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Mountain Medicine
in the Heart of the Himalayas

ABSTRACTS

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SUBCLINICAL HIGH-ALTITUDE PULMONARY EDEMA: AN ESTABLISHED CLINICAL ENTITY

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Introduction: High-altitude pulmonary edema (HAPE) is a serious medical condition, which develops in individuals who ascent to an altitude >3000 m. Troops are often air transported and hence are at risk of developing HAPE. The incidence of HAPE is 1.5%–5%. However, the incidence rises when chest radiography is used as a screening tool in subjects who are clinically asymptomatic.

Purpose of Study: Identifying personnel at risk and screening them using chest radiography.

Materials and Methods: A total of 50 young healthy soldiers on arrival at high-altitude base camp (3300 m) were selected for the study. All of them were examined immediately on arrival and on day 3. Clinical assessment was made using Lake Luis Questionnaire, electrocardiogram, echocardiography, PFT, hematological investigations, and followed by chest X-ray.

Results: None of the subjects developed clinical evidence of HAPE but all had pulmonary parameters consistent with the process of acclimatization. Two of these subjects developed a subclinical form of HAPE. Perihilar haziness, perivascular cuffing, and interstitial thickening were well appreciated on X-ray. Echocardiography revealed a higher pulmonary arterial pressure.

Conclusions: The study indicates that subclinical form of HAPE is actually important to identify and prevent complications and also to aggressively treat it. Chest radiography provides a cheap modality for detecting the same.

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COLD SUSCEPTIBILITY OF DIGIT STUMPS RESULTING FROM AMPUTATION AFTER FREEZING COLD INJURY IN ELITE ALPINISTS

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The aim of the study was to assess whether previous freezing cold injury (FCI) in fingers and/or toes might predispose alpinists to greater risk of further FCI, primarily due to a greater vasoconstrictor response to cold, resulting in a lower perfusion, reflected in lower skin temperature. Ten elite alpinists ($n = 10$; 8 males and 2 females) with amputations after FCI participated in a cold water (8°C) immersion stress test of the hands and feet. Digit skin temperatures of amputated digits, their noninjured counterparts, noninjured digits of the affected side, and noninjured digits of the corresponding side were measured. The skin temperatures were compared during three consecutive phases of the cold stress test: prewarming, cold water immersion, and passive heating. Amputated toes cooled much faster than their uninjured counterparts ($n = 26$, $p < 0.001$), and attained lower skin temperatures during the cold exposure test ($n = 26$, $p < 0.001$). Higher cooling rate

was observed in all the toes on the injured limb than on the toes on the uninjured limb ($n = 40$, $p < 0.001$). In contrast to the toes, the fingers on the injured limb after FCI were warmer during cooling phase than the uninjured fingers ($n = 15$, $p < 0.001$). Lower digit temperatures observed in the affected toe stumps during the cold stress test than in the nonamputated toes may indicate a heightened risk of future FCI with subsequent cold exposures, as a consequence of less perfusion, reflected in the lower skin temperature. This relationship was not confirmed in the fingers.

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KOROŠKA 8000 HIMALAYAN EXPEDITION: DIGIT RESPONSES TO COLD STRESS AFTER ASCENT TO BROAD PEAK (PAKISTAN, 8051 M)

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Purpose: Cold-induced vasodilatation (CIVD) is nonuniform and centrally mediated, observed in both the hands and feet. Exercise has been shown to enhance the response, specifically by increasing mean skin temperatures (Tsk), in part, due to the increased number of CIVD waves. In contrast, hypobaric hypoxia has been suggested to impair digit skin temperature responses, particularly during subsequent hand rewarming after the cold stimulus. This study examined the combined effect of exercise and hypobaric hypoxia on the CIVD response. Specifically, we compared the CIVD responses in the digits of both their hands and feet of a team of alpinists ($n = 7$) before and after a 35-day Himalayan expedition to Broad Peak, Pakistan (8051 m).

Methods: Seven elite alpinists participated in hand and foot cold water immersion tests 12 days before and immediately upon return from their expedition.

Results: Five of seven alpinists summited successfully without supplemental oxygen. Postexpedition, all alpinists demonstrated higher minimum Tsk in the hands (pre: 9.9 ± 1.1 , post: $10.1^\circ\text{C} \pm 0.7^\circ\text{C}$, $p = 0.031$). Four alpinists had either greater CIVD waves, and consequently higher mean Tsk in their hands, or larger recovery temperatures (pre: $26.0^\circ\text{C} \pm 5.5^\circ\text{C}$ post: $31.0^\circ\text{C} \pm 4.1^\circ\text{C}$, $p = 0.052$), or faster rewarming rate (pre: $2.6^\circ\text{C} \pm 0.5^\circ\text{C} \cdot \text{min}^{-1}$ post: $3.1^\circ\text{C} \pm 0.4^\circ\text{C} \cdot \text{min}^{-1}$, $p = 0.052$). In the feet, the responses varied: one of five alpinists had higher wave amplitudes, one of five alpinists had higher passive recovery temperatures, whereas three of five alpinists had lower mean toe temperatures during cold exposure.

Conclusions: The results of the cold stress test suggest a slight cold adaptation of the hands, but not of the feet, as a consequence of the 35-day expedition in cold and hypobaric hypoxia.

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SKI-EVEREST (8848 M) EXPEDITION: EVIDENCE OF SUSCEPTIBILITY TO COLD INJURY IN A MOUNTAIN CLIMBER

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Objectives: The risk of frostbite among alpinists is high, and may be attributed to external factors and an individual's predisposition to freezing cold injury (FCI). FCI sequelae may determine the risk of future frostbite. In this study we compare the responses to a cold stress test of an elite alpinist with those of a control group. The alpinist has much experience with high-altitude expeditions, but has subjective cold intolerance, including frostbite that resulted in toe amputations. The control group comprised age- and ability-matched noninjured alpinists.

Methods: The cold stress test involved sequential immersion of a hand and foot for 30 minutes in 8°C water, followed by 10 minutes recovery period. During this test, we monitored the finger and toe skin temperatures.

Results: The cold intolerant alpinist had a significantly attenuated cold-induced vasodilatation response and a lower skin temperature of all digits during both immersion (~3°C lower than control group) and recovery (~6°C lower than control group): in those who suffered FCI requiring medical attention and in those who did not.

Conclusions: The responses of the injured elite alpinist are indicative of a pre-existing but previously unrecognized enhanced susceptibility to FCI. Alpinists who have reported cold fingers or toes during their past climbs may benefit from a cold stress test to identify their susceptibility to cold injury.

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THE PLANICA PROTOCOL FOR FROSTBITE MANAGEMENT-2 CASE REPORTS

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Frostbite occurs as a consequence of tissue freezing due to the direct effects of cold on peripheral body areas (toes, fingers, ears, and nose). Frostbite most commonly occurs in the feet, where amputations do not leave considerable inability. In case of amputations on the hands, we speak of major functional impairment with permanent consequences. Case 1—Matterhorn (4478 m), north wall: A 24-year-old alpinist climbed the Matterhorn north face (Schmid route) in late autumn. After a night bivouac in the wall he did not feel his toes anymore. After hospital admission, deep frostbite of six toes was diagnosed. Case 2—frostbite during a winter ascent of Triglav (2864 m), north wall: A 25-year-old alpinist bivouacked with his teammate in sleeping bags after a successful day 1 of climbing the Triglav North Wall (route “Skalaska z ladjo,” 1000 m, V⁺). On day 2 of the climb, he lost his spare pair of climbing mittens and suffered deep frostbite on both hands. After admission, both alpinists were treated according to the Planica diagnostic and therapeutic algorithm of treating frostbite in the hospitals. During hospital treatment, both patients received the following medication: iloprost, pen-

toxifylline, enoxaparin, ibuprofen, pantoprazole, amoxicillin/clavulanic acid, and hyperbaric oxygen therapy. tPA was considered as an option in case 2. In the past few years, we implemented a diagnostic and therapeutic algorithm for treating frostbite—the Planica protocol. Frostbite is an emergency condition wherein early first aid, prompt emergency medical assistance, and standardized hospital treatment are key for a favorable outcome (without amputations).

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BLOOD TRANSFUSION IN MOUNTAIN EMERGENCY MEDICINE: EXPERIENCES FROM NORWEGIAN HELICOPTER-EMERGENCY-MEDICAL-SERVICE

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For the past century, the resuscitation fluids of choice in trauma patients with hemorrhagic shock have been blood products. After predominantly whole blood transfusion during several wars, component therapy became increasingly common during the 1970s. Recent studies recommend a 1:1:1 transfusion of red cells, plasma, and platelets in hemorrhagic shock and is currently a central part of damage control resuscitation. Although blood products have traditionally been reserved for hospitals and clear fluids dominated the prehospital field, the wind is changing. In Norway, most air ambulance and search and rescue helicopters have during the past years carried refrigerated packed red cells and freeze-dried plasma. One helicopter-emergency-medical-service base carries refrigerated whole blood. Due to “golden hour boxes,” the blood may be stored and used up to 72 hours after leaving base, allowing for blood transfusion during prolonged rescue operations. In addition, for severe trauma in extremely remote areas, the concept of a “walking blood bank” is gradually entering the civilian world. Already in practice on certain oilrigs and cruise liners, its protocols and feasibility are transferable to more or less any location in the world. Within a few minutes, a prescreened donor could provide a critical trauma patient with 450 mL of fresh warm whole blood with a hematocrit, coagulation factors, and platelet quality that far surpasses the initial 1:1:1 provided in most trauma centers. As blood transfusions in general are not risk free, solid protocols and indications for use are warranted.

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THE NORWEGIAN GUIDELINES FOR PREHOSPITAL MANAGEMENT OF ACCIDENTAL HYPOTHERMIA: A BRIEF REVIEW OF THE HISTORY OF HYPOTHERMIA AND THE DEVELOPMENT OF CONSENSUS GUIDELINES

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Man has for hundreds of years described the extraordinary ability for “apparent dead” victims of hypothermia to revive and survive with surprisingly good outcomes. Physiological research and the first scientific understanding of hypothermia date back to the 18th century and stories of both survival and death due to cold were abundant from the Napoleon times until present day. For the past 30 years, guidelines have attempted to describe the management and prognostic factors for hypothermic victims. Every few years, the guidelines

have changed to accommodate new findings, technology, and case reports. Development and increased availability of advanced resuscitation strategies such as ECPR, improved logistics, and prehospital care have changed the view of what is possible. However, when facing a hypothermic victim in a remote wilderness with only a first aid kit, we are not much better equipped to neither prognosticate nor manage the patients compared with our colleagues 200 years ago. The main difference is our current understanding of hypothermic physiology, survival possibilities, and how advanced prehospital care can bridge the patient to in-hospital reanimation. This talk briefly reviews the history of hypothermia management and the story of the process and challenges of the development and implementation of a national guideline for the prehospital management of accidental hypothermia in Norway.

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WINCH INSERTION OF AN INTERDISCIPLINARY RESCUE TEAM IN COMPLEX SEARCH AND RESCUE OPERATIONS

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In austere environments such as steep mountain areas, deep gorges, or in sea rescue operations, the rapid delivery of adequate help to severely injured patients is both imperative and complicated. In addition to the provision of advanced medical care, the logistics of an effective and safe extrication has to be solved. The Royal Norwegian Air Force search and rescue helicopter proposes that the parallel delivery of a rescue team comprising a specialist in anesthesiology and critical care and a technical rescue specialist will together be able to more efficiently provide optimal care during challenging conditions. As opposed to the single delivery of either a doctor or rescue specialists, this co-ordinated team is well enough trained in the others specialty to together make optimal priorities on scene whether it is medical or rescue, and aid and continuously assist each other in what is considered the most prudent intervention. The close cooperation between doctor and rescue specialist requires regular training and updates on both technical rescue and medical fields. This talk encompasses the advantages and challenges of the training and insertion of an interdisciplinary team in a variety of emergency medical situations in complex environments.

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ADVANCED RESUSCITATION STRATEGIES IN MOUNTAIN EMERGENCY MEDICINE

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Mountain accidents are characterized by considerable prolonged prehospital times in both time-to-treatment and transport times compared with urban trauma. Initial management must be on early hemostasis, stabilization of fractures, and aggressive prevention of hypothermia. Antifibrinolytic treatment should be considered and adequate analgesia should be provided to reduce stress and oxygen consumption. In prolonged field care, a thorough clinical examination and increased diagnostic precision utilizing modern aperture (i.e., ultrasound) should be utilized with the aim to increase the probability for diagnosing and managing reversible causes of

shock and detection of major hemorrhage. The health provider in austere environments must be aware of the low sensitivity of established prehospital "truths" for identifying development of hemorrhagic shock. In the deteriorating shocked patient with a high suspicion for hemorrhage, important decisions must be made regarding further management: although clear fluids will increase cardiac output and perfusion, this therapy will induce hemodilution with negative effects on hemoglobin and coagulation factors, and might also aggravate hypothermia. In contrast, prolonged hypoperfusion will at some point induce irreversible shock and death. Observational studies on "permissive hypotension" are mostly from urban penetrating trauma with extremely short transport times and cannot readily be transferred to prolonged mountain rescue situations. A tiered approach with individualized balanced resuscitation based on injury mechanism, diagnostic precision, meaningful on-scene interventions, and physiological understanding can aid in improving outcome for severely injured patients in the mountains.

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ARE THE EIGHT-THOUSANDERS PRONE TO BECOME MENTALLY RETARDED?

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Repeated exposure to hypobaric hypoxia in extreme altitudes of high-mountain environment may cause irreversible lesions on the cerebral structure as well as permanent impairment of neurocognitive functions. Within 3 years, we followed one subject, an elite Himalayan climber, during his two expeditions to 8000 m peaks and we looked for structural changes of his brain and we tested his neurocognitive performance. The magnetic resonance imaging scans of brain did not reveal in this subject any pathological changes. The neuropsychological tests did not present any deterioration in his neurocognitive performance after both expeditions. We concluded that some individuals might have special dispositions to resist the harmful effect of hypobaric hypoxia on the brain structure and function. We suggest that the key role in this disposition plays advantageous cerebral vessel network and unimpaired autoregulation of cerebrovascular system.

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ARE TRIPS TO HIGH ALTITUDE BENEFICIAL FOR PSYCHIATRIC PATIENTS?

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Based on the principles of the high-mountain physiology, we suppose that altitude-related hypoxia is likely to trigger a decompensation in any existing psychiatric disorder. At the same time, beneficial factors of mountaineering, such as healthy and peaceful environment, regular physical activity, or new mental stimuli, are to be considered. In our study, we decided to prepare one patient affected by different psychiatric disorders for a trip to a 4000 m peak. Before the ascent, 1 year of a thorough mental and physical training was implemented. Furthermore, mental and psychiatric conditions of the patient have been evaluated through different standardized tests, which were performed in three sessions: at the

beginning of the project, in the ascent days, and 1 month later. The ascent of a 4000 m peak has been successfully achieved and the patient proved a significant improvement mostly in her depressive and anxious symptoms. Whereas 1 month later, she presented a relapse, probably related to the withdrawal effect. We conclude that it is possible to climb a 4000 m peak for a psychiatric patient under stable condition of his or her disorder, although progressive training and precise preparation are mandatory. Further we observed that regular activities in the outdoor natural environment might have positive effect on patients with a psychiatric disorder.

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TIME AT HIGH ALTITUDE IS KEY CAUSAL FACTOR DICTATING EVOLUTIONARY RESPONSE TO HYPOXIA

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High-altitude species have evolved greatly increased capacities in the O₂-transport cascade for ventilation, pulmonary diffusion, circulation and tissue diffusion, mitochondrial function, and metabolism. However, the extent of interspecific variation in control of processes dictating hypoxia responses remains largely unknown. In this study we contrast two bird species, one migratory breeding on the Qinghai-Tibet Plateau, the Bar-headed Goose (*Anser indicus*), and the other a lifelong resident of the Andean Plateau, the Andean Goose (*Chloephaga melanoptera*). Surprisingly, and most likely by coincidence, these two species somewhat resemble the human populations where they are co-located. However, in comparison with many other species, the time elapsed since species first became established in the high-altitude environment appears to be a key causal factor dictating evolutionary outcomes and overall response to hypoxia.

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CEREBROVASCULAR REACTIVITY IN HEALTHY ADULTS AFTER RAPID ASCENT TO HIGH ALTITUDE

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A total of 59 subjects were divided into three groups. The low-altitude group (Beijing, 44.4 m) ascended rapidly to an intermediate-altitude area (Xining, 2200 m), and various indicators were measured before departure and 24 hours after arrival. After having rested for 48 hours, the low-altitude group, together with the intermediate-altitude group, ascended rapidly to a high-altitude area (Yushu, 3700 m), and various indicators were measured 24 and 48 hours after arrival. In the low-altitude group, the CRV and cerebrovascular reserve index significantly increased, but the rScO₂ significantly decreased after rapid ascent to the high altitude ($p < 0.001$). Compared with the preascent levels, the serum vasoactive substances of nitric oxide (NO), endothelial nitric oxide synthase (NOS), erythropoietin, vascular endothelial growth factor, and soluble vascular endothelial growth factor receptor had been decreased in the low-altitude group after rapid ascent to high altitude ($p < 0.001$). In the intermediate-

altitude group, the CRV and the CVRI significantly increased after rapid ascent to the high-altitude area ($p < 0.001$), but the rScO₂ slightly decreased ($p < 0.001$). Among these three groups, CRV was negatively correlated with rScO₂, highly positively correlated with NO and NOS. rScO₂ was highly positively correlated with red blood cell, HB, and vascular endothelial growth factor and moderately negatively correlated with NO and NOS. These changes reflect the hypoxia of local brain tissue in subjects at high altitude.

Keywords: acute hypoxia; cerebrovascular reactivity; rapid ascent to high altitude; regional cerebral oxygen saturation; vasoactive substances

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DOES INTERMITTENT NORMOBARIC HYPOXIC EXPOSURE INDUCE PREACCLIMATIZATION?

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Introduction: A growing number of commercial gyms are offering simulated-altitude training facilities and sleep chambers to aid performance in high-altitude ascents and endurance events. This review looked at the use of intermittent normobaric hypoxia and its effect on acclimatization.

Method: A systematic literature review was undertaken.

