenon are exacerbated by chronic inhalation is unclear. In the lone study to assess the effects of chronic xenon inhalation (12 sessions, 3 sessions/week, 2 minutes breathing FiXe 0.7), there was a relatively high incidence (15%) of adverse events, including symptoms resembling sleep paralysis and severe nausea (Dias et al., 2019).

## Other Aspects of Preparation for Rapid Everest Expeditions

Xenon inhalation was the aspect of expedition preparation that garnered the most attention with the 2025 Mount Everest expedition, but the climbers engaged in several other practices as part of the preparation for and conduct of the expedition—preacclimatization with hypoxic training systems in the weeks before the expedition and use of high oxygen flow rates while climbing the mountain—that were likely the key factors in the success of their expedition. The specific protocol for trip preparation and oxygen use on the mountain has not been made public, but information can be gleaned from the guiding company's website (Adventures) as well as reports and interviews in the lay press and on social media (Carns and Stazicker, 2025; Wolfe and Sharma, 2025).

# Hypoxic training systems

The climbers who used xenon prior to their 2025 Everest expedition spent 6–8 weeks sleeping in hypoxic tents with increasing doses of hypoxia up to a simulated altitude of 6,000–7,000 m. Two studies have examined the effects of such tents on acclimatization and suggest that this intervention likely results in some degree of acclimatization to high altitude. Fulco et al. (2011) randomized healthy, unacclimatized sea level residents to sleep in either normobaric hypoxia or "sham" hypoxia for seven nights and found that individuals who slept in hypoxic conditions—which steadily increased from the equivalent of 2,200 m at the start of the week to 3,100 m by the end of the week—had higher nocturnal oxygen saturation and lower AMS scores upon awakening each day at 4,300 m. In the other placebo-controlled double-blind study, Dehnert et al. (2014) randomized healthy

individuals to sleep in tents under either normoxia or hypoxia (>2,200 m, average 2,600 m) and found that the group that slept in hypoxic conditions for 14 days had lower AMS scores and a lower AMS incidence during the subsequent 20-hour exposure to the equivalent of 4,500 m. Given that benefit was seen with relatively short (1 to 2 week) exposures to lower simulated altitudes than experienced during an Everest climb, it is reasonable to expect that more weeks of exposure to greater degrees of hypoxia, as done by the climbers, should provide acclimatization to elevations approaching those of Everest Base Camp.

There is also some physiological rationale for combining the sleep protocols with hypoxic exercise training leading up to the climb. Breathing a reduced oxygen fraction during exercise causes a greater degree of hypoxemia (Sutton et al., 1988) and, thus, represents a stronger hypoxic stimulus. An example of such a training protocol is the one published by the current holder of the fastest time to summit Everest, in which up to 40% of his training volume was performed in hypoxic conditions simulating moderate-to-high altitude (Millet and Jornet, 2019). The literature on the benefits of this training approach for climbs at the extremes of elevation is, however, scarce. In a study by Brocherie et al. (2018), repeated maximal-intensity, short-duration hypoxic exercise elicited specific peripheral adaptations that were not observed with passive hypoxic exposure alone. Therefore, the combination of sleep in hypoxia and high-intensity hypoxic exercise may promote specific muscle adaptations that are not observed with sleep or exercise in hypoxia alone.

Beyond these data, additional indirect evidence in support of these systems is the fact that their use in preparation for climbing at extremely high altitude appears to have increased in recent years, as evidenced by reports in both the medical (Millet and Jornet, 2019; Tannheimer and Lechner, 2020) and lay literature (Bogage, 2019; Harrington, 2016). In fact, some guiding companies that lead expeditions to Mount Everest and other very high peaks recommend or require the use of these systems and have shortened the duration of expeditions to these mountains as a result of this practice. The company that led the xenon expedition, for example, incorporates 6–8 weeks of hypoxic tent use into their rapid or "Flash<sup>TM</sup>" Everest expeditions that are only 3 weeks in duration (Adventures). While such evolution in practice is certainly not proof of benefit, the fact that companies with

