Breathing at extreme altitudes. Scientific projects "EVEREST" (First part)

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Summary

Climbing to the highest height on Earth, the Mt. Everest (8.848 m), without supplementary oxygen equipment involves a physiological demand that is close to the maximum human tolerance. Exposures at extreme altitudes drastically conditions lung function, stores of oxygen and physical performance. This review brings interesting aspects about respiration, blood gases and aerobic exercise reported by those scientific projects that have carried out physiological measurements between 8,000 m and 8,848 m above sea level, under real or simulated altitude: the Operations "Everest I" (1946), "Everest II" (1985), "Everest III-COMEX" (1997), and the Expeditions "AMREE" (1981), "British 40th Anniversary Everest" (1993), and "Caudwell Xtrem Everest" (2007). These fascinating scientific research events, along with other outstanding biomedical expeditions performed above 5,500 m, like especially the "Silver Hut" (1960-61), "Italiana all'Everest" (1973), and "British Everest Medical" (1994), including those pioneer scientific reports made on the XIX century until the most recent research projects performed, have laid the foundations and knowledge on the human tolerance to such extreme levels of hypobaric hypoxia, where the lung, breathing and respiratory chain takes on a major role requiring fine physiological adjustments to ensure cellular oxygenation. Geophysical aspects, climatic factors and other environmental conditions that limit the biological viability and can affect the respiratory health of climbers on the upper troposphere zone at the subtropical latitude where that mountain is located are likewise reviewed and analyzed. Every year, hundreds of climbers try to reach the top of Mt. Everest, but only a few of them achieved their goal without inhaling supplemental oxygen, including some exceptionally gifted Sherpa natives, protagonist on unsuspected exploits in the highest mountain on terrestrial surface, whose summit touch the physiological limit of survival for the human being.

Key words:
Altitude. Oxygen uptake. Hypoxia. Mountaineering. Atmospheric pressure. Respiration.

Respirar en altitudes extremas. Proyectos científicos "EVEREST" (Primera parte)

Resumen

Escalar el punto más alto de la Tierra, el Mt. Everest (8.848 m), sin equipos de oxígeno conlleva una demanda fisiológica que está próxima a la máxima capacidad de tolerancia humana. Exponerse a altitudes extremas condiciona drásticamente la función pulmonar, el nivel de oxígeno y el rendimiento físico. Esta revisión reúne interesantes aspectos respiratorios, de gases sanguíneos y ejercicio aeróbico aportados por aquellos proyectos científicos que han llevado a cabo mediciones fisiológicas entre 8.000 m y 8.848 m, en altitud real o simulada, como las Operaciones "Everest I" (1946), "Everest II" (1985) y "Everest III-COMEX" (1997), y las Expediciones "AMREE" (1981), "British 40th Anniversary Everest" (1993) y "Caudwell Xtrem Everest" (2007). Estos fascinantes eventos de investigación, junto a otros destacados proyectos biomédicos realizados a más de 5.500 m, muy especialmente las Expediciones "Silver Hut" (1960-61), "Italiana all'Everest" (1973) y "British Everest Medical" (1994), incluyendo aquellas pioneras observaciones científicas llevadas a cabo en el s.XIX hasta los más recientes proyectos de investigación realizados, han sentado las bases del conocimiento sobre la tolerancia humana ante niveles de hipoxia hipobárica extrema, donde el pulmón y la cadena respiratoria adquieren un trascendente protagonismo requiriéndose de finos ajustes fisiológicos que garanticen la oxigenación celular. Asimismo, se exponen ciertos aspectos geofísicos, factores climáticos y otros condicionantes ambientales que limitan la viabilidad biológica y pueden afectar la salud respiratoria de los alpinistas situados en las cotas superiores de la troposfera a la latitud subtropical donde se encuentra ubicada dicha montaña. Actualmente cientos de alpinistas intentan alcanzar la cumbre del Mt. Everest todos los años, pero solo algunos consiguen su objetivo sin inhalar oxígeno suplementario, entre ellos algunos excepcionalmente dotados nativos Sherpa, protagonistas de insospechadas hazañas en la montaña más elevada de la superficie terrestre, cuya cima roza el límite fisiológico de supervivencia para el ser humano.

Palabras clave:
Altitud. Consumo de oxígeno. Hipoxia. Montañismo. Presión atmosférica. Respiración.

