ABSTRACTS

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It has long been claimed that Sherpa, a Mongolian tribe migrated from Tibet into Nepal (Himalaya), cope with hypoxia better than acclimatized lowlanders. Whereas respiratory, cardiovascular, and metabolic variables have been largely investigated, few data have been reported on oxidative stress. Aim of this study was to assess the reactive oxygen species (ROS) (using electron paramagnetic resonance) and related oxidative damage on lipids (TBARS, 8-iso), proteins (PC), and DNA; determinated antioxidant capacity (TAC), NO metabolites, and inflammatory biomarkers (using enzymatic assays) in Sherpas living at different altitudes versus Caucasian subjects living at sea level. Two groups of male Sherpas (30.2 ± 5.7 years) were investigated: the first ($n = 12$) living prevalently in Kathmandu (1355 msl, KTM) for, at least, 3 months; the second ($n = 12$) residing permanently in Khumjung (3790 msl, KHU) in the Khumbu valley. Our finding revealed significant differences between KHU versus KTM subjects in the following variables: ROS ($+12\%$; 0.18 ± 0.01 vs. $0.16 \pm 0.01\ \mu mol \cdot min^{-1}$) and TAC ($-19\%$; 155.2 ± 31 vs. 189.6 ± 18 nW). By contrast, PC was unchanged in both groups. Comparing the ROS and PC concentrations of both Sherpa groups with those obtained in the Caucasian subjects at sea level ($0.16 \pm 0.02\ \mu mol \cdot min^{-1}$, vs. $1.08 \pm 0.36\ nmol \cdot mg^{-1}$ protein, respectively), no significant differences were observed. On the basis of these findings, Sherpas appear to be better adapted to high altitude, in terms of redox balance, likely due to higher antioxidant levels than those of Caucasians (145 ± 20 nW). Present data may be useful to better understand the mechanisms of human adaptation to hypoxic environments and could improve our understanding of hypoxia physiopathology.

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HOW DIVING TAKES US HIGHER: NEW INSIGHTS INTO HIGH-ALTITUDE PHYSIOLOGY BY STUDYING FREEDIVING

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Breath-hold diving and high-altitude climbing share a general and naturally occurring exposure to hypoxia. The physiological stress caused is more or less chronic during rest at high altitude, but acute during apneic diving and during bouts of exercise at high altitude. Diving physiology research across decades has provided insights into human adaptations to and physiological defense systems against diving-induced hypoxia. Two protective responses are (1) the cardiovascular diving response and (2) spleen contraction, both of which humans share with, for example, seals. The responses are clearly separate, as the diving response is triggered by apnea before any hypoxia occurs and it is enhanced by facial chilling, whereas spleen contraction is elicited by hypoxia and enhanced by hypercapnia occurring during apnea. The diving response involves selective vasoconstriction, prioritizing bloodflow to the brain, heart, and working muscles to provide them with oxygen, and heart rate is reduced; both adjustments contribute to oxygen conservation. Spleen contraction boosts the blood with erythrocytes, which enhances our ability to store blood gases. We did a series of studies aiming to reveal how these mechanisms function in high-altitude environments. Both responses occurred at high altitude, revealing that they may provide a general protection against hypoxia. Elite freedivers have been found to have a more powerful diving response and larger spleens with more contractive ability than nondivers, and the same characteristics seem to be present in successful climbers. The magnitude of these natural defense responses may be involved in explaining individual tolerance to high altitude.

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GREATER SPLEEN VOLUME AND CONTRACTION DURING APNEA IN SHERPA HIGHLANDERS THAN IN NEPALESE LOWLANDERS MAY REFLECT ADAPTATION TO HIGH ALTITUDE

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Spleen volume is greater in divers than in nondivers and correlates with competitive apneic diving performance. Indonesian Bajau divers were recently reported to have genes associated with larger spleens than a nondiving population. Spleen contraction can transiently boost the blood with erythrocytes during hypoxia and a highland population could have developed larger spleens to cope with demanding hypoxic situations, for example, work at high altitude. Apnea can effectively trigger spleen contraction. We, therefore, investigated the spleen volume of seven male Sherpa highlanders and seven male Nepali lowland subjects during sitting rest and across three apneas spaced by 2 minutes breathing. Spleen diameters were measured in three axes using ultrasonic imaging and used for volume calculations. The first apnea was limited to 60 seconds, and the two subsequent apneas were of maximal duration: the last apnea was preceded by 15 seconds hyperventilation. Three of the Sherpas were professional climbers. Tests were done in Kathmandu in April before the climbing season. Sherpas were older than lowlanders (38 [8] vs. 27 [6] years) ($p = 0.012$). Height and weight were similar between groups, but vital capacity was greater in Sherpas: mean (SD) 4.6 (0.5) L vs. 3.7 (0.3) L ($p = 0.003$). Spleen volume during rest was greater in Sherpas (196 [+40] mL) than in lowlanders (139 [+35] mL; $p = 0.014$). Both groups showed spleen contraction during apneas, but mean volume change was greater in Sherpas (49 (26) mL vs. 18 (17) mL; $p = 0.023$). Maximal apneic duration was longer in the Sherpas: 92 (21) seconds versus 66 (12) seconds ($p = 0.016$). The greater spleen volume and contraction in the Sherpa population could reflect long-term adaptations to living at high altitude.