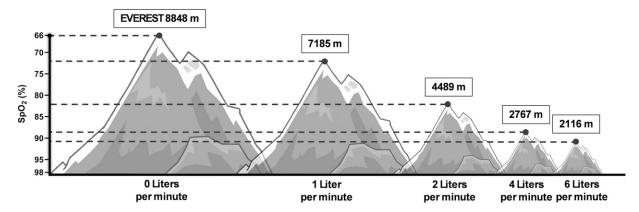
strong commercial interests in getting their clients to their intended summits have adopted the use of such systems and not reverted to prior practices provides some indirect evidence that hypoxic training systems yield benefit for climbers traveling at these extremes of high elevation.

#### Supplemental oxygen use

Another important intervention for the climbers who used xenon for their 2025 Everest expedition was their approach to the use of supplemental oxygen. Since the first documented attempt to summit Mount Everest in 1921, climbers have mitigated the extreme stress of climbing at very high elevations with supplemental oxygen. This practice is known to increase the odds of summit success and reduce the risk of acute altitude illness, frostbite, and hypothermia (Arnette, 2025; Kari and Huey, 2000). In fact, only a very few climbers (2.0% of all ascents) have succeeded in reaching the summit without this intervention, according to the Himalayan Database (2004).

The approach to supplemental oxygen on the xenon-assisted expedition differed from the typical approach used by most Western guiding agencies on Mount Everest in an important respect. Whereas western guiding agencies typically have their clients start using oxygen as they move from Camp II (6,494 m) to Camp III (6,800 m) and increase the flow rate as they climb higher (Madison G, personal communication), the climbers who used xenon on their 2025 expedition appear to have started supplemental oxygen on their way from Everest Base Camp (5,364 m) to Camp 1 (6,065 m) (Carns and Stazicker, 2025) and also used oxygen more or less continuously through the day and night.

The strong effects of supplemental oxygen administration can be appreciated by examining unpublished data from a study in which the investigators studied the effects of various flow rates of supplemental oxygen delivered via a typical mask system used on Mount Everest on the effective altitude experienced by the body at both rest and with varying levels of activity (Fig. 1) (Wakeham et al., 2023). There is a clear dose relationship between the flow rate of oxygen and the effective altitude experienced by climbers. For individuals at rest at the equivalent of the summit of Mount Everest (8,849 m), 2 l/min of oxygen lowered the effective altitude to 4,489 m, while breathing 6 l/min of oxygen brought the individual down to 2,116 m. In a second part of the study, they



**FIG. 1.** Equivalent "mask altitude" across various flow rates of supplemental oxygen during rest at 8,848 m (barometric pressure = 253 mmHg) (Wakeham et al., 2023). Mask altitude was calculated from peripheral oxygen saturation and barometric pressure using data from Operation Everest II (Sutton et al., 1988).

had subjects perform different levels of work at a slightly lower elevation and showed that oxygen's effect was somewhat diminished but was still significant. At 60 W of power output at the equivalent of 8,100 m, 1 l/min of oxygen flow rate had no effect on the effective altitude, 2 l/min lowered the effective altitude to 6,442 m, while 6 l/min lowered it to the equivalent of 2,545 m. Thus, it can be seen that application of sufficient flow rates while climbing significantly reduces the effective altitude and degree of hypoxemia experienced by climbers, thus mitigating the risks of climbing at the extremes of elevation and reducing the time necessary to acclimatize to severe hypoxia.