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Introduction

Since the summit of Mount Everest (8,848 m) was first reached in 1953 by Edmund Hillary and Tenzing Norgay, its summit has been climbed almost nine thousand times. Both pioneers used oxygen equipment, as climbing the summit with the provision of 3-4 L•min^{-1} of this gas[1] was equivalent to having an oxygen concentration in the body similar to that registered at an altitude 3,000 m lower[2]. The miraculous increase of physical capacity provided by inhaling the contents of the gas cylinders led the native Sherpas to call it "English air" [3]. It was not until 1978 when Reinhold Messner and Peter Habeler conquered the mountain without oxygen equipment, just over half a century after Edward Norton managed to scale 8,570 m in the same way in 1924[4]. This fact proves that the difficulty of ascending the final 300 m of the Everest pyramid is due to environmental factors rather than technical ones. Today, mountaineers that attack the final stretch of this mountain usually inhale 2-3 L•min^{-1} of supplementary oxygen[5], but over the history of this mountain less than 5% of climbs have been performed breathing environmental air alone. Trying to climb this way, even with previous altitude acclimatisation, entails a three-fold risk of death: Previous data indicates that 8.3% of mountaineers that reach the summit without using oxygen cylinders die, compared to the 3% of climbers that die whilst using them[6]. In general, the greatest probability of successfully climb Mt Everest and surviving is registered among mountaineers aged between 30-35 years[7]. Having previous experience in climbing at extreme altitude does not seem to reduce mortality rates on this mountain[8]. A third of fatal accidents are associated with hypoxia and low temperatures, generally occurring during the descent, and are attributed to serious traumatisms due to falls, probably furthered by brain swelling which induces neurocognitive dysfunctions, as well as fainting due to extreme fatigue[9,10]. It is worth highlighting that rapid exposure to such extreme heights without previous acclimatisation would cause a severe deterioration of the central nervous system, with the resulting loss of consciousness in less than 2-3 minutes[11].

The lungs are one of the most affected organs at high altitude. Breathing and pulmonary circulation take on a decisive role in adapting to hypoxia, as they must ensure cell oxygen demands are met, and during physical exercise one of the most critical physiological states is reached. Likewise, the respiratory channel is directly exposed to the other harmful environmental altitude factors, such as low temperatures and relative humidity or the presence of ozone. Knowledge available to us today regarding human exposure to height between 8,000 m and 8,848 m has been provided by numerous scientific publications, essentially produced by the following ambitious research projects carried out in hypobaric chambers: the US 1946 *"Operation Everest I"* and the 1985 *"Operation Everest II"*; the French *"Operation Everest III-COMEX"* in 1997; as well as the following scientific expeditions on Mt Everest: *"American Medical Research Expedition to Everest"* in 1981, the *"British 40th Anniversary Everest Expedition"* in 1993, and the British *"Caudwell Xtrem Everest"* in 2007[12-17]. Despite not having reached the same altitudes, particularly outstanding are the North American scientific expedition *"Silver Hut"* from 1960-1961, the *"Spedizione Italiana all'Everest"* of 1973, and the *"British Everest Medical Expedition"* of 1994[18-20]. Mention should also be made of more recent projects, such as the 1998-1999 North American *"Everest Extreme Expedition"*, the 2006 German "*Everest MedEx"*, and the 2013 British *"Xtreme Everest 2"* [21-23]. Finally, other noteworthy trials include the one performed in England in 1954 in a decompression chamber, simulating extreme altitudes[24], as well as two pioneering experiments carried out at the end of the 19th century, also in a hypobaric chamber, achieving depressurisation levels similar or greater to those felt at the summit of Mount Everest: in Italy in 1898 and in France in 1874[25,26], with the latter trial later called *"Operation Everest 0"* [27]. Similarly, in the first half of the 20th century, two pioneering British alpine expeditions are also noteworthy, carried out on Everest in 1933 and 1938, respectively; despite their main objective not being specifically scientific, parameters were obtained and biomedical samples were taken at extreme altitudes[28,29]. Table 1 details some aspects of all of these biomedical projects and alpine-scientific expeditions.

The main objective of this review article is to bring together and display essential aspects related to respiratory function, the transport of oxygen and/or maximum aerobic power that have been reported in these scientific projects. It is also an opportunity to display and analyse some geo-physical, climatic and meteorological aspects that could interfere in the human capacity to reach the summit of Mt. Everest without an oxygen supplement. To do this, an exhaustive search was performed on the PubMed database, with the main search strategy being the following combination: *"Respirat*[TW] OR Everest[TW] NOT mitral AND aerob*"*. In addition, the most important recent editions of international Mountain Medicine books and documents to date were reviewed. Furthermore, certain logistical and technical data from some of the alpine expeditions was obtained from official Internet websites published exclusively by the organisers of the respective events.