Results: The "hypoxic dose" generated by intermittent hypoxic exposure (IHE) falls short of that required to induce endogenous erythropoietin production and erythrocytosis, thus any benefit in acclimatization is likely to be due to other mechanisms. Repeated exposure to lower partial pressures of oxygen results in upregulation of transcription factors such as hypoxia-inducible factor 1a. In addition, skeletal muscle oxidative metabolism is altered by exposure to hypoxia with increased glycolytic capacity—a hypoxia-induced substrate switch.

Conclusions: Disparate studies have looked at a range of physiological end points in the study of normobaric hypoxia. Although these have allowed better characterization of the physiological responses to hypoxia, to suggest that these demonstrate evidence of preacclimatization is premature. The clinical ramifications of the mentioned molecular changes require clarification. An increasing body of research suggests that normobaric and hypobaric hypoxia induce different molecular and hormonal changes that may be key in successfully inducing a state of preacclimatization. Future research should target several key questions if normobaric hypoxia is to be safely used for recreation, rescue, and military preparedness: how persistent are the physiological effects of normobaric hypoxia? To what altitude would IHE preacclimatize an individual? What hypoxic dose is required and how is this best delivered?

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WHOLE BRAIN COMPUTED TOMOGRAPHY PERFUSION OF PATIENTS WITH VARYING DEGREES OF HIGH-ALTITUDE POLYCYTHEMIA: PRELIMINARY STUDY WITH A MULTIDETECTOR COMPUTED TOMOGRAPHY

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Objective: The aim of this study was to investigate the changes in computed tomography perfusion (CTP) in patients with varying degrees of high-altitude polycythemia (HAPC) using a multidetector CT (MDCT).

Methods: Patients who underwent whole brain CTP between March 2017 and January 2018 for various clinical indications were retrospectively reviewed. The study was approved by the institutional review board. Clinical data of 32 patients (group A: 8 cases with mild HAPC, group B: 7 cases with moderate HAPC, group C: 7 cases with severe HAPC, and group D: 10 cases without HAPC) were collected. All patients underwent whole brain CTP with a 256-MDCT (Revolution CT, GE Healthcare) after injection of iopromide 370 mg/mL (40 mL at the rate of 4.0 mL/s). The scanning parameters were as follows: 80 kVp tube voltage, 120 mA current, and 0.625 mm thickness. Whole brain CTP parameters including cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) on basal ganglia area were measured.

Results: The changes of CBV, CBF, and MTT in the basal ganglia area of the control group were 43.87 ± 7.89 , 3.21 ± 0.48 , and 5.00 ± 0.98 , respectively, compared to changes of 38.18 ± 5.25 , 3.82 ± 0.45 , and 6.53 ± 1.29 in patients with mild, moderate and severe HAPC ($p = 0.007$, 0.013 , 0.002).

Conclusions: Patients with different degrees of HAPC had lower perfusion changes than healthy volunteers. The amount of perfusion in basal ganglia area decreased with increasing severity of disease.

Clinical Relevance/Application: With the increase of HAPC severity, the cerebral perfusion parameters decreased gradually.

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EFFECT OF GEOGRAPHICAL ALTITUDE ON CORONARY ARTERY DIAMETER AND MYOCARDIAL PERFUSION IN HEALTHY VOLUNTEERS

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Objective: To determine whether there were any changes in coronary artery diameter and myocardial perfusion in healthy patients at different geographical altitudes.

Materials and Methods: This study was performed in healthy volunteers with approval from the institutional review board of Qinghai Provincial People's Hospital. Thirty-one healthy volunteers including 18 cases of moderate altitude (1500–2500 m) and 13 cases of high altitude (2500–4500 m) with no known cardiac disease were enrolled. All patients underwent coronary computed tomography angiography and myocardial perfusion imaging with a wide coverage CT scanner (Revolution CT, GE Healthcare). Two investigators independently measured the diameter of the left main coronary artery (LM) and right coronary artery (RCA). In addition, myocardial blood flow, myocardial blood volume, and mean transit time were calculated. Differences between groups (moderate altitude group and high altitude group) were analyzed using Mann–Whitney *U* test.

Results: There was a significant difference in the diameters of the LM (3.66 ± 0.25 ; 4.62 ± 0.50 , $p = 0.000$) and RCA (3.65 ± 0.40 ; 4.08 ± 0.44 , $p = 0.000$) between patients from moderate altitude and high altitude. No significant difference was observed in the perfusion parameters of the 16 segments of the myocardium between groups.

Conclusions: Based on the results of this study, the diameter of coronary artery increased with increasing altitude in healthy volunteers. However, the change of altitude had no significant influence on myocardial perfusion.

Clinical Significance/Application: The change of geographical altitude is associated with variability of anatomy in healthy volunteers.

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STUDY OF GLOBAL REGISTRY OF ACUTE CORONARY EVENTS AND THROMBOLYSIS IN MYOCARDIAL INFARCTION RISK SCORES' APPLICATION IN THE RISK STRATIFICATION AND PROGNOSTIC EVALUATION IN PATIENTS WITH ACUTE CORONARY SYNDROME IN QINGHAI

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Objective: To compare the risk stratification ability and prognostic evaluation values of global registry of acute coronary events (GRACE) and thrombolysis in myocardial infarction (TIMI) risk score in patients with acute coronary syndrome (ACS) in Qinghai.

Methods: The clinical data of 385 patients with ACS treated in our hospital from January 2014 to October 2015 were analyzed to calculate the GRACE and TIMI risk scores of each patient. The main adverse cardiovascular events (MACE) within 30 days of the onset and 1 year after discharge were followed up. The receiver operating characteristic (ROC) curves of two kinds of scoring are depicted and the area under the curve (AUC) is compared.

Results: There was no statistic difference between the risk stratification in patients with ACS by means of GRACE score and TIMI score ($\chi^2 = 0.316$, $p = 0.854$). What is more, the higher the GRACE and the TIMI risk scores were, the higher the incidence rate of MACE was in patients within 30 days of onset and 1 year after discharge ($p < 0.01$). Taking 143 points of GRACE risk score as the cut-off value, the sensitivity and specificity of predicting MACE within 1 year after discharge were 89.93% and 90.83%, respectively.

Conclusions: GRACE and TIMI risk scores could be used in the risk stratification of patients with ACS in Qinghai. GRACE risk score held a higher predictive value in predicting recent adverse cardiovascular events in patients with ACS.

Keywords: acute coronary syndrome; adverse cardiovascular events; global registry of acute coronary events risk score; risk stratification; the thrombolysis in myocardial infarction risk score

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CORRELATION OF VASCULAR ENDOTHELIAL GROWTH FACTOR EXPRESSION AND ACUTE MOUNTAIN SICKNESS DURING ASCENT TO HIGH ALTITUDE (MT FUJI, 3700 M) AND AFTER ACCLIMATIZATION

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Acute mountain sickness (AMS) may relate to hypoxia-induced increased expression of the permeability factor vascular endothelial growth factor (VEGF) and subsequent compromise of the blood–brain barrier (BBB). Dexamethasone and acclimatization are both established methods to treat AMS. Serial blood samples were taken from 12 volunteers who ascended Mt Fuji (3700 m) on two occasions separated by 48 hours (the first ascent served as acclimatization for the second). During the first ascent, the mean VEGF level for the seven AMS subjects rose from 23.8 to 30.3 pg/mL (statistically significant, $p = 0.080$)

compared with a decrease from 20.2 to 17.4 pg/mL for the five subjects who did not develop AMS (not significant, $p = 0.26$), concluding that AMS correlated with elevated VEGF levels on ascent to high altitude. Half the group ($n = 6$) were prescribed dexamethasone for the second ascent. The VEGF decreased from 35.2 to 22.4 pg/mL at high altitude (statistically significant, $p = 0.013$) for the dexamethasone group compared with the nontreated group wherein the level increased from 25.0 to 25.9 pg/mL (nonsignificant, $p = 0.79$). During the second ascent, dexamethasone tended to reduce plasma VEGF levels and this may be the mechanism by which it attenuates the hypoxia-induced BBB compromise in the treatment of AMS. Acclimatization did not modify the VEGF response to hypoxia in the nondexamethasone group.

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OXYGEN CONSUMPTION AND LACTATE CONCENTRATION DURING MAXIMUM EXERCISE AT SEA LEVEL AND HIGH ALTITUDE IN MINERS EXPOSED TO CHRONIC INTERMITTENT HYPOBARIC HYPOXIA AT 3800 M

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We previously showed that arterial oxygen content during maximum exercise at high altitude (HA) in chronic intermittent hypobaric hypoxia (CIHH) miners remains constant. However, information about oxygen consumption (VO_2) and lactate concentration [LA] in this population is scarce. Our aim was to determine aerobic capacity and [LA] at sea level (SL) and HA (3800 m) during maximum exercise in miners acclimatized to CIHH at HA. Eight volunteer miners acclimatized to CIHH at HA (>4 years) performed an exercise test at SL and HA (3800 m). The test was performed on the fourth day at SL or HA and consisted in three phases: warm-up (5 minutes); exercise test, wherein the load increased by 50 W every 3 minutes until exhaustion; and a recovery period of 30 minutes. During the routine, VO_2 , transcutaneous arterial saturation (SpO_2 , %) and HR (bpm) were assessed at each step by a pulse oximeter, and venous blood samples were taken to measure [LA]. No differences were observed in VO_2 and [LA], in contrast, a higher HR and low SpO_2 were observed at rest (SL vs. HA). During maximum exercise, a reduction in VO_2 was observed without differences in [LA] and HR. However, a decreased [LA] was observed during recovery (SL vs. HA). In agreement with previous studies, maximum VO_2 was reduced in CIHH by HA exposure. The slight decrease in maximal exercise and the reduction in [LA] during recovery suggest a different strategy to tolerate aerobic capacity in miners exposed to CIHH. Grant: 07 CN13ISM-152 INNOVA CORFO-CHILE.

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CORPORAL COMPOSITION, OXYGEN CONSUMPTION, AND [hsCRP] IN MINERS FROM 0 TO 2500 M

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Over the past 30 years, mining activities in Chile have re-located miners who normally live at sea level to work at altitude. This model of chronic intermittent hypobaric hypoxia exposure is characterized by alternating periods of work at high altitude and rest periods at sea level. Previous studies have shown a reduction in aerobic capacity at 3800 m. The aim of this study was to determine corporal composition, oxygen consumption (VO_2), and [hsCRP] in miners from 0 to 2500 m. A total of 153 subjects at sea level ($n = 54$), 1600 m ($n = 61$), and 2500 m ($n = 38$) were evaluated. We evaluated corporal composition and calculated the body mass index (BMI, kg/m^2), fatty mass (FM, %), and waist circumference (WC, cm). VO_2 max ($\text{mL O}_2/\text{kg}$) was determined at maximum exercise levels on a cycle ergometer. Venous blood samples were taken to quantify [hsPCR] by enzyme-linked immunosorbent assay. In the population at high altitude, we observed an increase in BMI, FM, and WC. A decrease in maximum VO_2 of 31% was observed at high altitude without changes in load (Watts) and heart rate. Increased [hsPCR] levels were observed with ascent to high altitude. The increased prevalence of overweight and obesity is related with ascent to high altitude. Maintenance of workload and heart rate with a decreased VO_2 max suggests a greater cardiovascular challenge in people who work at high altitude. This evidence is supported by increased levels of hsPCR. Grant: INNOVA CORFO 07CN13ISM-152.

3878

REGULATE THYROID FUNCTION TO TREAT OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME IN THE PLATEAU REGION

Luo Wei

Objective: To investigate the impact of the simple thyroid hormone therapy for the hypothyroidism with obstructive sleep apnea hypopnea syndrome in respiratory sleep indicators in plateau section.

Methods: A total of 216 cases of the hypothyroidism with obstructive sleep apnea hypopnea syndrome were collected, and simple thyroid hormone treatment was given for 4 months to compare the respiratory sleep indicators before and after treatment.

Results: Respiratory sleep indicators have been improved as with the improvement of thyroid function and body mass index after treatment ($p < 0.001$).

Conclusions: Simple thyroid hormone therapy can improve sleep disorders for hypothyroidism with obstructive sleep apnea hypopnea syndrome.

Keywords: hypothyroidism; obstructive sleep apnea hypopnea syndrome; plateau section; thyroid hormone

3879

REGULATING IRON AND HEMOGLOBIN LEVELS AT HIGH ALTITUDE

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At high altitude, erythropoiesis is increased to allow for the elevated demand of oxygen. In red blood cells, oxygen is bound to iron within the hemoglobin (Hb) molecule to circulate in the human body. Thus, iron levels have to be suf-

ficient to maintain adequate tissue oxygenation at high altitude. Iron metabolism is controlled by hypoxia by various mechanisms that is discussed in my presentation. The level of Hb defines anemia that adversely affects various aspects of human health, including cognitive performance, work productivity, and complications during pregnancy affecting mother and fetus. We analyzed “high altitude” as a well-established modifier of Hb concentration and show that Hb values in South American inhabitants increase more dramatically with altitude compared with all other regions of the world. By contrast, individuals of Tibetan origin show a significantly lower Hb concentration at all altitudes. All other ethnicities studied showed a comparable increase of Hb in response to altitude. We provide a multiple meta-regression model revealing the change in Hb concentration with increasing altitude in dependence of gender and ethnicity in adults.

3880

DISRUPTION OF THE HEPICIDIN/FERROPORTIN REGULATORY SYSTEM CAUSES PULMONARY IRON OVERLOAD AND RESTRICTIVE LUNG DISEASE

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Emerging evidence suggests that pulmonary iron accumulation is implicated in a spectrum of chronic lung diseases. However, the mechanism(s) involved in pulmonary iron deposition and its role in the *in vivo* pathogenesis of lung diseases remain unknown. We show that a point mutation in the murine ferroportin gene, which causes hereditary hemochromatosis type 4 (Slc40a1C326S), increases iron levels in alveolar macrophages, epithelial cells lining the conducting airways and lung parenchyma, and in vascular smooth muscle cells. Pulmonary iron overload is associated with oxidative stress, restrictive lung disease with decreased total lung capacity, and reduced blood oxygen saturation in homozygous Slc40a1C326S/C326S mice compared with wild-type controls. These findings implicate iron in lung pathology, which is so far not considered a classical iron-related disorder.

3881

PREVALENCE AND SHUNT TYPES OF RIGHT-TO-LEFT SHUNT IN PATIENTS WITH MIGRAINE IN PLATEAU AREA

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Objective: To analyze the prevalence, shunt types, and shunt volume of right-to-left shunt (RLS) in patients with migraine in middle-high-altitude area and further to analyze the relationship between migraine and RLS by conducting right heart contrast echocardiography on the patients.

Methods: Fifty-six patients diagnosed with migraine in neurology department of our hospital from June 2016 to August 2017 were enrolled. (Consistent with the diagnosis of The International Classification of Headache Disorders 3rd Edition Beta Version, ICHD-3 β). (Fifteen [female 11] had migraine with aura and 41 [female 21] were in the migraine without aura group and 50 were in the healthy group.) All patients underwent right heart contrast echocardiography. The test was performed during normal ventilation and during

Valsalva maneuver, recording the maximal microbubbles within 20 seconds as the extent of shunt volume of RLS.

Results: The prevalence of RLS and large RLS in the migraine with aura group (MA⁺) was higher than that of migraine without aura group (MA⁻) (60.3% vs. 34.5%, $p < 0.001$; 28.7% vs. 10.4%, $p < 0.001$). There was no difference among groups in terms of positive rate of medium and minor RLS ($p = 0.131$; $p = 0.065$). The prevalence of RLS and large RLS in the MA⁻ group was higher than that of healthy group (35.7% vs. 24.6%, $p < 0.001$; 15.7% vs. 8.2%, $p < 0.001$). There was no difference among groups in terms of positive rate of medium and minor RLS.

Conclusions: Prevalence of RLS in patients with migraine in plateau area (including MA⁺ and MA⁻) was higher than that of healthy group, and large shunts take a predominate percentage in all those shunts. There was no difference among groups in terms of positive rate and shunt types of medium and minor RLS. There is an association between RLS and migraine, especially when the shunt is large.

3884

COGNITIVE AND NEUROIMAGING CHANGES IN HEALTHY IMMIGRANTS UPON RELOCATION TO HIGH ALTITUDE: A PANEL STUDY

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Background: Cognitive and neuroimaging changes under chronic high-altitude exposure had never been followed up and dynamically assessed before.

Objectives: To investigate the cognitive and brain structural/functional alterations during chronic high-altitude exposure.

Methods: Sixty-nine college freshmen who immigrated to Tibet were enrolled and followed up for 2 years. Neuropsychological tests, including verbal/visual memory and simple/recognition reaction time, were utilized to determine whether the subjects' cognitive function had changed in response to chronic high-altitude exposure. Structural magnetic resonance imaging (MRI) and resting-state functional MRI were used to quantify brain gray matter (GM) volumes, regional homogeneity (ReHo), and functional connectivity (FC) alterations before and after exposure. Areas with both GM and ReHo alterations were used as seeds in inter-regional FC analysis.

Results: The subjects showed significantly lower accuracy in memory test and longer reaction time after exposure to high altitude. Neuroimaging analysis showed markedly decreased GM volume and ReHo in the left putamen. FC analysis seeding of the left putamen showed significantly weakened FCs with superior temporal gyrus, anterior/middle cingulate gyrus, medial frontal gyrus, and other brain regions. In addition, decreased ReHo was found in the superior temporal gyrus, superior parietal lobule, anterior cingulate gyrus, medial frontal gyrus, and anterior cerebellum lobe, whereas increased ReHo was found in the hippocampus. Differences of ReHo/FCs before and after high-altitude exposure in multiple regions showed significant correlation with the cognitive changes.

Conclusions: Cognitive functions such as working memory and psychomotor function are impaired during chronic high-altitude exposure. Putamen may play an important role in chronic hypoxia causing cognitive impairment.

3886

STUDY ON THE EXPRESSION OF p38MAPK IN RATS WITH SEVERE ACUTE PANCREATITIS-ASSOCIATED LUNG INJURY UNDER HIGH ALTITUDE AND LOW-OXYGEN ENVIRONMENT

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Objective: To investigate the expression of p38MAPK in the serum of severe acute pancreatitis (SAP) combined with lung injury and its clinical significance in hypoxic environment.