The specific flow rates used by the climbers are not entirely clear from publicly available information, but there is some information to suggest that they were using high enough flows to achieve the significant effects seen in the study cited above. While the lead guide indicated in one media report that they used 1 to 2 l/min for most of the climb before using higher flows above 7,900 m (Simicevic, 2025), the climbers have indicated that they adjusted their flow rates on an ongoing basis to maintain their  $S_pO_2 > 80\%$  (Carns and Stazicker, 2025). Information available on the company's website and other sources indicates that climbers on their company's Flash<sup>TM</sup> Everest expeditions are equipped with regulators that allow a flow of up to 8 l/min and travel with two Sherpas per climber, which allows them to maintain a supply of oxygen sufficient to support such high flow rates (Adventures; Schobersberger, 2019). Given that these Flash<sup>TM</sup> expeditions are longer in duration than the xenon-assisted expedition (21 vs. 7 days), it is highly likely that they employed similar oxygen protocols on the much shorter xenon expedition. The data cited above (Wakeham et al., 2023) strongly suggest that it is this oxygen support, rather than xenon, that was the critical factor in ensuring a successful climb.

## Conclusions

The use of xenon by four climbers ahead of their 2025 Everest expedition has garnered significant attention, as evidenced by the volume of articles in the lay press and discussion on social media before and after the expedition. This attention, however, stands in stark contrast to the lack of evidence supporting its role in aiding these climbers' ascents of Mount Everest. Aside from the fact that xenon inhalation increases serum EPO concentrations, there is no evidence that it enhances acclimatization or exercise capacity, prevents AMS, HACE, or HAPE, or interacts with the pathophysiology of those diseases in a clear and meaningful way, or protects against hypoxic injury in humans. There is also enough evidence to suggest that other practices on the part of the climbers—sleeping in hypoxic tents prior to the expedition and supplemental oxygen at high flows starting at a relatively low elevation during the expedition—likely played the critical roles in ensuring their successful ascent in a very short period of time rather than the xenon inhalation per se.

When these issues are viewed along with the expense of the intervention and the risks associated with xenon use outside of highly monitored settings, there is no basis for widespread adoption of the practice at this time, a conclusion supported by several other recent publications on this issue (Burtscher, 2025; Hilty et al., 2025). The experiences of the lead guide for this company in 2024 and the four climbers in 2025 are certainly intriguing, but are simply anecdotes rather

than evidence of benefit. Their experience demonstrates that xenon administration is feasible and safe when administered in a highly monitored setting by trained individuals, but further research should be conducted into the safety and efficacy of this intervention before xenon is used to support climbing at the extremes of elevation.

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#### References

Ainslie PN, Subudhi AW. Cerebral blood flow at high altitude. High Alt Med Biol 2014;15(2):133–140.

Al Tmimi L, Van Hemelrijck J, Van de Velde M, et al. Xenon anaesthesia for patients undergoing off-pump coronary artery bypass graft surgery: A prospective randomized controlled pilot trial. Br J Anaesth 2015;115(4):550–559.

Arnette A. Everest by the Numbers: 2025 Edition; Everest Publishers; 2025.

Bailey DM, Bartsch P, Knauth M, et al. Emerging concepts in acute mountain sickness and high-altitude cerebral edema: From the molecular to the morphological. Cell Mol Life Sci 2009;66(22):3583–3594.

Bantel C, Maze M, Trapp S. Noble gas xenon is a novel adenosine triphosphate-sensitive potassium channel opener. Anesthesiology 2010;112(3):623–630.

Baumert JH, Hecker KE, Hein M, et al. Effects of xenon anaesthesia on the circulatory response to hypoventilation. Br J Anaesth 2005;95(2):166–171.

Berger MM, Schiefer LM, Treff G, et al. Acute high-altitude illness: Updated principles of pathophysiology, prevention, and treatment. Dtsch Z Sportmed 2020;71(11–12):267–274.

Bogage J. (2019). A Mount Everest climb often takes two months. A California climber just did it in two weeks. In The Washington Post.

Breuer T, Emontzpohl C, Coburn M, et al. Xenon triggers proinflammatory effects and suppresses the anti-inflammatory response compared to sevoflurane in patients undergoing cardiac surgery. Crit Care 2015;19:365.