Barometric pressure, respiratory and blood gases at the summit of Mount Everest

The final pyramid that forms the great geological mass of Everest is located in the so-called "death zone" [30]. At its summit the barometric pressure (BP) is very low, which entails a severely reduced (~43 mmHg)[31,32] inspired oxygen pressure (PiO_2), but even so, it is possible to climb it without oxygen equipment. This is particularly true during the warm season, as the BP at the summit is higher (~251-255 mmHg)[33,34]. Pulmonary respiration must be able to ensure the mitochondrial cell respiratory chain, but at 8,848 m of altitude, the oxygen partial pressure of arterial blood (PaO_2) is just 27-31 mmHg[13,14,31,32,35], and average PaO_2 values of below 25 mmHg have even been registered upon descending from the summit[36]. However, the low alveolar partial pressure of carbon dioxide ($PACO_2$), due to pulmonary hyperventilation, helps keep the alveolar partial pressure of oxygen (PAO_2) stable at heights over ~7.000 m[32].

Table 1. Main biomedical scientific projects performed on humans, and mountaineering expeditions in which lung function and/or respiratory gas samples, blood gases and/or ergospirometry samples have been taken at altitudes exceeding 5,300 m in the area of Mount Everest, as well as using hypobaric chambers or hypoxic mixes that have simulated very extreme altitudes similar to those of this mountain (8,848 m).

Biomedical project or expedition	Year	Country	Scientific director	Max. altitude reached (m)	Max. altitude (m)* samples/parameters
Operation Everest 0 (a)	1874	France	Paul Bert	8,840	8,840
Camera Decompressione (b)	1898	Italy	Angelo Mosso	11,650	10,800
Everest Expedition (c)	1933	England	Raymond Greene	8,580	7,840
Mt. Everest Expedition (d)	1938	England	Charles Warren	8,300	6,400
Operation Everest I (e)	1946	USA	Charles Houston & Richard Riley	15,420	8,848
Himalayan Exped. to Mt. Everest (f)	1953	England	Griffith Pugh & Michael Ward	8,848	7,325
Decompression Chamber (g)	1954	England	John Cotes	8,240	8,240
Silver Hut (h)	1960-61	England	Griffith Pugh	8,362	7,830
Spedizione Everest (i)	1973	Italy	Paolo Cerretelli	8,848	6,500
AMREE (j)	1981	USA	John West	8,848	8,848
Operation Everest II (k)	1985	USA	Charles Houston & John Sutton	9,150	8,848
40th Anniversary Everest Exped. (l)	1993	England	Andrew Peacock & Peter Jones	8,848	8,000
Everest Medical Expedition (m)	1994	England	David Collier	8,848	8,000
Operation Everest III-COMEX (n)	1997	France	Jean-Paul Richalet	8,848	8,848
Everest Extreme Expedition (o)	1998-99	USA	Peter Angood	8,848	6,100
Everest MedEx (p)	2006	Germany	Klaus Mees	8,848	8,763
Caudwell Xtreme Everest (q)	2007	England	Michael Grocott	8,848	8,400
Xtreme Everest 2 (r)	2013	England	Daniel Martin & Edward Gilbert-Kawai	5,300	5,300

*Maximum real or calculated altitude depending on the intra-chamber pressure and/or FiO_2 applied. **(a)** Name given to the first trial performed in a hypobaric chamber; with pressures of below 410 mmHg, equivalent to >5,000 m, oxygen-enriched mixtures were inhaled intermittently, though the FiO_2 used was not specified. **(b)** Project in hypobaric chamber without a specific name; a FiO_2=29.2% to 11,650 m was used. **(c-d)** Not specifically scientific expeditions, though pulmonary gas samples were taken up to the specified respective altitudes. **(e)** The project refers to standard atmosphere in a hypobaric chamber; pulmonary gas samples with PiO_2=43 mmHg, equivalent to 8,848 m. **(f)** Not specific scientific expedition but ventilatory parameters were obtained to 6,470 m and pulmonary gas samples to 7,325 m. **(g)** Project in hypobaric chamber with no specific name; belonging to *"The Mount Everest oxygen mask-Medical Research Council High Altitude Committee".* **(h)** Also entitled *"Himalayan Scientific and Mountaineering Expedition";* exercise testings performed at 7,430 m; pulmonary gas samples at 7,830 m. **(i)** Exercise testings performed at 5,350 m and gas samples at 6,500 m. **(j)** International acronym for the *"American Medical Research Expedition to Mt. Everest";* exercise testings performed at 6,300 m with an FiO_2=14%, equivalent to 8,848 m; pulmonary gas samples obtained at a real altitude of 8,848 m. **(k)** The project refers to standard atmosphere in a hyperbaric chamber; exercise testings performed at 9,150 m with a PiO_2=43 mmHg, equivalent to 8,848 m. **(l)** Not specifically scientific expedition though alveolar gas and SaO_2 samples were obtained. **(m)** Also called *"MedEx";* alveolar gas and SaO_2 samples are obtained **(n)** Exercise testings performed at 7,000 m in hypobaric chamber; pulmonary gas samples with a PiO_2= 43 mmHg, equivalent to 8,848 m. **(o)** Also called *"Yale-NASA Mt. Everest Telemedicine Project"* or *"E3".* **(p)** Also called *"Ludwig Maximilians University Expedition to Mt. Everest";* polysomnograph is obtained at 7,500 m and SaO_2 at 8,763 m. **(q)** Exercise testings performed at 7,950 m and arterial gasometry at 8,400 m. **(r)** Project depending on the *"Caudwell Xtreme Everest Hypoxia Research Consortium";* numerous spirometry samples are obtained.