Method: An artificial SAP model was established by injecting sodium taurocholate into the pancreatic subcutum of Wistar rats. The models were randomly placed at four different altitudes of 400, 2300, 3500, and 4300 m, and each large group was randomized. The rats were divided into F group, P1h group, P6h group, P12h group, and P24h group. Western blot was used to detect the changes of p38MAPK activity in the pancreas and lung tissues, respectively. Reverse transcription-polymerase chain reaction (RT-PCR) was used to detect the expression of p38MAPK mRNA in the two tissues.

Result: In the same altitude, the expression of p38MAPK and p38MAPK mRNA in pancreas and lung tissue increased with the prolongation of rat SAP in each time group ($p < 0.05$). With the elevation of altitude, the expression of p38MAPK and p38MAPK mRNA in pancreas and lung tissues increased significantly ($p < 0.05$).

Conclusions: With the elevation of altitude and the prolongation of duration, the severity of SAP lung injury gradually increases. The activation and overexpression of p38 MAPK in the pancreas and lung tissue may be one of the causes of SAP lung injury.

Keywords: lung injury; p38MAPK; plateau hypoxia; SAP

3888

THE EXPRESS OF MMP-9 ON SEVERE ACUTE PANCREATITIS IN THE HIGH ALTITUDE

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Objective: To investigate the expression and changes of the concentration of matrix metalloproteinase 9 (MMP-9) in the serum of the severe acute pancreatitis (SAP) patient who lives in the high altitude and to explore clinical significance.

Methods: Using enzyme-linked immunosorbent assay, the level of the concentration of MMP-9 in the serum of people of the SAP (36 cases) and healthy persons (39 cases) was detected.

Results: The concentration of MMP-9 showed significant increase in values ($p < 0.05$) on the SAP patient, namely it was 12.56 ± 3.00 ng/mol and in the healthy group it was 3.49 ± 0.63 ng/mol. The concentration of MMP-9 in SAP patients with lung injury differed from those without lung injury ($p < 0.05$). The values were 13.60 ± 2.78 and 10.09 ± 1.94 ng/mol, respectively.

Conclusions: The results showed that the concentration of MMP-9 has significant changes in the serum of the SAP patient in the high altitude. This means that expression of MMP-9 may be involved in the progression of SAP and closely relates to lung injury in SAP patients.

Keywords: high altitude; MMP-9; severe acute pancreatitis

3889

CONSIDERATIONS FOR CANCER PATIENTS TRAVELING TO HIGH ALTITUDE

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Cancer patients and survivors increasingly travel to high altitude. Unfortunately, literature on such travel is lacking and few resources are available for clinicians advising oncology patients about altitude travel. As modern chemotherapies are allowing patients with cancer to live longer, more cancer patients and survivors are active in high-altitude setting. Therefore, clinicians must increasingly be familiar with the additional factors and considerations necessary to properly advise these patients about safe travel to altitude. In this presentation, we will review the important physiological interactions between malignancy, cancer treatments, and travel in the high mountains.

3890

THE DOCTOR WILL NOT SEE YOU NOW: TELE-MEDICINE AND CHANGING PARADIGMS IN MOUNTAIN MEDICINE

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Telemedicine can be defined as the provision of healthcare services at a distance. In the context of high altitude or expedition medicine, it may be different from other medical specialties in that the individual who requires medical support usually enters into a relationship with a doctor at that point and not earlier. "At that point" implies that they may be half way around the world or up a mountain. Many professional, legal, and ethical issues arise given absence of direct involvement by the physician and the use of digital media. Those include consent, confidentiality, and the data management as well as practice across jurisdictions and administration of treatment by nonhealthcare personnel. In our article, we propose tenets of telealtitude medical practice.

3891

INHIBITION OF SUICIDAL ERYTHROCYTE DEATH BY CHRONIC HYPOXIA

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Background/Aims: High-altitude polycythemia (HAPC) is defined by the increase of hematocrit and hemoglobin at high altitude. It is widely considered that excessive erythrocytes production leads to HAPC. Eryptosis is a process by which mature erythrocytes undergo self-destruction, sharing several characteristics with apoptosis. Eryptosis in high-altitude hypobaric hypoxia is unknown. The purpose of this study was to test whether chronic hypoxia influences eryptosis and, if so, to shed light on the mechanisms.

Methods: Biotin labeling and flow cytometry were employed to evaluate the volume of mature erythrocytes from forward scatter, phosphatidylserine scrambling from annexin-V binding, intracellular Ca^{2+} from Fluo-3-AM, reactive oxygen species (ROS) abundance from ROS probe, ceramide, and CD47 abundance utilizing specific antibodies.

Results: The volume was changed and percentage of annexin-V-binding cells was significantly decreased under chronic hypobaric hypoxia and the biotin-positive RBCs were increased in chronic hypoxia group. Furthermore,

chronic hypoxia increased CD47 and ceramide abundance and decreased intracellular Ca^{2+} but has no effect on ROS formation. **Conclusions:** Chronic hypobaric hypoxia inhibits eryptosis through decreasing intracellular Ca^{2+} and increasing integrin-associated protein CD47.

3892

HYPOXIA PROTECTS CARDIOMYOCYTES FROM ERASTIN-INDUCED FERROPTOSIS

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Objective: Ferroptosis is a newly iron-dependent form of cell death that is associated with many diseases, such as cancer, ischemia reperfusion injury, and neurotoxicity. The aim of this study was to investigate whether hypoxia regulates cardiomyocytes ferroptosis.

Methods: H9c2 cells were propagated in a hypoxic incubator and normoxic incubator. Proliferation of cells and effect of hypoxia on the lethality of erastin were determined by CCK8 assay. The migration ability was analyzed by transwell and wound healing assays. Lipid reactive oxygen species (ROS) was measured by C11-BODIPY staining coupled to flow cytometry. Immunoprecipitation and immunoblotting investigate whether SENP1 deSUMOylated HIF-1 α and ACSL4 in H9c2 cells.

Results: Compared with normoxic conditions, hypoxic H9c2 cells were decreased in cell viability, migration, invasion, and less sensitive to erastin. Moreover, we found that hypoxia increased the lipid ROS but attenuated the erastin-induced lipid ROS in H9c2 cells. The expression of ACSL4 was remarkably downregulated in hypoxic H9c2 cells that treated with erastin. SENP1 overexpression was also less sensitive to erastin and suppressed the erastin-induced ROS generation. Immunoprecipitation and immunoblotting investigation showed that SENP1 deSUMOylated HIF-1 α and ACSL4 in H9c2 cells.

Conclusions: Our studies have identified that hypoxia depresses ferroptosis of cardiomyocytes through regulating ACSL4 deSUMOylation.

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MECHANICAL CHEST COMPRESSION DURING MOUNTAIN RESCUE MISSIONS

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According to the European Resuscitation Council, mechanical chest compression (mechCC) can deliver higher quality chest compression in circumstances where this may not be possible with manual chest compression (manCC), for example, during prolonged resuscitations because of hypothermic arrest or during certain procedures such as terrestrial or helicopter winch rescue maneuvers in mountain rescue missions (MRMs). The Lund University cardiac arrest mechCC system (LUCAS) and the load distribution band mechCC system (AUTOPULSE) were successfully used for resuscitation in terrestrial and helicopter MRMs for patients after exhaustion, avalanche accidents, or hypothermic cardiac arrest when manCC was difficult to apply. Although the LUCAS device mainly uses the cardiac pump mechanism, the AUTOPULSE mainly uses the thoracic pump mechanism for forward blood flow during mechCC. According to Mair et al., the thoracic pump mechanism is important for the forward blood flow during CPR in hypothermic arrest victims because an open mitral valve is a common finding during chest compression in these patients. Especially in MRMs, the weight of the mechCC devices (8–10 kg) and the durability of the battery capacity must be taken into account. If mechCC devices are not available in MRMs, the CPR should be delayed or performed intermittently according to Gordon et al. A patient with core temperature $<28^{\circ}\text{C}$ or unknown with unequivocal hypothermic cardiac arrest should receive 5 minutes manual high-quality CPR followed by <5 minutes transport without CPR. With core temperature $<20^{\circ}\text{C}$ and after 5 minutes of manual high-quality CPR, the patient could be transported for <10 minutes without CPR.

3895

METHOXYFLURANE AS ANALGESIC IN MOUNTAIN RESCUE MISSIONS

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During mountain rescue missions (MRMs), most of the patients have to be rescued because of traumatic injuries (TIs) of the extremities with different pain intensities. Because of problems with the way of application, potential side effects, and medicolegal problems, the ideal analgesic drug for patients with TI, which could be supplied by volunteer paramedics in MRMs, is still under discussion. Methoxyflurane (MF) (PentroxR) was introduced in the early 1960s as an inhalation vapor for usage in general anesthesia. However, in anesthetic concentrations, it was found to cause hepatotoxicity

ABSTRACT WITHDRAWN

and irreversible dose-dependent nephrotoxicity, and its use as anesthetic agent was declined in the late 1970s in the United States and most of Europe. Nevertheless, MF has enjoyed considerable use in prehospital care in Australia and New Zealand. After about 40 years, MF is considered by many to be a safe and effective analgesic that is suitable for use in a remote environment as well as during MRMs. Therefore, and because of its easy way of application through inhalation, MF (as well as inhaled nitrous oxide in oxygen [EntonoxR]) is recommended by the ICAR Medical Commission as a pharmacological agent for the treatment of moderate or severe pain in mountain rescue. Unlike EntonoxR, which is applied as compressed gas in a canister, MF is easy to administer as 3 mL solution through an inhaler by the patient himself. Currently, MF will be introduced again in Central Europe as an analgesic drug that could be delivered in the preclinical setting (as well as in mountain rescue) by paramedics and volunteers.

3896

FATAL MOUNTAIN ACCIDENTS IN EUROPE: ARE THE NUMBERS INCREASING?

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Every year during summer, reports concerning acutely occurring fatal mountaineering accidents are published in the media with particular attention to dangerous mountain sports, followed by an unsightly discussion. These reports give the impression that the number of fatal mountain accidents, as well as the number of mountain tourists, is constantly increasing over the years. However, there is also country-specific reliable information available on the actual number of severe or fatal mountain accidents in recent decades that are worth being analyzed. In Switzerland, fatal accidents during classic mountain sport activities are documented by the Swiss Alpine Club for entire Switzerland. With year-to-year fluctuations, there has been no significant increase in fatal mountain accidents in Switzerland since 1984, with a long-term average of 123 deaths per year and a current number of 113 deaths in 2016. In Austria, fatal mountaineering accidents have been documented since 1984 by the "Austrian Alpine Safety Council" for entire Austria with a long-term average of 306 deaths each year and a current number of 267 deaths in 2016 and a slight increase over the years. The German Alpine Club has documented the number of alpine accidents of its members exclusively for >60 years. Since 1984, the number of fatal accidents of club members has constantly decreased with a long-term average of 56 deaths per year and a current number of 30 deaths in 2016. Unfortunately, these data statistics are only partially comparable due to the different underlying country-specific definitions of accident events.

3897

AVIATION ACCIDENTS IN THE AUSTRIAN ALPS: A RETROSPECTIVE 10-YEAR NATIONAL REGISTRY STUDY

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The injury patterns resulting from aviation accidents in alpine terrain, pertaining risk factors, prevention, and prehospital emergency care were analyzed. A total of 74,609 mountain accidents involving 114,595 injured persons are documented in the national registry. Data of Alpine Police Forces and Medical University Innsbruck could be merged in 120 persons suffering an aviation accident in alpine environment. Additional 1817 nationwide police data of aviation accidents were analyzed. Areas with an increased number of aviation accident events could be detected within Tyrol. The vast majority of victims were paragliders, followed by hang gliders. Unfavorable wind condition was the most common cause for aviation accidents. According to police data, most persons were seriously injured and rescued by helicopter. A total of 54.2% of people suffered an injury of the thoracic spine and/or the lumbar spine. Injuries of the head (19.3%), pelvic injuries (16.8%), injuries of the limbs (especially ankle injuries [13.4%]), and injuries of the spinal cord (10.1%) were common. The areas of head or neck were often injured severe to critical; chest, abdomen, and pelvic areas were mostly injured serious to severe. Operative treatment (51.5%) or intensive care treatment (20.8%) was common, in many cases (57.5%), persons were initially treated in trauma bay. Causes of death were head injuries (three times) and hemorrhagic shock (once). After an aviation accident, 13.3% of the persons suffered from paresis or plegia. The reported results are comparable with those of other publications. Protection for head, spine, and ankles is already required by decree, nevertheless these injuries are still common.

3898

CARDIOPULMONARY RESUSCITATION OF CARDIAC ARREST IN THE AUSTRIAN ALPS: A RETROSPECTIVE 10-YEAR NATIONAL REGISTRY STUDY

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No data exist regarding frequency and outcome of cardiac arrest, cardiopulmonary resuscitation (CPR), and automated external defibrillator (AED) for alpine areas. Millions of people visiting alpine areas are at a presumable risk for cardiovascular emergencies due to sportive activities and easy access to mountainous areas. Cardiac arrest in alpine areas of Austria and its outcome was analyzed using data of Austrian Alpine Police. A total of 136 persons suffered a cardiac arrest and received CPR from October 26, 2005 to December 31, 2015. Data were compared with data of Medical University Hospital Innsbruck. Additional CPR with AED cases could be found in the patient's data management system of Medical University Hospital Innsbruck. Eight alpine CPR cases were treated in Innsbruck. An Internet search in the lay press yielded only 10 cases. A total of 125 (92%) of 136 fatalities occur in men with average age of 59.2 years. Regarding distribution across the year, we found that most CPRs were

performed in summer (July, August) and in winter (December to February). During midday (28.7%), afternoon (30.9%), and on weekends (43.4%), cardiac arrest was more common. A total of 132 (97.1%) of cardiac arrest patients did not survive CPR. Five of the eight persons treated in Innsbruck were resuscitated with AED and survived without any neurological impairment. These patients showed shockable initial heart rhythm and CPR was performed for less time compared with persons deceased. There are cases of CPR with AED in Austrian mountains with favorable neurological outcome. Early recognition, immediate bystander CPR, use of an AED, and a short CPR are associated with a favorable neurological outcome.

3899

FROSTBITE INJURIES IN THE AUSTRIAN ALPS: A RETROSPECTIVE 11-YEAR NATIONAL REGISTRY STUDY

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Frostbite is a cold injury mostly affecting the extremities. The objective of this study was to reveal the incidence of frostbite injuries in the Austrian Alps, to search for frostbite risk factors, and thereby optimize prevention and treatment. Out-of-hospital data in the national registry of Alpine Accidents covering the period from January 1, 2005 to December 31, 2015 were retrospectively analyzed and screened for frostbite injuries. Cases in the registry were merged with clinical data from the major trauma center in western Austria, Innsbruck Medical University Hospital, and statistically analyzed. Documented in the national registry are 74,609 mountain accidents involving 114,595 injured persons in the 11-year study period. Thirty-one frostbite cases were documented nationwide, 18 (58%) of which occurred in the western states of Austria and were, therefore, potentially referred to Innsbruck Medical University Hospital. Six (19.6%) patients were female. Frostbite was almost exclusively related to fingers and toes (90% of cases). This translates to 0.1 clinically relevant frostbite cases per 100,000 inhabitants and year in Austria's western states versus 0.07 frostbite cases per 100,000 inhabitants and year in the Austrian Alps. Six patients were identified in the clinical data kept by Innsbruck Medical University Hospital. Frostbite injuries in the Austrian Alps are rare. With an incidence of approximately 0.07 per 100,000 inhabitants, three to four clinically relevant frostbite injuries occur annually. Men are at greater risk for frostbite injuries than are women. Fingers and toes are at greatest risk. Proper preparation of outdoor activities and cold-protective gear can help prevent frostbite injuries.

3900

LIGHTNING ACCIDENTS IN THE AUSTRIAN ALPS: A 10-YEAR RETROSPECTIVE NATIONWIDE ANALYSIS

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Lightning strikes are rare but potentially lethal. The risk for suffering a lightning strike in a mountain environment is unknown. The aim of this study was to determine the risk of a lightning accident in a mountain environment and describe the mechanism, injury pattern, and outcome. From 2005 to 2015, data from the national Austrian Alpine Police database as well as the Clinical Information System of Innsbruck Medical University Hospital were searched for the keywords lightning injury, lightning strike, lightning, and ICD-10 Code T75.0. In addition, the archive data of Innsbruck Medical University Hospital were searched manually. In the Austrian Alpine Police database for the years 2005–2015 109,168 patients were screened for lightning accidents. Sixty-four patients had been hit by lightning in the Austrian Alps, 54 were male. Four persons died on scene; survival rate was 93.8%. Two deceased persons were hunters, who were killed by the same lightning strike. Sixty-three patients suffered a lightning strike while doing a recreational activity, mostly hiking ($n = 55$), a few hunting, and only one doing occupational timberwork. Sixty-three patients suffered a lightning strike between June and August with nearly half (46.9%) of the accidents happening on a Saturday or Sunday, and mainly (95.3%) between 12:00 and 22:00 hours. Persons who perform recreational outdoor and occupational activities in an alpine environment during summer and afternoon incur a higher risk of sustaining a lightning strike. The primary risk group includes young male mountaineers and hunters. The mortality rate was low.

3901

DEVELOPMENT OF A SMARTPHONE APPLICATION TO ASSESS AND GUIDE TREATMENT OF ACUTE MOUNTAIN SICKNESS BY TELEMEDICINE IN THE SWISS ALPS

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Hikers, mountaineers, and people living in secluded high-altitude areas are at an increased risk of developing acute mountain sickness (AMS) and other altitude-related health problems. Medical facilities are generally scarce, and the only available medical care is by air rescue or telemedicine. To facilitate on-site diagnosis and decision-making in high-altitude areas of the Swiss Alps, we developed a smartphone application with integrated tools for patients to conduct a self-evaluation before consulting a medical doctor through telemedicine. Relevancy of the proposed application content, based on pre-existing user knowledge of AMS, was evaluated in a market study through a series of semistructured interviews and online surveys. The application was field-tested during a 6-month trial period in six Swiss mountain huts at an average altitude of 3153 m. Our call center received a total of 14 calls, 7 of which were test calls. The seven real patients

presented symptoms ranging from mild to severe AMS, according to the Lake Louise Score. All patients were able to receive advice and treatment through telemedicine. One patient needed to be airlifted to a regional hospital. The six other patients showed clinical improvement after on-site treatment and were able to continue or descend independently. In addition to guiding patients' decisions to call for help, the application data provided valuable information to medical doctors during the telemedical consultations. The application enabled differentiation between patients with severe AMS and patients presenting with mild to moderate symptoms, who could be treated on-site without the need for an immediate evacuation.