Brocherie F, Millet GP, D'Hulst G, et al. Repeated maximalintensity hypoxic exercise superimposed to hypoxic residence boosts skeletal muscle transcriptional responses in elite teamsport athletes. Acta Physiol (Oxf) 2018;222.

Burtscher M. Xenon - Propelling climbers to the summits of the world's highest mountains? N Engl J Med 2025;393:615–616.

Carns A, Stazicker A. Two Special Forces Legends in Death Zone: Alistair Carns & Staz. Woodall D, ed., YouTube; 2025.

Coburn M, Baumert JH, Roertgen D, et al. Emergence and early cognitive function in the elderly after xenon or desflurane anaesthesia: A double-blinded randomized controlled trial. Br J Anaesth 2007;98:756–762.

Cullen SC, Eger EI, 2nd, Cullen BF, et al. Observations on the anesthetic effect of the combination of xenon and halothane. Anesthesiology 1969;31:305–309.

Cullen SC, Gross EG. The anesthetic properties of xenon in animals and human beings, with additional observations on krypton. Science (1979) 1951;113:580–582.

- de Sousa SL, Dickinson R, Lieb WR, et al. Contrasting synaptic actions of the inhalational general anesthetics isoflurane and xenon. Anesthesiology 2000;92:1055–1066.
- Dehnert C, Berger MM, Mairbaurl H, et al. High altitude pulmonary edema: A pressure-induced leak. Respir Physiol Neurobiol 2007;158:266–273.
- Dehnert C, Bohm A, Grigoriev I, et al. Sleeping in moderate hypoxia at home for prevention of acute mountain sickness (AMS): A placebo-controlled, randomized double-blind study. Wilderness Environ Med 2014;25:263–271.
- Dias KA, Lawley JS, Gatterer H, et al. Effect of acute and chronic xenon inhalation on erythropoietin, hematological parameters, and athletic performance. J Appl Physiol (1985) 2019;127:1503–1510.
- Fink H, Blobner M, Bogdanski R, et al. Effects of xenon on cerebral blood flow and autoregulation: An experimental study in pigs. Br J Anaesth 2000;84:221–225.
- Francis RC, Hohne C, Klein A, et al. Endothelin-a receptor blockade does not debilitate the cardiovascular and hormonal adaptation to xenon or isoflurane anesthesia in dogs. Exp Biol Med (Maywood) 2006;231:834–839.
- Francis RC, Reyle-Hahn MS, Hohne C, et al. The haemodynamic and catecholamine response to xenon/remifentanil anaesthesia in Beagle dogs. Lab Anim 2008;42:338–349.
- Fries M, Nolte KW, Coburn M, et al. Xenon reduces neurohistopathological damage and improves the early neurological deficit after cardiac arrest in pigs. Crit Care Med 2008;36(8): 2420–2426.
- Frietsch T, Bogdanski R, Blobner M, et al. Effects of xenon on cerebral blood flow and cerebral glucose utilization in rats. Anesthesiology 2001;94(2):290–297.
- Fulco CS, Muza SR, Beidleman BA, et al. Effect of repeated normobaric hypoxia exposures during sleep on acute mountain sickness, exercise performance, and sleep during exposure to terrestrial altitude. Am J Physiol Regul Integr Comp Physiol 2011;300(2):R428–R436.
- Goetzenich A, Hatam N, Preuss S, et al. The role of hypoxiainducible factor-1alpha and vascular endothelial growth factor in late-phase preconditioning with xenon, isoflurane and levosimendan in rat cardiomyocytes. Interact Cardiovasc Thorac Surg 2014;18(3):321–328.
- Gruss M, Bushell TJ, Bright DP, et al. Two-pore-domain K+ channels are a novel target for the anesthetic gases xenon, nitrous oxide, and cyclopropane. Mol Pharmacol 2004;65(2):443–452.
- Gur D, Yonas H, Jackson DL, et al. Measurement of cerebral blood flow during xenon inhalation as measured by the microspheres method. Stroke 1985;16(5):871–874.
- Harrington E. Emily Harrington on her rapid ascent of Cho Oyu. UKClimbing 2016.
- Hartmann A, Dettmers C, Schuier FJ, et al. Effect of stable xenon on regional cerebral blood flow and the electroence-phalogram in normal volunteers. Stroke 1991;22(2):182–189.
- Hein M, Baumert JH, Roehl AB, et al. Xenon alters right ventricular function. Acta Anaesthesiol Scand 2008;52(8):1056–1063.
- Hilty MP, Hefti U, Bouzat P, et al. Xenon inhalation for expeditions to high altitude: A position statement from the international climbing and mountaineering federation (Union Internationale des Associations d'Alpinisme, UIAA) medical commission. High Alt Med Biol 2025.
- Himalayan Database. The Expedition Archives of Elizabeth Hawley. Club TAA., ed. Adventures F. Everest South Flash; 2004.
- Holl K, Nemati N, Kohmura E, et al. Stable-xenon-CT: Effects of xenon inhalation on EEG and cardio-respiratory parameters in the human. Acta Neurochir (Wien) 1987a;87(3–4):129–133.