According to the diagram by Rahn and Otis, the average PAO_2 usually remains over 35 mmHg in a subject acclimatised to hypoxia[37] (Figure 1), but the samples obtained at the summit of Mt. Everest, or simulating the same height, oscillate between 21-37.6 mmHg with $PACO_2$ values between 7.5-14.2 mmHg, demonstrating the extreme hypocapnic hypoxia that occurs under these environmental conditions[14,31,32,35,38,39]. Despite all of these surprising biological figures, the acid-base balance remains within a physiologically viable range, even when faced with such intense respiratory alkalosis with a blood pH that reaches values of up to 7.78[32]. Due to the Bohr effect, this alkalosis reduces the P_{50} of the oxyhemoglobin to values of ~19 mmHg, achieving a resting arterial oxygen saturation (SaO_2) of 58-70% at 8,848 m[31,32], despite values having been registered of ~50% between 8,400 and 8,763 m[22,36]. Still breathing oxygen at the rate of 2 $L \cdot min^{-1}$, some subjects at 8,000 m do not achieve SaO_2 over 80%[16]. Table 2 displays some average oxygen gas values at sea level and at the summit of Mount Everest.

Figure 1. Alveolar oxygen pressure in correlation to alveolar carbon dioxide pressure under exposure to acute or chronic hypoxia. Based on Rahn and Otis[37].

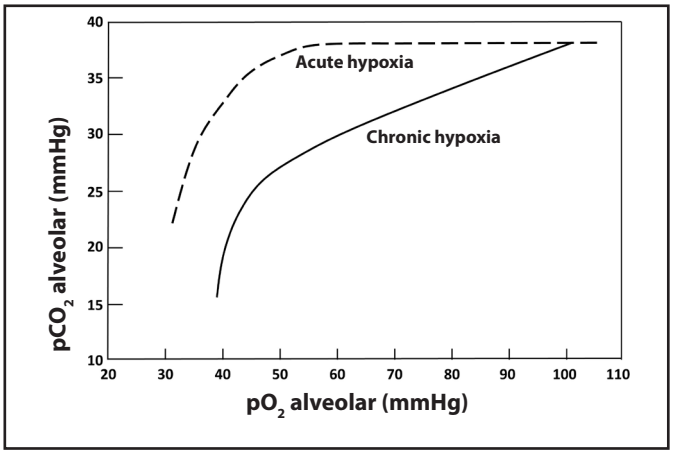

Table 2. Physiological oxygen values at the altitude equivalent to Mount Everest (8,848 m) when resting and during maximum physical exercise. The approximate average values are displayed, calculated based on the data reported from various studies[13-15,31,32,38,39,48,84].

Altitude (m)	BP (mmHg)	PiO_2 (mmHg)	PAO_2 (mmHg)	PaO_2 (mmHg)	SaO_2 (%)	VO_2max (%)
Sea level*	760	149	100	95	97	100
8,848 resting	252	43	31	29	64	—
8,848 exercise	252	43	35	25	41	25

BP: barometric pressure (model atmosphere); PiO_2, PAO_2, PaO_2: partial pressure of oxygen at an inspiratory, alveolar and arterial level, respectively; SaO_2: arterial oxygen saturation; VO_2max: Expected percentage of maximum oxygen uptake. *Resting PAO_2, PaO_2 and SaO_2 values.