3903

MULTIGENE INTERACTIONS UNDERLYING GENETIC ADAPTATION TO HIGH ALTITUDE IN HIGHLANDER TIBETANS

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The Qinghai-Tibetan Plateau represents the highest elevation of human occupation. It serves as the ideal geographic region of studying genetic adaptation of human populations to high altitude. Previous genetic studies have identified many candidate genes showing signals of Darwinian positive selection in indigenous Tibetans. Combining population genetic approaches with functional assays, we have demonstrated that EPAS1 and EGLN1 are the two key genes showing dramatic allelic divergence between highlander Tibetans and lowlander Han Chinese, and the Tibetan-enriched mutations in these two genes contribute to the blunted regulation of hemoglobin levels at altitude. We also identified other genes explaining the adaptive physiological changes of Tibetans, including genes involved in heme metabolism, blood nitric oxide regulation, and pulmonary arterial pressure. Importantly, these genes interact with each other to maintain physiological homeostasis in Tibetans to cope with hypobaric hypoxia.

3905

EXPRESSION OF MERLIN PROTEIN IN FEMALE CERVICAL CANCER OF HAN, TIBETAN, AND HUI NATIONALITIES IN QINGHAI

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Objective: To explore the expression of the Merlin protein in normal cervix and cervical normal cervix were 90.0%, 91.9% and 86.7% respectively cancer of the Han, Tibetan and Hui nationalities in Qinghai.

Methods: Immunohisto-chemical staining was performed to detect the expression of Merlin in 108 cases of cervical carcinoma (40 cases of Han, 38 cases of Tibetan and 30 cases of Hui nationality) and 107 cases of normal cervix (40 cases of Han, 37 cases of Tibetan and 30 cases of Hui nationality).

Results: The positive expression rates of Merlin in and those in cervical carcinoma were 17.5%, 18.4% and 16.7% respectively. There was significantly statistical difference ($P < 0.05$). However, there was no significant difference in the positive rates of Merlin between cervical carcinoma among different ethnic groups ($P > 0.05$). The expression of Merlin was not correlated

with age, FIGO stage, lymph metastasis and cell differentiation ($P > 0.05$) in cervical carcinoma of three ethnic groups.

Conclusions: The decrease or even deletion of Merlin may be involved in the development of cervical cancer, and it plays an important role in cervical cancer. The expression of Merlin exerts no effect on the occurrence of cervical cancer and it is not associated with the clinical characteristics of the patients, suggesting that it may not be involved in the invasion and metastasis of cervical cancer.

3907

BLUNTED NITRIC OXIDE REGULATION IN TIBETANS UNDER HIGH-ALTITUDE HYPOXIA

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Nitric oxide (NO) is an important molecule for vasomotor tone, and elevated NO signaling was previously hypothesized as a unique and adaptive physiological change in highland Tibetans. However, there has been lack of NO data from Tibetans living at low altitude and lowlander immigrants living at high altitude, which is crucial to test this hypothesis. In this study, through cross-altitude (1990–5018 m) and cross-population (Tibetans and Han Chinese) analyses of serum NO metabolites (NOx) of 2086 individuals, we demonstrate that although Tibetans have a higher serum NOx level than lowlanders, Han Chinese immigrants living at high altitude show an even higher level than Tibetans. Consequently, our data contradict the previous proposal of increased NO signaling as the unique adaptive strategy in Tibetans. Instead, Tibetans have a relatively lower circulating NOx level at high altitude. This observation is further supported by data from the hypoxic experiments using human umbilical vein endothelial cells and gene knockout mice. No difference is detected between Tibetans and Han Chinese for endothelial nitric oxide synthase (eNOS), the key enzyme for circulating NO synthesis, suggesting that eNOS itself is unlikely to be the cause. We show that other NO synthesis-related genes (e.g., GCH1) carry Tibetan-enriched mutations significantly associated with the level of circulating NOx in Tibetans. Furthermore, gene network analysis revealed that the downregulation and upregulation of NOx are possibly achieved through distinct pathways. Collectively, our findings provide novel insights into the physiological and genetic mechanisms of the evolutionary adaptation of Tibetans to high-altitude hypoxia.

3908

A RELIABLE NOMOGRAM MODEL TO PREDICT THE RECURRENCE OF CHRONIC SUBDURAL HEMATOMA AFTER BURR-HOLE SURGERY

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Objective: We established a reliable nomogram model to predict the recurrence of chronic subdural hematoma (CSDH) after burr-hole surgery.

Methods: We retrospectively analyzed 514 patients who were treated in our hospital between January 2010 and November 2017, and included 231 patients in this study. We used univariate and binary logistic regression analyses to select the significantly

related predictors for recurrence. Subsequently, we established the nomogram model using these predictors and validated it.

Result: The total rate of recurrence after initial surgery for CSDH was 14.29% (33 of 231 patients) during the following 3 months. We found that preoperative hematoma volume (> 121 mL), postoperative residual cavity volume (> 72 mL), computed tomography scan imaging appearance (hyperdense and mixed-dense type), and age (> 65 years) were significantly related to recurrence. By using these predictors, a nomogram model was established to predict the recurrence. We used 50% recurrence rate as the classification cut-off, with the corresponding points of 252 to validate the nomogram model. The accuracy of predicting the recurrence of CSDH calculated by the binary logistic regression model was 91.7%.

Conclusions: This nomogram model had a high preciseness to predict the recurrence of CSDH and needs more external validation in the future.

3909

ULTRASOUND-GUIDED PERCUTANEOUS MICROWAVE ABLATION FOR HEPATIC ALVEOLAR ECHINOCOCCOSIS: A PRELIMINARY STUDY

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Objectives: To evaluate safety and efficacy of ultrasound-guided percutaneous microwave ablation (MWA) for hepatic alveolar echinococcosis.

Methods: A total of 26 lumps of hepatic alveolar echinococcosis in 21 patients were treated with ultrasound-guided MWA from January 2016 to December 2017 in Qinghai Provincial People's Hospital. The 21 patients were selected based on the following inclusion criteria: (1) for single lesion: diameter = 5 cm; (2) for multiple lesions: diameter of each lesion = 3 cm, and the number of lesions = 3; and (3) for palliative treatment: 5 cm < single lesion diameter < 10 cm. Therapeutic efficacy was assessed by computed tomography imaging, liver function laboratory examination, volume reduction rate, and complication at 1-, 3-, and 6-month follow-up after MWA treatment.

Results: All of the procedures were technically successful, and the average volume reduction rate of the 26 lumps was 74.1% at 6-month follow-up. After the treatment, the patients' abdominal pain was relieved apparently. And liver functions were not affected by MWA. In addition, 21 lumps (80.8%) were completely ablated with obvious volume reduction and significant calcification (> 70%) at 6-month follow-up, and no evidence of recurrence was demonstrated. Five lumps (19.2%) were partially ablated, with volume reduction and partial calcification (> 50%). Besides, complications and metastasis were not observed.

Conclusions: Ultrasound-guided percutaneous MWA for hepatic alveolar echinococcosis is safe and effective, without apparent complications and metastasis.

3910

DIFFERENCE IN COMMUNICATION STYLES OF WESTERN TEACHERS AND NEPALESE LEARNERS IN AN INTERCULTURAL FACULTY DEVELOPMENT PROGRAM FOR MOUNTAIN RESCUERS IN NEPAL

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We conducted a research on intercultural competence of Western instructors (WIs) and Nepalese instructor candidates (NICs) during a pilot instructor course for future instructors in mountain rescue in Nepal. Data collection was based on self-assessments and semistructured interviews with randomly selected NICs.

Results: In a conflict situation in their own culture, half of WIs prefer exchanges that are dispassionate and another half of them want to reveal people's true feelings and emotions. All [17 of 18, 1 missing] the NICs declared to reveal people's true feelings and emotions. When disagreeing in their own culture, most of the WIs [7 of 8] and half the NICs [9 of 18] prefer to be told directly. One WI and half of NICs prefer not to speak openly so as not to offend anyone. The semistructured interviews with six NICs highlighted the importance of language, time, and dedication of teachers. Prior exposure with the host culture clearly was an advantage for WIs. In our research, we found significant differences in communication styles between NICs and WIs: NICs establish relationship before talking about business, and in conflict situations, they prefer not to speak openly so as not to offend anyone. WIs are much more direct. Such differences are relevant for intercultural medical education. Unless addressed, they can heavily disturb teaching and learning. Faculty members should be prepared before going abroad. Content of the training should include knowledge about the host culture, language and communication skills, and attitudes such as empathy or respect.

3911

STRENGTHENING ALTITUDE RESEARCH: THE "STAR" DATA REPORTING GUIDELINES FOR CLINICAL HIGH-ALTITUDE RESEARCH

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Despite previous efforts to standardize clinical parameters of high-altitude (HA)-related illnesses, such as the Lake Louise consensus definitions, there remains a lack of uniformity in defining and reporting basic parameters in clinical HA research. This makes it difficult to reproduce or to compare studies and to perform reliable meta-analyses. The goal of the STAR (strengthening altitude research) initiative was to

produce a uniform set of key elements for research and reporting in clinical HA medicine. The STAR initiative was inspired by research on treatment of cardiac arrest, in which the establishment of the Utstein style, a uniform data reporting protocol, substantially contributed to improving data reporting and subsequently the quality of scientific evidence. The STAR core group used the Delphi method, in which a group of experts reaches a consensus over multiple rounds using a formal method. We selected experts in the field of clinical HA medicine based on their scientific credentials and identified an initial set of parameters for evaluation by the experts. Twenty-one experts completed both rounds. They identified 42 key parameters in six categories (setting, individual factors, acute mountain sickness, high-altitude cerebral edema, high-altitude pulmonary edema, and treatment) that were considered essential for research and reporting in clinical HA research. An additional 47 supplemental parameters were identified that should be reported depending on the nature of the research. Regular updates of the guidelines are required as new evidence is published in the dynamic field of clinical HA research.

3913

ASSOCIATIONS OF HIGH-ALTITUDE POLYCYTHEMIA WITH POLYMORPHISMS IN ITGAV AND EPAS1 IN CHINESE HAN AND TIBETAN POPULATIONS

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High-altitude polycythemia (HAPC) is characterized by hyperplasia of erythrocyte, a chronic plateau disease characterized by headache, dizziness, and fatigue. Although chronic hypoxia is the main cause of HAPC, the fundamental pathophysiological process and related molecular mechanisms responsible for its development remain largely unclear. In this study, we hope to explore the pathogenesis of HAPC by studying the differences between the susceptible genes (ITGAV and EPAS1) in Han and Tibetan populations. The study recruited 200 subjects, 140 of whom were HAPC patients (70 Han and 70 Tibetans), and 60 healthy people were randomly selected as healthy controls. We sequenced the ITGAV and EPAS1 genes through the second-generation sequencing technology, and obtained rs3832041, rs3738918, and rs16828136 in ITGAV that were associated with decreased HAPC susceptibility in Han populations. The rs75591953 and rs75984373 of EPAS1 gene were associated with reduced risk of HAPC. The rs3738919, rs3795865, and rs2887831 of the ITGAV gene in the Tibetans were related to the increased risk of the disease. Our results showed that the polymorphisms of ITGAV and EPAS1 were significantly correlated with susceptibility to HAPC in Chinese Han and Tibetan populations. This work was supported by the National Natural Science Foundation of China (Grant Nos. 31460286, 31660307, and 31260252).

3914

IMPACT OF TIBETAN MEDICINE QISHIWEI ZHENZHU WAN ON BEHAVIOR OF PARKINSON'S DISEASE MODEL RATS

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To observe the effect of Tibetan medicine Qishiwei Zhenzhu Wan on behavior of Parkinson's disease (PD) model rats. Tibetan medicine low-, median-, and high-dose groups were given 90, 180, and 360 mg/kg by gavage, respectively. Rats in each group were gavaged once every day for 4 weeks. After intervention, rotational behavior experiment, balancing rod experiment, and body torsion pendulum experiment were carried out. Compared with that in the model group, the latency time in the medication groups was shortened in balancing rod experiment; total layout time in the Tibetan medicine low- and high-dose groups was shortened. In body torsion pendulum experiment, rats' uninjured side torsion pendulum frequency in the Tibetan medicine low- and high-dose groups was lower than that in the model group. The Tibetan medicine Qishiwei Zhenzhu Wan might improve PD rats' motor function.

3916

STUDY ON THE BIOLOGICAL VIABILITY AND BOUNDARY RANGE OF HEPATIC ALVEOLAR ECHINOCOCCOSIS BY THE CONTRAST-ENHANCED ULTRASONOGRAPHY AND ARFI IN THE PLATEAU AREA

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Objective: To study the biological viability and boundary range of hepatic alveolar echinococcosis (HAE) by the contrast-enhanced ultrasonography (CEUS) and acoustic radiation force impulse elastography (ARFI).

Methods: Twenty-seven cases with HAE underwent ARFI and CEUS examination and were confirmed by operation and pathology.

Results: Two-dimensional sonography of HAE showed unclear boundary, heterogeneous middle hyperechoic nodules, and the maximum area was $(6.08 \pm 4.47) \text{ cm}^2$ in 27 lesions. CEUS of HAE showed nonenhancement in three phases and black hole sign. Circumferential enhancement on the periphery of the lesion was seen synchronized with the liver parenchyma and showed fast in and slow out. The maximum area was $(8.87 \pm 4.83) \text{ cm}^2$. The area of ECUS was larger than two-dimensional sonography in HAE ($p < 0.05$). The mean shear wave velocity of the interior and the boundary range and the surrounding liver tissues of HAE were statistically different by ARFI ($p < 0.05$), there were significant differences between groups ($p < 0.05$).

Conclusions: CEUS and ARFI examination can determine the biological viability and boundary range of migrating zone around HAE, which is valuable for guiding treatment, judging curative effect, and predicting prognosis.

3917

STUDY ON SUSCEPTIBILITY OF TUBERCULOSIS AND GENE POLYMORPHISM IN TIBETAN POPULATION IN CHINA

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Chinese Tibetans live in the plateau area and have relatively special geographical environment and genetic characteristics. Tuberculosis is a disease affected by interaction of environmental and genetic factors. Hence, studies on the relationship between susceptibility to tuberculosis and gene

polymorphism in Chinese Tibetans are of great significance for the prevention and control of tuberculosis in Tibet. However, there are few related studies on genes except HLA-II genes and vitamin D receptor (VDR) genes. Chen et al. have showed that VDR-ff genotype may be a susceptibility genotype of mycobacterium tuberculosis-positive tuberculosis patients among Chinese Tibetans by detecting the FokI and TaqI polymorphisms in the VDR gene in their population and analyzing the relationship between the two polymorphisms and culture and acid-fast staining of mycobacterium tuberculosis. Li Suzhi et al. used the polymerase chain reaction/sequence-specific primer method to analyze the polymorphisms of HLA-II genes in Tibetan patients with tuberculosis. The results showed that HLA-DRB1 0901, DQA1 0101, and -DQB1 0301 were closely related to tuberculosis susceptibility. Our study found five loci that may be associated with increased risk of tuberculosis in them for the first time. These studies have provided some pieces of evidence for the role of immune and genetic factors in the pathogenesis of tuberculosis in Tibetans in China.

3918

DEADAPTATION OF THE CARDIORESPIRATORY SYSTEM IN HIGH-PLATEAU TIBETAN YOUTH AFTER MIGRATION TO THE PLAINS: A CASE-CONTROL STUDY

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To study the cardiorespiratory changes in Tibetan plateau youth after migration to the plains, and to investigate the correlation between these changes and the time spent in the plains. We randomly chose 60 native Tibetan youth who had moved to the plains and were examined to ensure that they had no disease caused by other factors (case group) and 60 healthy students (control group). The cardiac structure and function, pulmonary artery pressure, mitral and tricuspid valve flow velocity, and other indicators were measured at three time points: just after moving to the plains, 1 year after moving to the plains, and 3 years after moving to the plains. The differences between the case and control group were then statistically analyzed. The Tibetan youth had enlarged right heart structure (anteroposterior diameter of the right atrium and right ventricle) that did not show recovery changes with the extension of time spent in the plains. After entering the plains, the initially altitude-induced increases in pulmonary artery pressure gradually returned to normal, heart rate increased over time to the level of controls, mitral and tricuspid flow velocity significantly increased, and cardiac function indicators tended to gradually increase. The changes in the mentioned indicators were associated with the time spent in the plains. These preliminary findings need to be confirmed by further studies. This study was supported by Natural Science Foundation of Xizang (Tibet) Autonomous Region (2011-150-18).

3919

EFFECTIVENESS OF PEER EDUCATION ON PULMONARY TUBERCULOSIS PREVENTION AMONG COLLEGE STUDENTS IN TIBET, CHINA: A CLUSTER-RANDOMIZED TRIAL

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Tuberculosis is an infectious disease and is a leading cause of death worldwide. In China, the province with the highest incidence of tuberculosis among students is Tibet. This study aimed to evaluate the effectiveness of peer education on pulmonary tuberculosis prevention among nonmedical college students in Tibet, China. Stratified cluster sampling was used, four colleges' students in Tibet were enrolled and randomly divided into intervention group (571 people) and control group (563 people). In the intervention group, peer education was conducted; in the control group, the publicity pages were released. A self-designed questionnaire was used to investigate the knowledge, attitude, and behavior level of the two groups before and 1 month and 6 months after intervention. Analysis of variance of repeated measurement data showed the scores of pulmonary tuberculosis prevention knowledge, attitude, and behaviors in the intervention group were all higher than those in the control group, and the difference was statistically significant ($p < 0.05$). In both groups, the difference of knowledge and attitude scores among different time points were also statistically significant ($p < 0.05$). But, in the intervention group, scores of behaviors had no significant statistical difference between 1 month and 6 months after the intervention ($p > 0.05$). The opposite results were obtained in the control group. Therefore, peer education and releasing publicity pages could both improve college students' knowledge and attitude toward pulmonary tuberculosis prevention. But, on behavior level, the effectiveness of peer education was more persistent. This study was supported by the Natural Science Foundation of Xizang (Tibet) Autonomous Region (2016-ZR-15-16).