- Holl K, Samii M, Gaab MR, et al. EEG changes during five minutes of inhalation of a 33% xenon-O2 mixture. Neurosurg Rev 1987b;10(4):309–310.
- Jin Z, Piazza O, Ma D, et al. Xenon anesthesia and beyond: Pros and cons. Minerva Anestesiol 2019:85(1):83–89.
- Kari JS, Huey RB. Size and seasonal temperature in free-ranging Drosophila subobscura. J Therm Biol 2000;25(4):267–272.
- Laitio RM, Kaisti KK, Laangsjo JW, et al. Effects of xenon anesthesia on cerebral blood flow in humans: A positron emission tomography study. Anesthesiology 2007;106(6):1128–1133.
- Law LS, Lo EA, Gan TJ. Xenon anesthesia: A systematic review and meta-analysis of randomized controlled trials. Anesth Analg 2016;122(3):678–697.
- Lawley JS, Gatterer H, Dias KA, et al. Safety, hemodynamic effects, and detection of acute xenon inhalation: Rationale for banning xenon from sport. J Appl Physiol (1985) 2019; 127(6):1511–1518.
- Liang M, Ahmad F, Dickinson R. Neuroprotection by the noble gases argon and xenon as treatments for acquired brain injury: A preclinical systematic review and meta-analysis. Br J Anaesth 2022;129(2):200–218.
- Limatola V, Ward P, Cattano D, et al. Xenon preconditioning confers neuroprotection regardless of gender in a mouse model of transient middle cerebral artery occlusion. Neuroscience 2010;165(3):874–881.
- Lo EA, Law LS, Gan TJ. Paradox of the incidence of postoperative nausea and vomiting after xenon-based anaesthesia. Br J Anaesth 2016;116(6):881–883.
- Luks AM, Ainslie PN, Lawley JS, et al. Acute mountain sickness. In Ward, Milledge and West's High Altitude Medicine and Physiology. Taylor & Franciss Group: Boca Raton, FL; 2021a.
- Luks AM, Ainslie PN, Lawley JS, et al. High altitude cerebral edema. In Ward, Milledge and West's High Altitude Medicine and Physiology. Taylor & Franciss Group: Boca Raton, FL; 2021b.
- Luks AM. Physiology in medicine: A physiologic approach to prevention and treatment of acute high altitude illnesses. J Appl Physiol (1985) 2015;118(5):509–519.
- Lundby C, Robach P, Boushel R, et al. Does recombinant human Epo increase exercise capacity by means other than augmenting oxygen transport? J Appl Physiol (1985) 2008; 105(2):581–587.
- Luttropp HH, Romner B, Perhag L, et al. Left ventricular performance and cerebral haemodynamics during xenon anaesthesia. A transoesophageal echocardiography and transcranial Doppler sonography study. Anaesthesia 1993;48(12):1045–1049.
- Ma D, Lim T, Xu J, et al. Xenon preconditioning protects against renal ischemic-reperfusion injury via HIF-1alpha activation. J Am Soc Nephrol 2009;20(4):713–720.
- Manferdelli G, Marzorati M, Easton C, et al. Changes in prefrontal cerebral oxygenation and microvascular blood volume in hypoxia and possible association with acute mountain sickness. Exp Physiol 2021;106(1):76–85.
- Maze M, Laitio T. Neuroprotective properties of xenon. Mol Neurobiol 2020;57(1):118–124.
- McGuigan S, Marie DJ, O'Bryan LJ, et al. The cellular mechanisms associated with the anesthetic and neuroprotective properties of xenon: A systematic review of the preclinical literature. Front Neurosci 2023;17:1225191.
- Millet GP, Jornet K. On top to the top-acclimatization strategy for the "fastest known time" to Mount Everest. Int J Sports Physiol Perform 2019;14:1438–1441.
- Nair AS, Christopher A, Pulipaka SK, et al. Efficacy of xenon anesthesia in preventing postoperative cognitive dysfunction