It is worth highlighting that at altitudes near 8,000 m, there are already significant physiological differences between an environmental condition of normobaric hypoxia and hypobaric hypoxia[40], or between measurements carried out at real altitudes on the mountain and the equivalent altitude in a hypobaric chamber[41]. PiO_2 values close to those estimated at the summit of Everest have been registered at 8,400 m and even extreme values of PaO_2 (19.1 mmHg) have been registered at this height upon descending from the summit[36,42]. As such, it should be considered that there are differences between the type of "international standard atmosphere" of aviation or the "model atmosphere", as in Operation Everest I and II standard atmosphere was used as a benchmark. The intra-chamber BP reached in Operation Everest II (240 mmHg) was equivalent to 9,150 m, a discrepancy corrected by the fraction of inspired oxygen flow (FiO_2) of 22%, a fact that conferred a PiO_2 of 42-43 mmHg[39,43] corresponding to that at the summit of Everest[34].

Lung adaptation and ventilatory function at extreme altitudes

Hypoxia is a powerful pulmonary arteriolar vasoconstrictor, distributing blood throughout the entire vascular bed of the lungs. This physiological response is designed to optimise the ventilation-perfusion rate (VA/Q) and therefore, gas exchange, despite a major increase of vascular resistance causing pulmonary hypertension (PHT)[44-47]. However, at very extreme altitudes, the existence of a certain imbalance in the VA/Q and the limitation of the alveolar-capillary diffusion seem to play a major role in reducing the PaO_2[45,48,49] and this seems to partly explain the great increase of pulmonary blood volume and the presence of interstitial oedema, precisely due to the rapid hypertension caused by hypoxic vasoconstriction[50]. This situation can set off a spiral of negative effects, in which interstitial oedema, low SaO_2, hypoxic vasoconstriction and PHT can be triggered and worsen reciprocally, causing massive pulmonary oedema with mortal consequences. These facts, as well as the effect caused by hypoxia on the respiratory muscles, are decisive in the early appearance of severe fatigue at high altitude[51].

A determining factor in correctly adapting to altitude is to have a fast and intense hypoxic ventilatory response (HVR)[52-54]. However, in elite mountaineers that are used to high altitudes, a more attenuated HVR seems to be beneficial. Despite this fact causing a certain degree of controversy[55], a lower HVR with greater ventilatory efficiency could help mountaineers to achieve an increased ventilatory store at extremely high altitudes[56]. Today, it is accepted that tolerance to altitude increases with age, and in large part, this is due to an improvement in HVR among males, in accordance with a study performed on 4,675 individuals (2,789 men and 1,886 women aged between 14-85 years), but the cardiac response to hypoxia reduced with age in both sexes. Similar results were found in the same study, in 30 subjects examined with an average interval of 10.4 years, revealing a reduction in heart rate and an increase in HVR with age. These adaptive responses were less marked or absent in post-menopausal women with no physical training[57].

In turn, the maximum voluntary ventilation (MVV) increases progressively with altitude, reaching values of over 200 L•min^{-1} at 8,240 m, due to the low density of the tracheal air[24]. At 8,848 m it is just ~30% compared to sea level. During a simulated ascent to the summit of Mount Everest, forced vital capacity (FVC) reduces progressively to 14%, the mid-expiratory flow (MEF25-75%) increases to 82%, but the forced expiratory volume in the first second (FEV1) does not reveal significant changes regarding lower altitude[50]. Other studies do detect slight FEV1 reductions, even at a much lower altitude[58], revealing a direct correlation between subjects that show lower FVC and FEV1 values with lower SaO_2 levels[59]. The FVC reduction is probably due to changes in pulmonary blood volume and/or the presence of interstitial oedema[60]. The expiratory volume (VE) resting at 7,500 m is ~23 L•min^{-1}[61] and at the summit of Everest is ~40 L•min^{-1}, i.e., some 5 times greater compared to sea level[62]. Mountaineers take on the final pyramid of this mountain at an extraordinarily slow rate, and despite this, they need to keep an VE of ~100-120 L•min^{-1}, hyperventilation characterised by shallow rapid breathing, given that their respiratory frequencies (RF) reach 60 breaths•min^{-1}[48]. But if the exercise is maximum intensity during the ascent to 8,848 m, some subjects can even exceed 200 L•min^{-1}[39] and 80 breaths•min^{-1}[48]. However, such extreme hyperventilation, even with a lower RF, is more common during maximum exertion performed with PiO_2 corresponding to altitudes between 5,000 and 7,000 m, as at higher altitudes the capacity for exercise is considerably depleted[48]. The isocapnic and hypercapnic ventilatory response to hypoxia only increases slightly at altitudes over 8,000 m[61]. It is worth highlighting the high rate of apnoea-hypopnea phases that appear during sleep at high altitudes, and also that at 7,500 m up to 148 phases•h^{-1} have been registered, reaching SaO_2 values of 48%, lower than those recorded in a waking state at 8,763 m in the same subject[22].

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