3920

THE CHANGES ON LYMPHOCYTE SUBSETS OF THE PATIENTS WITH HIGH-ALTITUDE POLYCYTHEMIA AT DIFFERENT PLATEAU ALTITUDES

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Objective: High-altitude polycythemia (HAPC) is a common chronic altitude disease, which occurs in people who live in the plateau. The patients with HAPC have a series of pathological and physiological change such as excessive erythrocytosis and increased blood viscosity. To observe the changes on lymphocyte subsets of the patients with HAPC, we detected the lymphocyte subsets ($CD3^+$, $CD4^+$, $CD8^+$, $CD4/CD8$, $CD56^+$, and $CD19^+$) of the patients (35 cases in altitude between 3300 and 4200 m and 43 cases in altitude >4200 m) with HAPC (according to the 2004 international conference on plateau medical standard $HGB > 210$ g and $HCT > 65\%$).

Methods: From the patients, 2 mL of fasting blood was collected, which are mixed with EDTA anticoagulant. Lymphocyte subsets were detected by using the U.S. Beckman-Coulter company EpicsXL flow cytometer and reagents.

Results: The lymphocyte subsets ($CD3^+$ [84.8 ± 7.80], $CD4^+$ [46.34 ± 11.51], and $CD4/CD8$ [1.48 ± 0.74]) of the patients in 4200 m compared with the lymphocyte subsets ($CD3^+$ [73.4 ± 7.58], $CD4^+$ [29.98 ± 6.30], and $CD4/CD8$ [0.9 ± 0.38]) of the patients in 3300 m were significantly different ($p < 0.05$). The lymphocyte subsets ($CD8^+$ [35.71 ± 10.96], $CD56^+$ [20.06 ± 10.1], and $CD19^+$ [8.35 ± 3.69]) of the patients at 4200 m compared with the lymphocyte subsets

(CD8⁺ [36.7 ± 10.3], CD56⁺ [18.35 ± 6.24], and CD19⁺ [10.07 ± 3.13]) of the patients at 3300 m were not statistically different ($p > 0.05$).

Conclusions: The changes in the physiopathology such as excessive erythrocytosis, increased blood viscosity, and disordered circulation may be caused by hypoxia, hypobaric hypoxia, and poor environment. It is very significant to research the changes of cellular immune function in the patients with HAPC, and then enhance the cellular immune function.

3922

EFFECT OF HYPOXIA ON ANGIOGENESIS-RELATED FACTORS IN K562 CELLS

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Objective: The purpose of this study was to investigate the mechanism of angiogenesis under hypoxia in K562 cells.

Method: The K562 cells were transfected with HIF-1a^{+/−} gene. K562 cells transfected with the empty virus were used as the control group. The cells were harvested after 72 hours of cultivation under hypoxia. The expression of HIF-1a and angiogenesis-related factors mRNA was detected by RT-PCR. The concentration of angiogenesis-related factors in the culture supernatant was detected by enzyme-linked immunosorbent assay.

Results: The expression of ANG-II and VEGF mRNA in the HIF-1a[−] group was lower than that in the HIF-1a⁺ group. The expression of TGF-β1 mRNA was higher in the HIF-1a[−] group than in the control group and the HIF-1a⁺ group. ANG-II mRNA expression in the HIF-1a⁺ group was higher than that in the control group. TGF-α was not detected and the culture supernatant concentration of ANG-II in the HIF-1a⁺ group was lower than that in the control group. Whereas the VEGF concentration in the HIF-1a⁺ group was higher than that in the control group. The levels of TGF-β, VEGF, and TNF-α in the HIF-1a[−] group were lower than those in the control group.

Conclusions: HIF-1a mRNA positively regulates the expression of ANG-II and VEGF mRNA. And it inhibits ANG-II and promotes the autocrine ability of VEGF and TNF-α in K562 cells. High HIF-1a upregulates the expression of TGF-α mRNA without stimulating autocrine of TGF-α under hypoxia. The effect of high HIF-1a mRNA on TGF-β1 is exactly the opposite of TGF-α. It is suggested that hypoxia and HIF-1a affect the expression and autocrine of angiogenesis-related factors in K562 cells.

3923

EFFECT OF HIF-1A ON ANGIOGENESIS-RELATED FACTORS IN K562 CELLS UNDER NORMOX

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Objective: The aim of this study was to observe levels of angiogenesis-related factors in K562 cells.

Method: The K562 cells were transfected with HIF-1a^{+/−} gene. Transfected K562 cells were used as overexpression and interference group, respectively. K562 cells transfected with the empty virus were used as control group. The cells were harvested after 72 hours of cultivation under normoxic conditions. HIF-1a expression and angiogenesis-related fac-

tors mRNA were detected by RT-PCR. The concentration of angiogenesis-related factors in the culture supernatant was detected by enzyme-linked immunosorbent assay.

Results: HIF-1a mRNA expression in the overexpression group was higher than that in the control and interference groups. HIF-1a mRNA expression in the interference group was lower than that in the control group. Expression of ANG-I, ANG-II, TGF-α, and VEGF mRNA in the interference group was lower than that in the overexpression group, and TGF-β1 mRNA expression in the interference group was higher than that in the overexpression group. Expression of ANG-I and VEGF mRNA in the interference group was lower than that in the control group. TGF-α was not detected and the culture supernatant concentration of ANG-I and TNF-α in the interference group was lower than that in overexpression group, whereas VEGF concentration in the interference group was higher than that in the overexpression group.

Conclusions: HIF-1a mRNA positively regulates ANG-I, ANG-II, TGF-α, and VEGF mRNA and promotes the ability of ANG-I and TNF-α to secrete itself in K562 cells, but does not stimulate autocrine of TGF-α. HIF upregulation can inhibit the expression and autocrine ability of TGF-β1. It is suggested that HIF-1a affects mRNA expression and autocrine of angiogenesis-related factors in K562 cells.

3924

EFFECT OF HYPOXIA ON THE EXPRESSION OF ERYTHROID TRANSCRIPTION FACTORS

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Objective: The purpose was to observe the expression levels of HIF-1a and erythroid transcription factors in bone marrow erythrocytes in chronic altitude sickness and K562 cells. To investigate the effect of hypoxia and erythroid transcription factors on the erythrocytes hematopoiesis.

Method: Bone marrow erythroid CD235a cells of chronic mountain sickness (CMS) were obtained by using magnetic activated cell sorting as CMS group and healthy persons as control group. The expression of HIF-1a and erythroid transcription factor mRNA was tested by RT-PCR in bone marrow CD235a cells of CMS. K562 cells were transfected by interfered with HIF-1a gene. Transfected K562 cells with carried and interfered with HIF-1a gene were used as overexpression and interference groups, respectively. The cells were harvested after culture under normoxic conditions for 72 hours. The expression of HIF-1a and erythroid transcription factors was detected by RT-PCR.

Results: The results showed that the expression of HIF1- and GATA1 mRNA in the CMS group was higher than that in the control group, whereas there was no significant difference in the mRNA levels of NFE2, c-MYB, FOG-1, LMO2, β-globin, and α-globin. The expression of FOG-1 and α-globin mRNA in the overexpression group was higher than that in the interference group. The mentioned differences were statistically significant ($p < 0.05$).

Conclusions: The axis of hypoxia-HIF-1-erythroid-specific genes (GATA-1, FOG-1, and β-globin) plays an important regulatory role in hypoxia-induced erythroid hematopoiesis.

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ABSTRACT WITHDRAWN

3926

CIRCULATION MICRORNAs IN HIGH-ALTITUDE POLYCYTHEMIA

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Objectives: To clarify the differences of miRNAs expression in patients with high-altitude polycythemia (HAPC) and establish the circulating miRNAs and target genes network.

Methods: We used microarray and real time polymerase chain reaction to investigate the differential expression of circulating miRNAs. miRBase, Miranda, and Targetscan were utilized to analyze the potential targets for miRNAs. We appraised the predicted target genes of miRNAs in gene-term enrichment analysis using KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway analysis.

Results: Thirty-three miRNAs were significantly down-regulated and six miRNAs were upregulated in HAPC patients. A total of 2322 candidate genes were predicted as target genes by Targetscan, and 23,513 genes by miRanda, and 7560 genes by miRbase. Taken together, we selected 863 genes to ascertain target genes for HAPC associate miRNAs. To overview HAPC-associated miRNAs and candidate genes, a network draft was mapped that involved miRNAs and the target genes. Furthermore, top 10 signaling pathways including MAPK signaling pathway, insulin signaling pathway, fatty acid metabolism, and so on were found by KEGG pathway.

Conclusions: These results suggest that the network involving miRNAs and target genes may play an important role in HAPC. However, the specific mechanism needs further verification. This study was funded by the Natural Science Foundation of China (Grant No. 31571231), Natural Science Foundation of China (Grant No. 81360300), Natural Science Foundation Innovation team Project of Qinghai Province, China (Grant No. 2014-ZJ-922), The Program of International S&T Cooperation of Qinghai Province, China (Grant No. 2015-HZ-810).

Keywords: circulating miRNAs; high-altitude polycythemia; network

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RELATIONSHIP BETWEEN CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ARTERIOSCLEROSIS IN THE ELDERLY AT HIGH ALTITUDE

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Objective: To explore the relationship between chronic obstructive pulmonary disease (COPD) and arteriosclerosis in the elderly at high altitudes, risk factors for atherosclerosis in elderly COPD patients at high altitudes.

Methods: Forty-two patients with COPD stabilization in Xining area were selected as observation group and 40 patients from health examination group were taken as control group. The two groups were recorded and compared for age, gender, smoking index, homocysteine (HCY), triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL-C), low density lipoprotein (LDL-C), pulmonary function, and carotid intima-media thickness (IMT).

Results: Smoking index, FEV1%, and IMT comparison of the two groups were statistically significant ($p < 0.05$). Gender ratio, HCY, and lipid (TG, TC, HDL-C, and LDL-C) levels of the two groups were compared, and the difference was not statistically significant ($p > 0.05$). Correlation analysis showed that IMT was positively correlated with age and smoking index ($r = 0.081$ and 0.596 , $p < 0.05$) and negatively related to FEV1 ($r = -0.540$, $p < 0.05$). Dual Logic regression analysis showed that age, smoking index, and FEV1 are risk factors for IMT.

Conclusions: Elderly COPD patients at high altitudes are prone to arteriosclerosis; age, smoking index, and FEV1 % may be the risk factors for arteriosclerosis?

Keywords: arteriosclerosis; risk factors; chronic obstructive pulmonary disease; high altitude; old age

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EFFECT OF BOSENTAN IN HYPOXIA-INDUCED INCREASE IN PULMONARY ARTERY PRESSURE: A META-ANALYSIS

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Pulmonary vasoconstriction in response to hypoxia during ascent to high altitude leads to an increase in pulmonary artery pressure (PAP) that may trigger high-altitude pulmonary edema. Bosentan, an endothelin-1 antagonist is known to reduce pulmonary hypertension but fewer studies have been done in case of hypoxia-induced increase in PAP. In this meta-analysis, we analyze all existing data on the effect of bosentan in hypoxia-induced increase in PAP. PubMed, Scopus, Google Scholar, and reference lists were searched for

studies. Clinical trials were selected if they compared the effect of bosentan on PAP with placebo in patients being exposed to hypoxic environment. The extracted data were employed to obtain weighted mean difference (MD) and 95% confidence intervals using the inverse variance random-effects model. Heterogeneity between studies was assessed using I² statistics. Four clinical trials were included in this study with 33 subjects in each arm. Meta-analysis indicates that hypoxic subjects treated with bosentan have no statistically significant difference in PAP relative to placebo. (Weighted MD -2.92; 95% confidence interval: -9.48 to 3.64, $p = 0.38$.) Significant heterogeneity was seen among studies ($I^2 = 79\%$, $p = 0.008$). Bosentan was not effective compared with placebo for the prevention and treatment of hypoxia-induced increase in PAP. However, further larger population studies comparing bosentan with nifedipine or dexamethasone are required to provide more evidence of its efficacy and safety profile.

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AIRWAY MANAGEMENT AND VENTILATOR CHOICES IN HELICOPTER HUMAN EXTERNAL CARGO EVACUATION

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In remote areas such as in the mountains, helicopter-emergency-medical-service (HEMS) is an integral part of mountain rescue. Most HEMSs are able to access patients in difficult environments using winching or long-line operation with human external cargo (HEC). Falls are major causes for traumatic injury in mountains, with >50% traumatic brain injuries (TBI) occurring in fatal trauma accidents. In most cases of major trauma, a rapid evacuation to a less exposed terrain using basic trauma life support interventions is a reasonable, if not preferable, alternative. However patients with TBI and a Glasgow-Coma-Scale <8-9 should be endotracheal intubated (EI) to prevent secondary brain injury from hypoxemia or hypercapnia as part of advanced trauma life support. For an experienced emergency physician, EI is associated with a 90% success rate despite the difficulties in mountain rescue evacuation of an intubated person using HEC; it is a rare and highly complex scenario which only occurs in 2%-13% of cases. Whether the patient should be intubated before or after HEC operation, as well as how to artificially ventilate the patient after EI, is still under discussion. Artificial ventilation during HEC operations can be delivered manually using self-inflating bags (manVent) or using automated mechanical ventilators (mechVent). ManVent allows good tactile feedback about adequate ventilation for the experienced provider but is prone to hypo- or hyperventilation. MechVent allows normoventilation and provides additional safety for patients and attendants because of reduced work load during HEC. However, monitoring of mechVent during HEC evacuation without visual or acoustic feedback due to the noise level and light reflection on the monitor is very difficult.

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PORTERS, PILGRIMS, AND PICKERS

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Each year thousands of people make their way to high-altitude destinations scattered across the Himalayas. Although they may be just a scenic attraction for some, for many such as porters and herb collectors, it is a way to make their ends meet. For some others such as pilgrims, these hold places for spiritual purification. Whatever the desire be, all meet their common grounds at human physiology in hypoxic and hypothermic conditions there. For people who are bound to the journey by socioeconomical or strong spiritual devotion, these journeys often hold dangerous challenges. With poor knowledge and preparation regarding high-altitude environments, people often succumb to various illnesses. These situations are often complicated because of lack of adequate healthcare facilities and evacuation opportunities. We summarize and compare the challenges faced by these unique populations at high altitude, porters, pilgrims, and pickers (herb collectors), and identify areas for possible intervention.

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miR-17 REGULATES HYPOXIA-INDUCED ANGIOGENIC GROWTH FACTOR SECRETION IN MESENCHYMAL STEM CELLS BY TARGETING HIF-1A

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Hypoxia affects the angiogenic activity of bone marrow-derived mesenchymal stem cells (BM-MSCs) through multiple signal pathways and post-transcriptional regulation of functional genes. miR-17-92 is a hypoxia response microRNA cluster that plays important roles in tumor initiation and development. However, little is known about the roles of miR-17-92 in hypoxia-induced angiogenic growth factor secretion in MSCs. In this study, we detected that miR-17, miR-18, and miR-19 are downregulated in BM-MSCs under hypoxia condition, whereas miR-92 is upregulated. Meanwhile, the secretion of angiogenic growth factors such as hepatocyte growth factor (HGF), vascular endothelial growth factor (VEGF), and angiopoietin-1 was significantly upregulated. Transduction of miR-17 inhibitors resulted in increased HGF and VEGF secretion in BM-MSCs. miR-17-92-transduced BM-MSCs grow slower in hypoxia than that in normoxia. Furthermore, we also validated that HIF-1a is a target of miR-17 by using dual-luciferase reporter assay. Transduction of miR-17 mimics also results in the downregulation of HIF-1a in BM-MSCs. We concluded that hypoxia-induced downregulation of miR-17 regulates the secretion of angiogenic growth factors of BM-MSCs under hypoxia.

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HIGHER SERUM FERRITIN IN TIBETAN AND HAN POPULATIONS WITH DIABETES LIVING ON THE TIBETAN PLATEAU

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Objective: Tissue iron has emerged as a significant risk factor for diabetes. Pathways that sense and regulate iron and oxygen interact, but few studies examined the interactions of hypoxia and iron in determining diabetes risk in human populations. Accordingly, metabolic phenotyping with

analysis of iron homeostasis in both Tibetan and Han Chinese living at 2300–3900 m altitudes was conducted.

Research design and methods: Data were collected on Tibetan and Han Chinese living at intermediate altitudes. Iron homeostatic and metabolic parameters including homeostasis model assessments (HOMA), hemoglobin A1c, serum ferritin, and transferrin saturation were determined.

Results: Serum ferritin is higher in both Tibetan groups than in the respective Han groups, and higher in each diabetic group than in nondiabetic people of the same ethnicity. Serum iron and transferrin saturation were also higher in the Tibetan diabetic population than in the Tibetan nondiabetic population. Serum iron was significantly correlated with ferritin levels in the four combined groups ($r^2 = 0.07313$, $p < 0.05$) and even stronger in the Tibetan diabetic group ($r^2 = 0.2702$, $p < 0.05$). HOMA- β was negatively correlated with ferritin in the Tibetan combined groups ($r^2 = 0.020$, $p < 0.05$), and HOMA-IR tended to be positively correlated with ferritin ($r^2 = 0.018$, $p < 0.05$).

Conclusions: Iron parameters differ both between Han and Tibetans and between diabetic groups and nondiabetic groups of both populations. High ferritin, which in these cohorts reflects iron status, is a risk factor for diabetes in both groups, although how iron status relates to the diabetes phenotype differs between the two groups, possibly related to their differing histories of adaptation to high altitude.

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CLINICAL STUDY ON THE COMBINED TARGETED THERAPY OF HER-2 PROTEIN POSITIVE CHEMOTHERAPY IN ADVANCED GASTRIC CANCER IN XINING*

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Objective: To observe the effect of trastuzumab combined with chemotherapy in advanced gastric cancer in Xining.