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TELEMEDICINE IN ITALIAN MOUNTAIN AREA: THE E-RES@MONT PROJECT

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A teleconsultation system was developed as part of the of e-Rés@mont (European Interreg Alcotra) project, aimed to improve the healthcare for mountain inhabitants and tourists. Accessing a Web system, through a tablet equipped with a mobile 3G/4G connection, trained nurses from remote shelters of north-west Italian mountain area (between 1544 and 3500 m) can send multimedia data (physiological parameters, electrocardiogram, echography, etc.) to the hospital (Aosta, Italy) where a doctor determined a diagnosis. This system provided an *ad hoc* videoconference built using the most recent technologies with autoadapting videoband. When connection was not available, a decision support system, on an off-line app, provides scores and suggestions to the nurse to evaluate the severity, to dispense emergency aids, and to call rescue services when needed. When the connection turned available, locally stored data were sent to the hospital. On the basis of acquired information, the presence of acute mountain sickness was also automatically assessed. A total of 702 teleconsultations were performed during last summer and winter. The system fully performed the functions it was designed for in mountain areas: all data were correctly received at the hospital and teleconsultations allowed specialist checks. The average diagnosis time was 42 minutes: 333 white, 356 yellow, and 13 red severity; moreover, in 12 cases, this system avoided inappropriate helicopter rescue intervention. Our mountain teleconsultation system was effective in improving people emergency treatments, allowing proper diagnoses and reducing waiting time. Further studies are needed to establish the effectiveness of this system in a high-altitude setting (>3500 m).

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THE EFFECT OF AN EXPIRATORY RESISTANCE MASK WITH DEAD SPACE ON SLEEP, ACUTE MOUNTAIN SICKNESS, COGNITION, AND VENTILATORY ACCLIMATIZATION IN NORMOBARIC HYPOXIA

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We examined the hypothesis that an expiratory resistance mask containing a small amount of dead space (ER/DS) would reduce the apnea–hypopnea index (AHI) during sleep, attenuate the severity of acute mountain sickness (AMS), and offset decrements in cognitive function compared with a sham mask. In a double-blinded randomized sham-controlled cross-over design, 19 volunteers were exposed to two nights of normobaric hypoxia ($FIO_2 = 0.125$), using an ER/DS mask (3.5 mm restrictive expiratory orifice; 125 mL dead space volume) and sham mask (zero flow resistance; 50 mL dead space volume). Cognitive function, AMS, and ventilatory acclimatization were assessed before and after the 12-hour normobaric hypoxia exposure. Full polysomnography was conducted during sleep. AHI was significantly reduced using the ER/DS sleep mask compared with the sham (30.1 ± 23.9 events$\cdot$hour^{-1} vs. 58.9 ± 34.4 events$\cdot$hour^{-1}, respectively; $p = 0.01$). Likewise, oxygen desaturation index and headache ratings were reduced (both $p < 0.05$). There were also significant benefits on limiting the hypoxia-induced reductions in reaction time and attention with the ER/DS mask when compared with the sham ($p < 0.05$). Our study indicates that a simple noninvasive and portable ER/DS mask resulted in marked reductions (49%) in AHI, and improved headache severity and aspects of cognitive function. The field applications and clinical utility of this ER/DS sleep mask should be investigated further.

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INFLAMMASOME PATHWAY PLAYS AN IMPORTANT ROLE IN PATHOPHYSIOLOGY OF HIGH-ALTITUDE-INDUCED PULMONARY HYPERTENSION

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Inflammation is a key feature in pathogenesis of several cardiovascular diseases, including pulmonary hypertension, but the molecular mechanisms by which hypoxia triggers inflammation and pulmonary hypertension remain poorly understood. The members of nod-like receptor (NLR) family are reported to be a key immune sensor that recognizes endogenous danger signals. NLRP3, a member of NLR family, is known to regulate the assembly of inflammasome and may play an important role in pathogenesis of high-altitude-induced pulmonary hypertension. A cross-sectional randomized controlled study was carried out at an altitude of 10,000 ft on 100 healthy male troops on their way back after their prolonged stay at high altitude ($\sim$16,789 ft) in Western Himalayas for 6–8 months. The following physiological parameters such as anthropometry, blood pressure (BP), heart rate (HR), electrocardiogram (ECG), oxygen saturation (SPO_2), hematology, renal function, lung function, echocardiography, heart rate variability (HRV), and circulatory cytokine profile were monitored during the study. Around 30% of studied population showed elevated systolic pulmonary arterial pressures (sPAPs, >35 mmHg). An increase in sympathetic activity was observed in subjects with higher sPAP. Furthermore, Q-PCR, WB, and enzyme-linked immunosorbent assay demonstrated a significant increase in levels of activated caspase-1, interleukin-1β, interleukin-18, NLRP3, and interleukin-6 in subjects with increased sPAP. In conclusion, our study demonstrated that prolonged hypoxia induces activation of inflammasome pathway and is involved in pathophysiology of high-altitude-induced pulmonary hypertension.

Keywords: HAPH, inflammasome, inflammation, NLRP3, sympathetic nerve activity

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APPLICATION AND EFFECT OF OBSERVATION OF NRS2002 ON NUTRITIONAL RISK SCREENING OF ELDERLY CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS AT HIGH-ALTITUDE AREA TO DETECT MALNUTRITION

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