after cardiac and major non-cardiac surgeries in elderly patients: A topical review. Med Gas Res 2021;11(3):110–113.

- Neukirchen M, Hipp J, Schaefer MS, et al. Cardiovascular stability and unchanged muscle sympathetic activity during xenon anaesthesia: Role of norepinephrine uptake inhibition. Br J Anaesth 2012;109(6):887–896.
- Pagliaro P, Weber NC, Femmino S, et al. Gasotransmitters and noble gases in cardioprotection: Unraveling molecular pathways for future therapeutic strategies. Basic Res Cardiol 2024;119(4):509–544.
- Pain CF, Glazier JB, Simon H, et al. Regional and overall inequality of ventilation and blood flow in patients with chronic airflow obstruction. Thorax 1967;22(5):453–461.
- Plougmann J, Astrup J, Pedersen J, et al. Effect of stable xenon inhalation on intracranial pressure during measurement of cerebral blood flow in head injury. J Neurosurg 1994;81(6):822–828.
- Ramsay W, Travers MW. On a new constituent of atmospheric air. Proc. R. Soc. Lond 1898;63:405–408.
- Sartori C, Allemann Y, Scherrer U. Pathogenesis of pulmonary edema: Learning from high-altitude pulmonary edema. Respir Physiol Neurobiol 2007;159(3):338–349.
- Schaefer MS, Piper T, Geyer H, et al. Xenon elimination kinetics following brief exposure. Drug Test Anal 2017;9(5):666–670.
- Schaefer W, Meyer PT, Rossaint R, et al. Myocardial blood flow during general anesthesia with xenon in humans: A positron emission tomography study. Anesthesiology 2011; 114(6):1373–1379.
- Schobersberger B. Flash der neue Expeditionsstil mit Zukunft? Die praxisorientierte Seite. In Alpinmedizinischer. Rundbrief; 2019. pp. 16–21.
- Simicevic V. When Climbing the World's Tallest Mountains. What Counts as Cheating? In National Geographic 2025.
- Stoppe C, Ney J, Brenke M, et al. Sub-anesthetic xenon increases erythropoietin levels in humans: A randomized controlled trial. Sports Med 2016;46(11):1753–1766.
- Stoppe C, Ney J, Brenke M, et al. Correction to: Sub-anesthetic xenon increases erythropoietin levels in humans: A randomized controlled trial. Sports Med 2018;48(3):751.
- Sutton JR, Reeves JT, Wagner PD, et al. Operation Everest II: Oxygen transport during exercise at extreme simulated altitude. J Appl Physiol (1985) 1988;64(4):1309–1321.
- Swenson ER, Bartsch P. High-altitude pulmonary edema. Compr Physiol 2012;2(4):2753–2773.
- Tannheimer M, Lechner R. Rapid ascents of Mt Everest: Normobaric hypoxic preacclimatization. J Travel Med 2020; 27(6):taaa099.
- Tassel C, Le Dare B, Morel I, et al. [Xenon: From rare gaz to doping product]. Presse Med 2016;45(4 Pt 1):422–430.
- Thomsen JJ, Rentsch RL, Robach P, et al. Prolonged administration of recombinant human erythropoietin increases submaximal performance more than maximal aerobic capacity. Eur J Appl Physiol 2007;101(4):481–486.
- Tissot van Patot MC, Leadbetter G, Keyes LE, et al. Greater free plasma VEGF and lower soluble VEGF receptor-1 in acute mountain sickness. J Appl Physiol (1985) 2005;98(5): 1626–1629.
- Van Hese L, Al Tmimi L, Devroe S, et al. Neuroprotective properties of xenon in different types of CNS injury. Br J Anaesth 2018;121(6):1365–1368.
- Wakeham DJ, Tomlinson AR, Hackett PH, et al. The effects of stepwise reductions in supplemental oxygen on oxygen saturation