Method: Between January 2013 and December 2015, we randomly assigned 40 HER-2-positive advanced gastric cancer patients in Xining to chemotherapy combined with trastuzumab and chemotherapy alone. The chemotherapies used in this trial were XELOX and FOLFOX4. According to the RECIST criteria to evaluate the objective effect after 6 weeks treatment, the patients who achieved PR and SD continue the original chemotherapy until 126 days. Then they were continued on maintenance treatment. The overall survival, progression-free survival, and objective response rate were compared between the two groups.

Result: All patients in the groups completed the expected treatment. Median overall survival was 13.87 months for the group of chemotherapy combined with trastuzumab versus 11.14 months for the chemotherapy alone ($p = 0.0032$). Median progression-free survival was 6.71 months for the group of chemotherapy combined with trastuzumab versus 5.49 months for the group of chemotherapy alone ($p = 0.0241$). Objective response rate was 45.0% for the group of chemotherapy combined with trastuzumab versus 35% for the group of chemotherapy alone ($p = 0.5186$).

Conclusions: The overall survival and progression-free survival were significantly longer in chemotherapy combined with trastuzumab than in chemotherapy alone in HER-2 overexpression advanced gastric cancer patients in Xining. Note: *The altitude of Xining is about 2200 m.

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ANTIOXIDANT ACTIVITY OF A SU5416/HYPOXIA-INDUCED EMPHYSEMA AND PULMONARY HYPERTENSION MODEL IN RATS

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Rationale vascular endothelial growth factor (VEGF) has close relationship with hypoxia environment. In animal models, previous studies revealed that chronic treatment of rats with the VEGF receptor blocker SU5416 led to enlargement of the air spaces, indicative of emphysema. In contrast, previous studies also revealed that the SU5416/hypoxia/normoxia-exposed rats develop severe pulmonary hypertension. Based on these reports, this study was conducted to determine whether SU5416/hypoxia model has a chronic hemodynamic deterioration pattern and development of emphysema similar to that of human pulmonary hypertension with emphysema. We also examined the influence of the antioxidant activity in this model by using the serum.

Methods: Male Sprague-Dawley rats were injected subcutaneously with SU5416 on days 1, 8, and 15, and were exposed to hypoxia for 6 weeks. The animals were sacrificed on day 42 after the first SU5416 injection to perform hemodynamic and histological examinations.

Results: SU5416/hypoxia rats showed enlarged airspaces that were quantified by mean linear intercept, suggesting a development of emphysema in comparison with the control group. Also, SU5416/hypoxia rats showed pulmonary hypertension that was determined by increased mean pulmonary arterial pressure. The serum antioxidant activity was significantly decreased in the SU5416/hypoxia rats.

Conclusions: Our findings suggest that rats that were treated with a VEGF receptor inhibitor and a concomitant exposure to hypoxia cause pulmonary hypertension and emphysema. Decreasing of the antioxidant ability may influence pulmonary hypertension and pulmonary emphysema onset.

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STUDIES ON APOPTOSIS, CYTOCHROME C, AND MITOCHONDRIAL MEMBRANE POTENTIAL IN CD71⁺ NUCLEATED ERYTHROCYTES IN PATIENTS WITH CHRONIC MOUNTAIN SICKNESS

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Objective: The aim of this article was to investigate the changes of apoptosis, cytochrome C (Cyt-C), and mitochondrial membrane potential (MMP) in CD71⁺ nucleated erythrocytes in patients with chronic mountain sickness (CMS), and to further explore the possible role of apoptosis in the path of mitochondrion of CD71⁺ nucleated erythrocytes in CMS patients.

Methods: The study included 14 CMS patients and 15 normal people. Bone marrow was collected and the bone marrow mononuclear cells (BMMNCs) were separated. The BMMNCs were marked with CD71 monoclonal antibody and stained with Annexin V-FITC/PI. Then the apoptotic index of CD71⁺ nucleated erythrocytes was determined by flow cytometry. CD71⁺ nucleated erythrocytes were sorted out by magnetic column separation technique. Cyt-C mRNA and MMP were detected by RT-qPCR and flow cytometry with JC-1 staining, separately.

Results: The results showed that the apoptotic index of CD71⁺ nucleated erythrocytes was significantly different between the two groups ($p = 0.031$). The expression of Cyt-C mRNA was significantly different between the two groups ($p < 0.001$). MMP was significantly different between the two groups ($p = 0.017$). The apoptotic index of CD71⁺ nucleated erythrocytes was negatively correlated with hemoglobin in the CMS group ($r = -0.569$, $p = 0.034$). But there was no significant correlation among apoptosis index, MMP, and Cyt-C mRNA.

Conclusions: The decline of apoptosis index of CD71⁺ nucleated erythrocytes may be related to the accumulation of red blood cells in CMS. The increased MMP and decreased Cyt-C mRNA suggest that the change of mitochondrial pathway of apoptosis might be involved in the down-regulation of apoptosis in CD71⁺ nucleated erythrocytes of CMS patients.

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HYPOBARIC HYPOXIA-INDUCED CHANGES IN THE SEX HORMONES AND THEIR UNDERLYING REGULATORY PATHWAYS IN ADULT FEMALE RATS

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Despite extreme environmental conditions, high altitude (HA) attracts both male and female visitors for recreational activities and occupational commitments. Hypobaric hypoxia, the main characteristic of HA, showed to affect the male reproductive system. Comparatively fewer studies were done on females at HA, where varied hormonal level irregular menstrual cycles were reported. The reasons behind these alterations were not well established. This study was undertaken aiming to evaluate the hormonal changes, induced by hypobaric hypoxia and their underlying mechanism in female rats by measuring circulatory estradiol and progesterone level, 17 β hydroxysteroid dehydrogenase (HSD), and 3 β HSD enzyme activity along with estrous cycle, ovarian, and adrenal morphology. Female Sprague–Dawley rats were grouped ($n = 6$): control, acute hypobaric hypoxia (AHH) (simulated altitude: 9144 m, 6 hours), 3CHH, and 7CHH (chronic hypobaric hypoxia) (simulated altitude: 7620 m, 3 and 7 days, respectively). The estrous cycle was found to be stuck in diestrous phase from 4 $\pm$ 1 days onward in the 7CHH group; body weight was significantly decreased till the third day of exposure, and then recovered afterward. In the AHH group, few atretic follicles were found. Degenerated cumulus oophorus and corpus luteum with a declining percentage of adrenocortical cells in both 3CHH and 7CHH groups were observed. A significant decrease in circulatory progesterone level and ovarian 3 β HSD activity was found with increasing days of hypoxic exposure. In conclusion, CHH induces more degenerative changes in female ovary and adrenal glands that interferes with 3 β HSD activity and is likely the reason for a state of low progesterone level in circulation.

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ELEVATION IN ALTITUDE LEVERAGES PHYSIOLOGICAL AND GENETIC ASPECTS

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Hypobaric hypoxia at high altitude (HA, 2500–3500 m) has leveraged distinctive morphological and physiological characteristics in HA natives. This study attempts to understand these adaptive patterns in Ladakh population living at four different altitudes, that is, at 3048 m ($n = 142$), 3812 m ($n = 104$), 4200 m ($n = 170$), and 4522 m ($n = 74$), delineated by a difference of 3% ambient oxygen availability among them. Clinical parameters including age, gender, blood pressure (BP), and arterial oxygen saturation (SaO₂) were documented for all the subjects. Genotyping of functionally relevant SNPs associating with HA adaptation was performed using customized Illumina assay. Our analyses revealed a significant negative correlation between increasing altitude and BP and SaO₂. The lowest study altitude population depicted highest BP (systolic (SBP) = 130 $\pm$ 24 mmHg; diastolic (DBP) = 77 $\pm$ 12 mmHg). Unanticipatedly, the lowest and highest study altitude populations witnessed a difference of $\sim$ 13.5 and $\sim$ 5.0 mmHg in SBP and DBP, respectively ($p < 0.01$). Furthermore, SaO₂, the measure of hypoxemia, showed a negative trend with altitude, with a difference of $\sim$ 6.0% SaO₂ among the lowest and highest study altitude populations ($p < 0.01$). Reduction in SaO₂ elicits the response required to maintain cellular O₂ homeostasis during hypoxia and helps in signaling adaptive mechanisms under hypobaric hypoxia. Furthermore, at the genetic level, nine SNPs spanning oxygen-homeostasis pathway genes depicted a positive trend in adaptive allele frequency with increasing altitude ($p < 0.001$). Furthermore, the correlation analyses revealed significant role of adaptive alleles in augmented SaO₂ ($p < 0.001$). To conclude, the summative levels of oxidative stress over the progressive altitudes shape the clinical, physiological, and genetics patterns favoring adaptation of the native populations.

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GENOME-WIDE ANALYSIS REVEALS HIGH-ALTITUDE HYPOXIA-INDUCED RAS/RAP1 SIGNALING AS AN ACCLIMATIZATION RESPONSE IN KYRGYZ AS COMPARED WITH INDIAN MALES

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Acclimatization is essential for healthy stay at high altitude (HA). Different ethnic groups have distinct HA response and this leads to our insight in understanding HA acclimatization pattern in two groups. Age-matched healthy volunteers ($n = 20$) of Indian and Kyrgyz origin participated in the study and data were collected at basal and day 7 of HA (4111 m) exposure. Total cellular RNA was isolated from whole blood using PAX gene blood RNA kit. RNA quality and concentration were measured using spectrophotometer (NanoDrop). Illumina HiSeqX sequencing system was used to perform 2 $\times$ 150 paired end sequencing. The sequence reads were mapped to the human reference genome (HG19) with STAR aligner (V.2.0). Differential expression analysis was performed using edgeR package for R statistical analysis. Genes with absolute log₂FC $\geq \pm 0.67$ and p -value = 0.05 were considered as statistically significant and were further used

for pathway enrichment analysis using David. Top upregulated pathway was Ras and Rap1 signaling pathway (twofold enrichment) in Kyrgyz. Ingenuity pathway analysis reveals vascular endothelial cell functions to be upregulated in Kyrgyz. Furthermore, ERK and p-ERK (extracellular regulated kinase), consecutive downstream regulator in Ras/Rap1 signaling, were found to be upregulated in Kyrgyz at HA, and growth factor, VEGF-A, indicated Kyrgyz have significantly higher values than Indians at HA (p -value = 0.04). Taken together, genes obtained by *in silico* analysis, also validated by RT-PCR, are known for their function in cellular growth and proliferation through Ras/Rap1 pathway. Kyrgyz have different ethnic origin thus they may show acclimatization response through this pathway for better oxygen delivery at HA.

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HIGH-LEVEL MATRILIN-2 EXPRESSION IN THE OSTEOARTHRITIS PATIENTS IN XINING AREA

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Background: Osteoarthritis (OA) is one of the most common and disabling diseases in the elderly, affecting nearly 80% of individuals of older than 75 years. Our previous results suggested that all the family members of matrilins contributing to the balance of matrilins filament network of extracellular matrix matrilin-2 consist of a large filamentous network in the body, which may act as adapter molecule connecting other proteins and proteoglycans in the extracellular matrix and play an important role in communication or balance between the extracellular matrix and epithelial cells.

Materials and Methods: Articular cartilage from 18 total knee arthroplasty patients from Xining area (2260 m high altitude) was studied by immunohistochemistry. Immunohistochemistry was carried out using the avidin-biotin complex methods. Control sections on the same slide were treated with pre-immunized rabbit serum to replace the primary antibody.

Results: Expression and distribution of matrilin-2 in OA articular cartilage were studied by immunohistochemistry. In this study, matrilin-2 significantly increased expression in articular cartilage, including surfacing area, proliferating, and hypertrophic areas.

Conclusions: Matrilin-2 may play an important role in the communication of matrix to matrix and matrix to cells and may be used as a potential biomarker in the early stage of OA of articular cartilage.

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HYPOMETHYLATION SEEMS TO DRIVE CLINICAL FAILURE AT HIGH ALTITUDE

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High-altitude pulmonary edema (HAPE), a noncardiogenic pulmonary edema, occurs in otherwise healthy sojourners at 2500 m altitude. Although HAPE phenotypes can be distinguished through clinical characteristics, epigenetic aberrations seem to play a potential role in the pathogenesis.

Therefore, clinical characteristics and methylation patterns of oxygen sensing gene, EGLN1, were investigated under the hypobaric hypoxia of high altitude in three well-characterized groups namely, HAPE-free (HAPE-f), HAPE-patient (HAPE-p), and highlanders (HLs). The clinical characteristics namely blood pressure, oxygen saturation (SaO₂), and pulmonary artery systolic pressure (PASP) were measured. Methylation heterogeneity in EGLN1 was evaluated by Methylation Gold™ Kit (Zymo Research, USA) and Bismark Methylation Software Suit. Higher pulse rate (>90 rate/min), mean arterial pressure ($\sim 100.0 \pm 12.0$ mmHg), PASP (~ 2 -fold), and $\sim 12\%$ – 15% lower SaO₂ level were observed in HAPE-p as compared with HAPE-f and HLs ($p < 0.01$). In addition, EGLN1 was found to be hypomethylated in HAPE-p as compared with HAPE-f and HLs ($p < 0.05$) in the CG context; however, near similar blueprint was observed between HAPE-f and HLs ($p > 0.05$). Contrary to this, cytosine methylations of EGLN1 in the context of CHH and CHG (where, H = A, T, or C) were comparable among the three groups ($p > 0.05$). The negative correlation of all the clinical characteristics with methylation was observed, whereas SaO₂ level was positively correlated with methylation in HAPE-p ($p < 0.05$). In conclusion, the results indicate that aberrant clinical characteristics are associated with hypomethylation of EGLN1 that may lead to HAPE pathogenesis due to dysregulation of oxygen homeostasis.

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ABSTRACT REMOVED

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CLINICOPATHOLOGICAL AND MOLECULAR CHARACTERISTICS OF SYNCHRONOUS GASTRIC ADENOCARCINOMA AND GASTROINTESTINAL STROMAL TUMORS IN XINING AREA

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Gastric synchronous tumors that consist of both gastrointestinal stromal tumor (GIST) and adenocarcinoma are rare. We reported six cases of adenocarcinoma with GIST and five cases of GIST in the stomach with special immunohistochemical characteristics (positive for CD117, Dog1, and CD34) and direct sequencing for c-kit and PDGFR- α . By means of immunohistochemical analysis, all GIST cells expressed CD117, CD34, and Dog1 in all six concurrent adenocarcinomas and GIST. The direct sequencing analysis demonstrated that exon 11 c-kit mutations were present in two of six synchronous tumors and four of five GISTs alone. One of the two exon 11 c-kit mutations in synchronous adenocarcinomas with GISTs was an uncommon mutation of CTT>CCA at amino acid 576, and the other was GTT deletion at amino acid 560. The mutation was a homozygous A > G mutation in exon 12 of the gene (amino acid 567) of PDGFR- α . We concluded that exon 11 mutations were the most important mutations in both synchronous cases of adenocarcinoma and GIST and GIST alone of the stomach. The mutation rate was higher in the GIST alone than in synchronous adenocarcinoma with GIST.

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miR-122 INHIBITS ERYTHROID DIFFERENTIATION OF HEMOPOIETIC STEM CELL IN CHRONIC HYPOXIC ENVIRONMENT

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Background/Aims: In our previous study, we found that miR-122 was upregulated in Tibetan versus Chinese Han, whether it regulates erythropoiesis and its detail mechanisms are unknown.

Methods: Circulating miR-122 in plasma was detected in patients with chronic mountain sickness (CMS) through real time polymerase chain reaction. To evaluate the function of miR-122 during erythroid differentiation, CMS mice were injected with miR-122 mimics (100 μ g/20 g per 3 days) and miR-122 inhibitors (100 μ g/20 g) through tail vein, and flow cytometry was employed to detect the expression of Ter119⁺. We screened the potential target protein of miR-122 through bioinformatics software such as Target scan 6 and Pictar and identified it through luciferase report and performing miR-122 gain and loss of function experiments on HepG2 cells and CMS mice. The level of EPO in HepG2 cells and mice plasma was detected through Western blotting and enzyme-linked immunosorbent assay.

Results: The expression of miR-122 was significantly reduced in CMS patients versus control ($p = 0.01$). miR-122 inhibited erythroid differentiation. Overexpression of miR-122 suppresses the expression of Ter119⁺ in bone marrow mononuclear cells of CMS mice ($p = 0.01$). miR-122 directly target EPO *in vivo* and *in vitro*. Overexpression of miR-122 led to decreased EPO expression ($p = 0.05$), and

EPO was upregulated when miR-122 expression was inhibited ($p = 0.01$).

Conclusions: miR-122 plays an important biological function by regulating EPO in the differentiation of hematopoietic progenitor cells in chronic hypoxic environment. This study was funded by the Natural Science Foundation of China (No. 31571231), Natural Science Foundation of China (No. 81360300), Natural Science Foundation Innovation team Project of Qinghai Province, China (No. 2014-ZJ-922), and The Program of International S&T Cooperation of Qinghai Province, China (No. 2015-HZ-810).

Keywords: EPO; erythropoiesis; microRNA; miR-122

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HIGH-ALTITUDE PULMONARY EDEMA AMENABLE INTERACTION BETWEEN RS479200 OF EGLN1 AND RHO GDI-1Kavita Sharma,¹ Ghulam Mohammad,² Tashi Thinlas,² and Qadar M.A. Pasha¹¹CSIR-Institute of Genomics and Integrative Biology, Delhi, India; ²Department of Medicine, Sonam Norboo Memorial Hospital, Leh, India

High-altitude pulmonary edema (HAPE) is one of the serious conditions faced by sojourners at high altitude. This study explores the clinical and genetic aspects of HAPE and HIF-prolyl hydroxylase 2 (EGLN1) by undertaking extensive sequential experiments and analyses in three groups, namely HAPE patients (HAPE-p), HAPE-free sojourners (HAPE-f) and healthy highland natives (HLs). Among the study groups, clinical investigation provided insights into the significance of the elevated mean arterial pressure, pulmonary arterial systolic pressure, and decreased SaO₂ levels in HAPE-p ($p = 0.05$). Furthermore, the protein level and expression of EGLN1 were significantly upregulated in HAPE-p ($p < 0.001$) than in HAPE-f and HLs. Among the several significant single nucleotide polymorphisms (SNPs) of EGLN1 ($p < 0.05$), the regulatory region SNP (rSNP) rs479200C/T seemed to be involved with gene regulation. The protein-DNA interaction assay revealed allele-specific differences of transcription factors by highlighting the lower signal intensity for the protective C allele than for the risk T allele. Furthermore, identification of the interacting proteins showed RhoGDP-dissociation inhibitor 1 (RhoGDI-1) as the candidate mediator of the interactive complex involving the risk allele. RhoGDI-1 acts as the principal member that regulates both Fas signaling and pentose phosphate pathways as protective and risk pathways, respectively, for uncovering the basis of the molecular mechanism underlying hypobaric hypoxia. We, thus, define a functional network between the rSNP rs479200 of EGLN1 and its nuclear transcription factor RhoGDI-1 that could be a potential therapeutic target regulating the cellular system under hypoxic stress.

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DOES REAL-TIME FEEDBACK SOFTWARE IMPROVE SKI-PATROLLER CARDIOPULMONARY RESUSCITATION TRAINING UNDER SNOW CONDITIONS?Iñigo Soteras,¹ Miguel Pla,² Marc Ayala,³ Maria A. Nerin Rotger,⁴ and Enric Subirats¹¹Hospital de Cerdanya, Spain; ²Bombers Gencat, Spain; ³061 Aragón, Spain; ⁴Jose Ramón Morandeira Mountain Medicine Association, Benasque, Spain.

Intense physical activity, cold, and altitude make ski slopes sports a cause of increased risk of out-of-hospital cardiac arrest. Ski patrollers have positive impact in the survival chain on the slope; therefore, they should be trained in basic life support and automatic external defibrillation (BLS + AED) under real snow conditions. Training based on real-time feedback software (RTTS) has been demonstrated to be more effective than standard instructor-based feedback (SIBF), but this effectiveness has not been demonstrated in rough terrain. The aim of this study was to assess the effectiveness of a real-time training software in ski slopes setting compared with SIBF for chest compression and ventilation. We randomized 48 ski patrollers after a 30-minute lesson of BLS + AED to two types of training. Group 1: Using a real-time training software and Group 2: Based on SIBF. Ski patrollers in the RTTS group had a significantly higher chest compression score (median 96%, interquartile range [IQR] 93–98) than those in the SIBF group (median 92%, IQR 76–95) $p = 0.002$. Ski patrollers in the RTTS group had higher percentage of fully released chest compression (median 92%, IQR 76–95 vs. 39%, IQR 10–86.5) $p = 0.002$, better compression rate (median 113 c/min [IQR 108–120] vs. 121 c/min [116.5–124]; $p = 0.004$), and better ventilation score (median 95%, IQR 88–97 vs. 89%, IQR 47.5–91.0) $p = 0.033$.

Conclusions: In ski patrollers, under ski slope conditions, BLS training based on real-time feedback software is more effective than SIBF.

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TANKYRASE: A PROMISING TARGET TO EXPLICATE THE ADAPTATION/MALADAPTATION PHENOMENA AT HIGH ALTITUDE

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At high altitude (HA), oxidative stresses augment reactive oxygen species production that may damage the telomeres. Tankyrase (TRF-1 interacting ankyrin-related ADP-ribose polymerase) performs post-translational modification during DNA damage, thereby acting as a positive regulator of telomere length. It thus could be an important marker with respect to HA adaptation or maladaptation. This study investigated the plausible roles of tankyrase single nucleotide polymorphisms (SNPs) and protein levels in three well-defined groups, namely high-altitude pulmonary edema patients (HAPE-p), HAPE free sojourners (HAPE-f), and healthy highlanders (HLs) comprising 200 samples each. Genotyping was performed using PCR-RFLP and the protein level was estimated using enzyme-linked immunosorbent assay and correlations between genotype/allele with protein levels were analyzed. Three tankyrase SNPs, rs7015700G/A, rs12541709, and rs11991621, were genotyped. SNP rs12541709 did not fall in HWE. Remaining two SNPs could reveal a strong trend. The heterozygote rs7015700GA was prevalent in HLs than in HAPE-f, hence it may contribute toward adaptation. HLs have the highest telomere length followed by HAPE-f and HAPE-p ($p < 0.05$). In a correlation analysis between the heterozygotes and the telomere length, greater length was observed in HLs than in the patients. This phenomenon also suggests that the telomere effect could be

multifactorial. HAPE-p had significantly decreased and HLs had marginally reduced concentration of tankyrase as compared with HAPE-f ($p = 0.05$). These results suggest that perhaps telomere length is more regulated by telomerase enzyme than the tankyrase. Our findings suggest that tankyrase is critical to study adaptation/maladaptation at HA.

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RESEARCH ON RESTING HEART RATE, QTc INTERVAL, TP-Te INTERVAL, AND BLOOD PRESSURE BETWEEN TWO HEALTHY YOUNG PEOPLE OF TIBETAN AND HAN NATIONALITY IN THE PLATEAU AREA AT DIFFERENT ELEVATIONS

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Objectives: To investigate the differences in resting heart rate, QTc interval, TP-Te interval, and blood pressure between two healthy young people of Tibetan and Han nationality in the plateau area at different elevations and degrees of hypoxia; To preliminarily clarify the effects of different elevations on healthy young people and the risks of them getting potential cardiovascular diseases; and to provide the basis for the prevention of the occurrence and development of cardiovascular disease.

Methods: The subjects were divided into eight groups according to elevation, ethnicity, and gender. In the same period of time, medical and physical examinations and all routine tests were carried out. Electrocardiograph was used to record the 12-lead body surface electrocardiogram. Meanwhile, mercury sphygmomanometer was used to monitor the blood pressure of the subjects.

Results: Resting heart rate and blood pressure of young people in Yushu were lower than those who were in the same ethnic group in Xining. The resting heart rate of Tibetans was lower than that of Han nationality at the same elevation. Compared with those in Xining, the QTc interval and TP-Te interval of the people in Yushu were prolonged. These differences were statistically significant. At the same elevation, there was no statistically significant difference in QTc interval, TP-Te interval, and blood pressure between young people of different nationalities.

Conclusions: Resting heart rate and blood pressure in young healthy population in Yushu were lower than those in Xining. QTc interval and TP-Te interval were longer than those in Xining. The resting heart rate of Tibetan was lower than that of Han nationality at the same elevation. Moreover, the risk of cardiovascular and cerebrovascular diseases of different nationalities may not be different.

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TEACHING ROAD TRAFFIC ACCIDENT SAFETY TO LAY PEOPLE: INFOGRAPHIC DETAILING EVIDENCE-BASED FACTORS THAT IMPROVE SURVIVAL

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Rock climbing and mountaineering adventure tourism activities are increasingly being promoted in low-income countries (LICs) and middle-income countries (MICs); however, 93% of the burden of death from road traffic accidents (RTAs) is in LICs/MICs where there is often incomplete implementation of evidence-based practices that reduce

the risk of death from RTAs. This project aimed to summarize international guidance about factors that impact RTA survival in a simple infographic to help climbing and mountaineering councils promote road safety and injury prevention. World Health Organization guidelines targeted at LICs/MICs were read. Evidence-based practices that reduce the risk of being involved in an RTA and improve chance of survival were identified, these practices are summarized in an infographic. Five main themes were identified: prevention through reducing behavioral risk factors, allowing for human error through the “safe systems approach” such that the energy is low enough to avoid serious injury or death, prompt response with activation of a prehospital care system, upon reaching a healthcare facility the patient receives trauma-focused care in a timely manner, and enabling meaningful recovery through further surgery, rehabilitation, and follow-up. It is essential for rock climbers and mountaineers to be aware of the dangers and difficulties at all stages of being involved in an accident in an LIC/MIC, in doing so they can develop strategies to minimize their own risk of morbidity and mortality. This infographic can be used by climbing and mountaineering councils as a teaching aid to highlight areas of improvement in LIC/MIC destinations.

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UP-TO-DATE FIRST AID TRAINING ASSOCIATED WITH GREATER CONFIDENCE DEALING WITH HEALTH-RELATED RISKS AMONG ROCK CLIMBING TOURISTS IN INDIA

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Climbing tourists traveling to low income countries (LICs) and middle income countries (MICs) assume health-related risk from sources, including, but not limited to, illness (e.g., communicable disease), climbing injury, and nonclimbing injury (e.g., road traffic accident [RTA]). This is the first study to investigate whether first aid training affects climbing tourists' confidence about dealing with these risks. Climbers in the bouldering destination of Hampi, India were invited to complete a self-administered questionnaire, 161 responses were collected (95% response rate) between January 18 and March 1, 2017. Confidence dealing with illness, climbing injury, and nonclimbing injury was assessed using a Likert-type scale (1, not confident at all; 5, very confident). First aid training was considered up-to-date if completed within the past 3 years. One-way analysis of variance was performed with Prism (Version 5). Sixteen percent of participants had no first aid training and 55% had up-to-date first aid training. Participants were most confident dealing with illnesses (mean 3.64, confidence interval [CI] 3.47–3.81), then climbing injuries (mean 3.38, CI 3.19–3.57), and least confident with nonclimbing injuries (mean 3.13, CI 2.94–3.31) ($p < 0.0001$). Mean score was highest in those with up-to-date first aid training (up-to-date > out-of-date > none) for illnesses ($p < 0.0001$), climbing injuries ($p < 0.0001$), and nonclimbing injuries ($p = 0.0003$). Up-to-date first aid training is associated with higher levels of confidence dealing with health-related risks when traveling among climbing tourists in India. Participants were least confident dealing with nonclimbing injuries, yet in LICs/MICs,

this health risk is the one most likely to result in death. Rock climbing tourists could consider first aid training before travel, ideally this should include how to deal with an RTA.

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ABSTRACT WITHDRAWN

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ABSTRACT WITHDRAWN

ABSTRACT WITHDRAWN

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CLIMBING INJURIES WHEN TRAVELING TO A LOWER-MIDDLE INCOME COUNTRY: DOES KNOWLEDGE TRANSLATE INTO PRACTICE?

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Bouldering is particularly suited to adventure tourism in low-income countries (LICs) and middle-income countries (MICs) requiring minimal equipment, having few objective dangers, and injuries are mostly mild/moderate not requiring urgent medical attention. This is the first study to evaluate rock climbing tourists' knowledge, attitudes, and practices relating to climbing injuries when traveling to a lower-middle income country. The author visited preselected climbing areas and hostels on a weekly rotation (January 18–March 1, 2017) in the bouldering destination of Hampi, India. Climbers were invited to complete a self-administered questionnaire, 161 responses were collected (95% response rate). Student's paired *t*-test was performed with Prism (Version 5). Seventy percent had >3 years climbing experience, 61% had been on a climbing trip to an LIC/MIC previously. The majority recognized bouldering has few objective dangers (82%) and causes mainly mild/moderate injuries (93%). Sixteen percent always carry a first aid kit and 55% have travel insurance. The severity of injury (UIAA injury and illness severity classification) that would prompt the participant to seek medical attention was higher in India (mean 2.68, confidence interval [CI] 2.58–2.77) than in their home country (mean 2.41, CI 2.30–2.51) ($p < 0.0001$). This research shows that rock climbing tourists are experienced climbers and repeat visitors to LICs/MICs. Participants would only seek medical attention for a more serious injury in India than at home, this severity of injury would likely require medical intervention and possibly repatriation; however, not all participants had appropriate travel insurance.

The majority recognize that most bouldering injuries are relatively minor, these would be amenable to first aid, despite this very few carry a first aid kit.

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CROSS-ALTITUDE ANALYSIS SUGGESTS A TURNING POINT AT THE ELEVATION OF 4500 M FOR POLYCYTHEMIA PREVALENCE IN TIBETANS

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Tibetans are well adapted to high-altitude environments, and with a great majority of them living at the elevation of 4500 m. It is understood that the relatively low hemoglobin (Hb) concentration in Tibetans protects them from polycythemia (red cell overproduction). In general, Tibetans showed lower Hb concentration than Han immigrants residing in Tibet, and there was a linear correlation of Hb concentration with altitude. To test whether there is a turning point of elevation for polycythemia incidence in Tibetans, we collected data of Hb concentration from nearly 8000 Tibetan individuals residing in 20 geographic regions throughout the Qinghai–Tibetan Plateau, with elevations ranging from 2227 to 5018 m. For populations living <4500 m, the average Hb levels are low and incidences of polycythemia are rare, an indication of adaptation for Tibetans at relatively low altitude. In contrast, the average Hb levels and incidences of polycythemia deviated from the linear expectation for the high elevations (>4500 m). In particular, at 5000 m, the majority of the population (67% in males and 65% in females) are subject to polycythemia. The nonlinear regression curves indicate that the Hb levels increase slowly with elevations from 2200 to 4500 m, and then sharply after 4500 m. The same pattern was observed for the curve of incidence of polycythemia. We showed that the elevation of 4500 m marks a sharp increase of Hb concentration and incidence of polycythemia in Tibetan populations living above the elevation of 4500 m, which may reflect the altitude limit for Tibetans' adaptation to high altitude.

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ASSOCIATION BETWEEN GENETIC POLYMORPHISMS OF HIF-2A GENE AND HIGH-ALTITUDE PULMONARY HYPERTENSION IN HAN POPULATION

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Objective: To test the hypothesis that the single nucleotide polymorphisms (SNPs) in HIF-2a gene are associated with the susceptibility to high-altitude pulmonary hypertension (HAPH) in Han population in China.

Methods: To those who emigrated to plateau (average altitude 3300 m) and have been living there for >20 years from the Han population, the method of overall random was used to enroll 49 HAPH patients as the case group (HAPH group) and 39 people free of HAPH as the control group. The Sanger chain termination method was used to detect the SNPs in HIF-2a gene.

Results: The genotype and frequencies of rs1562453 were CC (49.0%), CT (46.9%), and TT (4.1%) in the HAPH group, and the locus's genotype and frequencies were CC (76.9%), CT (17.9%), and TT (5.1%) in the control group. The alleles

and frequencies of rs1562453 were C (72.4%) and T (27.6%) in the HAPH group, and the locus's alleles and frequencies were C (85.9%) and T (14.1%) in the control group. Their genotypes and alleles frequencies were of significant difference between the two groups (genotypes $p = 0.017$; allele $p = 0.031$). Meanwhile, the genotype and frequencies of rs1867785 were AA (46.9%), AG (46.9%), and GG (6.1%) in the HAPH group, and the locus's genotype and frequencies were AA (74.4%), AG (25.6%), and GG (0.0%) in the control group. The alleles and frequencies of rs1867785 were A (70.4%) and G (29.6%) in the HAPH group, and the locus's alleles and frequencies were A (87.2%) and G (12.8%) in the control group.

Conclusions: The SNPs of rs1562453 in HIF-2a gene may be associated with the development of HAPH among Chinese Han population, and individuals with the genotype CT may be more vulnerable to HAPH than those who carry the genotype CC, and allele T may be a risk factor for HAPH.

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THE RESEARCH ON VON WILLEBRAND FACTOR, VON WILLEBRAND FACTOR CLEAVING PROTEASE, AND THROMBOSPONDIN 1 LEVELS IN PLASMA OF PATIENTS WITH CHRONIC MOUNTAIN SICKNESS AND CHRONIC HYPOXIA EXPOSURE

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Objective: To explore the role of von Willebrand factor (vWF), von Willebrand factor cleaving protease (vWF-CP), and thrombospondin 1 (TSP1) in the occurrence of chronic mountain sickness (CMS) and chronic hypoxia exposure.

Methods: Enzyme-linked immunosorbent assay was used to assess plasma level of vWF, ADAM13, and TSP1 in 28 CMS patients, 28 healthy plateau natives, and 28 healthy Xining citizens.

Results: Plasma vWF level of the CMS group was higher than that in the plateau healthy group and Xining healthy group ($p < 0.05$). Plasma level of vWF-CP in the CMS group and plateau healthy group was lower than that in the Xining healthy group ($p < 0.05$). The plasma TSP1 level in the CMS group was higher than that in the plateau healthy group and Xining healthy group ($p < 0.05$).

Conclusions: vWF, vWF-CP, and TSP1 may be related to the occurrence of CMS. vWF-CP has been changed in chronic hypoxia exposure, which may have guiding significance for the early prevention of CMS.

Keywords: chronic mountain sickness; thrombospondin 1; von Willebrand factor; von Willebrand factor cleaving protease

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OBSERVATION OF THE EFFICACY OF LEFLUNOMIDE COMBINED WITH HORMONE TREATMENT ON PATIENTS WITH IgA NEPHROPATHY IN HIGH-ALTITUDE AREA

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Objective: Observing the efficacy of leflunomide combined with hormone treatment on patients with IgA nephropathy in high-altitude area.

Methods: Thirty patients with IgA nephropathy were selected and were divided into the experimental group and the control group randomly. The experimental group was treated

with hormone combined with leflunomide and the control group was treated with only hormone. The urine protein quantitation and serum albumin of those patients were detected after weeks 12 and 24 of treatment.

Results: After 24 weeks of treatment, four patients were completely relieved, six patients were effective, and two patients were treated ineffectively in the experimental group; therefore, one patient was completely relieved, five patients were effective, four patients were treated ineffectively, and three patients relapsed in the control group. After 12 weeks of treatment, urine protein quantification decreased and serum protein increased in the experimental group, of which the difference between the experimental group and the control group was statistically significant ($p < 0.05$).

Conclusions: Compared with using only hormone, leflunomide combined with hormone has a significant effect on patients with IgA nephropathy at high-altitude area, which can reduce urinary protein effectively, increase serum albumin, and reduce recurrence rate.