at rest and during exercise at extreme (simulated) altitude. In International Hypoxia Symposia. Wiley: Lake Louise, Alberta. Canada; 2023.

- Wappler F, Rossaint R, Baumert J, et al.; Xenon Multicenter Study Research G. Multicenter randomized comparison of xenon and isoflurane on left ventricular function in patients undergoing elective surgery. Anesthesiology 2007;106(3):463–471.
- Wilson MH, Edsell ME, Davagnanam I, et al.; Caudwell Xtreme Everest Research Group. Cerebral artery dilatation maintains cerebral oxygenation at extreme altitude and in acute hypoxia—an ultrasound and MRI study. J Cereb Blood Flow Metab 2011;31(10):2019–2029.
- Wolfe J, Sharma B. Up Everest in a Flash, Assisted by Xenon Gas. In The New York Times. The New York Times Company: New York; 2025. p. 26.
- Yagi M, Mashimo T, Kawaguchi T, et al. Analgesic and hypnotic effects of subanaesthetic concentrations of xenon in human volunteers: Comparison with nitrous oxide. Br J Anaesth 1995;74: 670–673.
- Yang SR, Hua KF, Chu LJ, et al. Xenon blunts NF-kappaB/NLRP3 inflammasome activation and improves acute onset of accelerated and severe lupus nephritis in mice. Kidney Int 2020;98(2):378–390.
- Yao L, Nemoto EM, Boston JR, et al. Effect of 80% Xe on whole brain blood flow and metabolism in awake monkeys. J Neurosurg Anesthesiol 1992a;4(4):268–271.
- Yao LP, Bandres J, Nemoto EM, et al. Effect of 33% xenon inhalation on whole-brain blood flow and metabolism in awake and fentanyl-anesthetized monkeys. Stroke 1992b;23(1):69–74.
- Yonas H, Grundy B, Gur D, et al. Side effects of xenon inhalation. J Comput Assist Tomogr 1981;5(4):591–592.
- Yonas H, Gur D, Good BC, et al. Stable xenon CT blood flow mapping for evaluation of patients with extracranial-intracranial bypass surgery. J Neurosurg 1985;62(3):324–333.
- Zardini P, West JB. Topographical distribution of ventilation in isolated lung. J Appl Physiol 1966;21(3):794–802.
- Zhang M, Cheng Y, Zhai Y, et al. Attenuated iron stress and oxidative stress may participate in anti-seizure and neuroprotective roles of xenon in pentylenetetrazole-induced epileptogenesis. Front Cell Neurosci 2022;16:1007458.
- Zhao H, Huang H, Ologunde R, et al. Xenon treatment protects against remote lung injury after kidney transplantation in rats. Anesthesiology 2015;122(6):1312–1326.
- Zhao H, Luo X, Zhou Z, et al. Early treatment with xenon protects against the cold ischemia associated with chronic allograft nephropathy in rats. Kidney Int 2014;85(1):112–123.

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