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A CROSS TALK IN EPAS1 BETWEEN GENETIC AND EPIGENETIC REGULATIONS IN TIBETAN HIGH-ALTITUDE ADAPTATION

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While recent genome-wide studies have found hundreds of Tibetan adaptation-related genes with the majority of variants in noncoding regions, the molecular mechanisms of these candidates to adaptation remain elusive. In this study we examine whether EPAS1 noncoding mutations may influence enhancer activity by altering transcription factor binding. First, our dual luciferase reporter assays evidenced that five noncoding regions near or in EPAS1 are enhancers, and four of them show allele specificity. Furthermore, we observed two polymorphic sites, one creates novel CpG dinucleotide, and another wipes out one known CpG. Gel shift assays demonstrated that different alleles of these two single nucleotide polymorphisms (SNPs) and their methylation status affect the enhancer binding to proteins and such binding is also oxygen concentration dependent. In addition, we observed that SNPs in one enhancer (E4) significantly altered the protein binding spectrum. To further explore the genes interacting with E4 and whether those interactions are oxygen dependent, 4C-seq of E4 in hypoxia and normoxia-treated HepG2 was conducted. Despite the concordance between two treatments in most interactions, we identified several specific interactions including one hypoxia-related interaction linked with protein coding isoform of PRKCE. Our current results suggest that one function of EPAS1 related to Tibetan hypoxia adaptation is through its allele-specific enhancers, whose targets may be oxygen status dependent.

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GENETIC AND EPIGENETIC SIGNALS INFLUENCE ADAPTATION UNDER HYPOBARIC HYPOXIA

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Hypoxia-inducible pathways, owing to their significance in oxygen sensing, accentuate their relevance in high-altitude

(HA) physiology. Consequently, HIF-1A, EPAS1, and HIF-prolyl hydroxylase-2 (EGLN1) have emerged as the intriguing genes concerning HA health and diseases such as high-altitude pulmonary edema (HAPE). In this study, we report the genetic and epigenetic involvement of EGLN1 in three well-characterized groups, that is, highland natives (HLs), HAPE-free (HAPE-f) controls, and HAPE patients (HAPE-p). High-throughput screening of genetic variants and CpG islands unveiled the important SNPs/regions of EGLN1. It also delineated the transcription factors interacting with the regulatory SNPs and their associated pathways. Lastly, primary human cells validated the enhancer effect due to the allelic variants. Clinical characteristics varied significantly among the three groups ($p < 0.001$). The genetic study revealed a significant association of EGLN1 SNPs with both HA adaptation and HAPE ($p < 0.001$). Of note, however, HLs depicted an increase in adaptive allele frequency with increasing altitude ($p < 0.001$), with a strong positive correlation with SaO_2 ($p < 0.05$). Furthermore, the highly methylated 5'UTR of EGLN1 in HLs ($> 50\%$ CG, $p < 0.01$) and a reverse trend in HAPE demonstrated the involvement of a strong epigenetic component under HA stress. We deduce complex genetic and epigenetic interactions with the environmental factors.

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LUNG FUNCTION AMONG ADULT TIBETAN POPULATION LIVING AT 2300 AND 5300 M IN TIBET

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Tibetans have lived at high altitude longer than any other high-altitude population. We previously reported the data of lung function among 9- to 10-year-old children in Tibet. This study compared lung function values of forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), forced expiratory flow at 25% of FVC (FEF25), forced expiratory flow at 50% of FVC (FEF50), and forced expiratory flow at 75% of FVC (FEF75) in adults living at various altitudes in Tibet. A cross-sectional study of lung function was performed among adult native Tibetans living at 2300 and 5300 m above sea level. The crude value of FVC and PEF was significantly higher in Tibetan adults living at 2300 m than in Tibetans living at 5300 m above sea level. Linear regression models were constructed for determining the relationship between the outcome variable (FVC) and the selected covariates. The difference between the Tibetans living at two different altitudes disappeared after adjusting by gender and height. Furthermore, the predicted value for lung function was significantly lower than the measured value.

Keywords: adult; high altitude; lung function; Tibet

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MICRORNA-29A EXERTS AN ANTICANCER EFFECT BY MODULATING Sp1 IN GLIOMA CELLS

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Objective: To explore the microRNA regulatory mechanism of Sp1 expression in gliomas, and to provide the exact ex-

perimental theoretical basis for the diagnosis and treatment of glioma.

Methods: (1) The expression levels of Sp1 mRNA and miR-29a were detected by real-time polymerase chain reaction (PCR) in human normal glial cells and four glioma cells, respectively. The expression of Sp1 protein was detected using Western blot. (2) The expression of Sp1 mRNA and protein was detected after miR-29a overexpression by miR-NC/29a mimics and si-NC/Sp1, real-time PCR, and Western Blot, respectively, after transient transfection with Lipofectamine 2000. (3) Bioinformatics analysis software TargetSpy and online database Targetscan, miRBase prediction shows that miR-29a can target Sp1 3'UTR region, with dual fluorescence experiment testing whether miR-29a directly binds with the specific sequence of Sp1 3'UTR region.

Results: In glioma cells, the expression of miR-29a is low and transcription factor Sp1 is highly expressed, and miR-29a is capable of direct targeting of 3'UTR specific sequences of Sp1. Of miR-29a and Sp1 functional analysis showed that miR-29a can inhibit tumor metastasis and invasion, whereas Sp1 can enhance the ability of tumor metastasis and invasion. After the overexpression of miR-29a, the expression of Sp1 mRNA and protein was downregulated.

Conclusions: miR-29a may be a tumor suppressor gene, during the progression of gliomas, by inhibiting the expression of Sp1 to inhibit the development of tumors. By studying the inhibitory effect of miR-29a on Sp1 gene, it may be helpful to improve our understanding of the pathogenesis of gliomas and provide a reliable theoretical basis for the diagnosis and treatment of gliomas.

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ABSTRACT WITHDRAWN

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CONTINUOUS MEASUREMENTS OF OXYGEN SATURATION FOR FIVE CONSECUTIVE NIGHTS AT ALTITUDE OF 3000 M IN A FAMILY WHILE ASLEEP

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Oxygen saturation (SpO₂) was measured for five consecutive nights in a Japanese family while asleep at an altitude of 3050 m. The family comprised a father (aged 43 years), mother (aged 39 years), two boys (aged 13 and 10 years), and a girl (age 7 years). They lived essentially at sea level in Japan and had visited Telluride, Colorado, USA, for a conference in 2016. None of the family members had been exposed to altitudes >2000 m for 6 months before arriving at Telluride. We used a Pulsox-300i, pulse oximeter (KONICA MINOLTA), to measure SpO₂ values every second, then separately analyzed the results for the children and the parents. The mean nocturnal SpO₂ of the children ($97.4\% \pm 0.1\%$ at sea level) decreased to $87.1\% \pm 2.0\%$ on night 1, then increased to $89.0\% \pm 0.6\%$ and $91.1\% \pm 0.2\%$ on nights 2 and 4, respectively. The mean nocturnal SpO₂ of the parents ($95.7\% \pm 1.2\%$ at sea level) decreased to $83.6\% \pm 0.6\%$ on night 1, then increased to $84.7\% \pm 0.9\%$ and $88.3\% \pm 0.3\%$ on nights 2 and 5, respectively. The SpO₂ values of the children were 3.5%–4.3% higher than those of their parents and reached a plateau between nights 3 and 5, which did not occur in the parents. Hemoglobin oxygenation levels during sleep for five nights at 3050 m were higher in children aged 6 to 13 years than in their parents aged 39 and 43 years.

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THE CHANGES AND SIGNIFICANCE OF PERIPHERAL AND CENTRAL IMMUNE CELLS AFTER HYPOXIC PRECONDITIONING AND ISCHEMIC BRAIN DAMAGE IN RATS

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In 1990, Kitagawa K carried out cerebral ischemic preconditioning (2 minutes $\times$ 2 times) in the gerbil. During this experiment, the majority of hippocampal neurons in the most vulnerable area of the hippocampal CA1 region survived 1 day later after a severe repeated cerebral ischemia lasted for 5 minutes, which thus confirmed the protective effect of hypoxia (ischemic) preconditioning. In the present experiment, rats in the simple cerebral infarction group, hypoxic preconditioning group (under simulated 5500 m altitude using low pressure oxygen cabin, 3 hours at the same time period per day for 7 days), and hypoxic preconditioning + cerebral infarction group were selected as the subjects of the study. The changes and effect of the immune system in brain protection under hypoxic preconditioning were investigated by comparing the scores of nerve function, the area of cerebral infarction, and the changes of expression in peripheral immune cells (T lymphocytes and natural killer cells) and central immune cells (microglia, oligodendrocytes, and astrocytes).

Conclusions: First hypoxia preconditioning can alleviate neurological defect symptoms and reduce the cerebral infarction area after ischemic brain damage, playing a role in brain protection; second, the expression level of microglia in rats with cerebral infarction is decreased after hypoxic preconditioning, with a reduction in activated number of cells,

indicating that hypoxia preconditioning is likely to inhibit further activation of microglia cells and thereby to inhibit their neurotoxicity and exert the neural protect function; oligodendrocytes and astrocytes may be involved in cerebral protection in case of hypoxia preconditioning.

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INTERVENTIONAL TREATMENT OF ACUTE MASSIVE HEMOPTYSIS OF TUBERCULOSIS IN THE QINGHAI-TIBET PLATEAU

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To study the clinical value of bronchial arterial embolization in the treatment of acute massive hemoptysis of pulmonary tuberculosis in the plateau area. Thirty-two patients with acute massive hemoptysis with pulmonary tuberculosis underwent conservative medical treatment and were treated with interventional embolization. Selective bronchial artery embolization therapy on the bronchial artery, internal mammary artery, intercostal artery, and infraorbital artery was performed, as well as contralateral bronchial arteriography. Among the 32 patients, 26 cases were successfully embolized once, and hemostasis was achieved immediately; hemoptysis was significantly reduced in 5 cases, and 1 case was treated with embolization again to stop bleeding with an effective rate of 100% without serious complications. Clearly showing the blood supply artery, standard catheter operation, and reasonable choice of embolization agent are the keys to successful operation and reduction of complications. The development of primary pulmonary disease and the establishment and opening of collateral vessels are the main factors for recurrent bleeding after embolization; familiar with the anatomical variation of bronchial arteries and side branch involvement in bleeding is an important guarantee for the safety and effectiveness of interventional treatment of tuberculous hemoptysis.

Keywords: big hemoptysis; bronchial arteries; interventional therapy; plateau tuberculosis

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APOPTOSIS OF PANCREATIC CELLS IN RATS WITH SEVERE ACUTE PANCREATITIS AT HIGH ALTITUDE

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Objective: To evaluate the role of apoptosis in plateau severe acute pancreatitis (SAP) and the mechanism of apoptosis in SAP by measuring the serum amylase, histopathology score, and the expression of apoptosis index, HIF-1A and Fas/FasL, of pancreatic adenoid cells at different altitudes, and to explore the pathogenesis of SAP in high altitude to better explore the pathogenesis of SAP in plateau. The diagnosis and treatment of SAP provide a theoretical basis.

Methods: Ninety-six SPF grade healthy male Wistar rats were randomly divided into three large groups, all rats were sacrificed and the serum and pancreas tissues were collected. The content of serum amylase was measured with an automatic biochemical analyzer, the pathological changes were observed by HE staining in some pancreatic tissues, the apoptosis index of pancreatic adenoid cells was measured by TUNEL, and the expression of HIF-1, Fas, and FasL in

pancreatic tissue was measured by immunohistochemical SP method.

Results: There was a significant difference in HE score and FasL expression between the three elevation groups ($p < 0.05$). Compared with AI at the same time point, the AI of pancreatic adenocarcinoma in P group at three elevations decreased gradually with the increase of altitude, and there was a significant difference ($p < 0.05$).

Conclusions: (1) SAP in plateau area is caused by hypoxia that leads to the decrease of apoptosis; (2) Fas/FasL participates in the pancreatic acinus, the conduction of apoptosis; (3) FasL can represent the high and low levels of inflammation to some extent.

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EMERGENCY MEDICINE IN NEPAL

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Emergency medicine is the youngest medical specialty recognized in Nepal. The growth of emergency medicine in academics and clinical practice has been tough as most of the emergency departments in Nepal have been staffed by general practitioners/family physicians and untrained medical officers. Most hospitals manage their emergency departments by on-call multispecialist approach, which has stalled the development of emergency medicine as a specialty. The national standards in training and certification for emergency physicians are nonexistent. So, the quality of care delivered in the emergency departments of different hospitals varies greatly. Efforts have been made in the right direction by international organizations to produce necessary human resources. ICAR, ISMM, and EURAC have come together in the past to train Nepali medicos and mountain guides to form the rescue team. For the development of emergency medicine as a specialty, a strong step from the Nepalese leadership and focused guidance from international emergency medicine community is required. This is paramount for the establishment of proper emergency medical services and promoting prehospital medicine. In the long run, this may result in a good and sustainable model of emergency medical care in Nepal.

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ABSTRACT REMOVED

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WILDERNESS AND OUTDOOR ACTIVITIES FOR THE DISABLED: RECENT CHALLENGES AND PERSPECTIVES

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Every year wilderness and outdoor activities become more popular in persons with disabilities. Nevertheless, there is a dearth of research, published guidelines, and recommendations on that topic. We reviewed outdoor recreational possibilities available for the disabled, ways of becoming travel active, and rehabilitation effects of these activities. A remarkable diversity of wilderness activities is available for persons with various physical, visual, and intellectual impairments, such as trekking, rock climbing, kayaking, skydiving, mountaineering, and alpine skiing. Specific preparticipation examination is required to assess health problems that might put persons at risk of injury or any kind of deterioration of an existing disorder, along with a detailed assessment of all environmental risks of the future wilderness activity. As a result, an individual emergency action plan should be created. Presumably people with disabilities are at a lower risk of accidents during such activities than the able bodied as the former are aware of their limitations and ready to cope with them. There are many barriers faced by the disabled, hindering them from leading an active lifestyle: intrinsic, environmental, and societal, among others. Practicing outdoor activities impact greatly not only upon overall well-being and socialization, but also upon adaptation to acquired physical disability. Leisure pursuits are an essential component of the quality of life, particularly if a person's full engagement in society is confined by a physical impairment. So, communities should develop more opportunities for wilderness and outdoor recreation for the disabled in the future.

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ENDOTHELIAL NITRIC OXIDE SYNTHASE RE-VISITED: *IN SILICO* PROFILING REVEALS NINE POTENTIAL RISK MARKERS FOR HIGH-ALTITUDE PULMONARY EDEMA

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Endothelial nitric oxide synthase (eNOS) is vital to vascular homeostasis. Until now, few select eNOS variants have been investigated in the pathogenesis of a high-altitude disorder high-altitude pulmonary edema (HAPE); whereas several other potential variants are needed to be investigated. This study, therefore, focused on *in silico* analyses to identify the most relevant eNOS risk markers toward HAPE susceptibility. The Ensembl human genome browser was used to secure the significant polymorphisms of eNOS. Furthermore, the variants located on promoter and UTR regions, showing association with vascular homeostasis, were filtered out. Lastly, to annotate the obtained SNPs, three SNP-annotation tools were utilized: (1) RegulomeDB tool to study the effect of variants in transcriptional factor binding regulation; (2) SNPinfo for functional annotation of SNPs; and (3) DIANA for specification of particular SNP-bound miRNA. A total of 31,315 sequence variants of eNOS were extracted. However, only nine SNPs were found to be localized either in promoter flanking region/UTRs and associated with the vascular homeostasis. Seven SNPs, that is, rs3918227, rs3918162, rs3918166, rs1800781, rs753482, rs3918226, and rs2070744, were located at promoter flanking region and were strongly suggestive of affecting the binding of transcriptional factors. Other two SNPs, rs7830 and rs3918211, were localized at the 3'UTR and may silence eNOS function. Our *in silico* analyses suggest the variants of these nine SNPs to contributing extensively to the pathophysiology of HAPE. Taking lead from the present findings, the experimental validation of the determined markers is in progress.

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IMPROVING READERSHIP OF UIAA MEDICAL COMMISSION ADVICE AND RECOMMENDATION PAPERS IN FIRST TIME MOUNTAINEERS: A FOCUS ON MOUNT KILIMANJARO

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A total of 20,000–40,000 people summit Mount Kilimanjaro each year, the majority are on commercially organized treks and have little previous altitude experience. Concerns have been raised about the high prevalence of altitude illness on Kilimanjaro, the UIAA produces advice papers for lay people about such travel risks. This review aims to identify ways to increase readership of online UIAA medical commission (MedCom) advice papers by first time mountaineers attempting Mount Kilimanjaro. Research conducted on Kilimanjaro shows trekkers are predominantly aged 20–50 years. The 2014 Kilimanjaro Park Authority statistics recorded highest number of trekkers from the United States and United Kingdom. The Internet is the most commonly used resource for trip planning in 25–54-year olds. Pretravel altitude health information is sought from a variety of sources commonly including the Internet. Climbing/trekking websites are most often reached through Google and Facebook. The most popular search terms are “climb Kilimanjaro” for trip planning and “altitude sickness” for altitude-related illnesses. First time mountaineers are unlikely to already follow the UIAA Facebook page; increasing followers on Facebook and increasing postshares improve chances of reaching new audiences, this can be achieved through optimization of posts, for example, short engaging posts and use of trending hashtags. These recommendations can be used by the UIAA to improve

engagement of first time mountaineers with online high-altitude advice; however, as many are unlikely to return to altitude, it is essential for the mountaineering community to continue to attempt to improve trek ascent profiles, carriage of altitude illness medications by trekking companies, and guide/porter education about high-altitude illness.

3975

LONG-TERM EFFECTS OF HIGH-ALTITUDE CEREBRAL EDEMA

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High-altitude cerebral edema (HACE) is a life threatening condition. Most HACE patients recover quickly after descent, but in some patients recovery is delayed. The purpose of this study was to provide more insight into post-HACE symptoms. We conducted a retrospective cohort study in patients who had been diagnosed with HACE. Patients were identified by approaching mountain medicine doctors per e-mail ($n = 760$). Eligible patients received a link to an online questionnaire. Post-HACE symptoms were defined as ongoing symptoms (e.g., headache, memory loss, and concentration problems) in a HACE patient, 1 week after descent to 1000 m. We included 15 patients. Post-HACE symptoms occurred in seven (47%) patients. There were significantly more women in the post-HACE symptom group than the group that recovered quickly (71% vs. 12%, $p = 0.041$). The main symptoms were headache (86%), concentration problems (86%), memory loss (86%), dizziness (43%), fatigue (29%), and intolerance of stimuli (29%). The maximum duration of symptoms was 69 weeks and in this patient the symptoms were still ongoing. In most patients, the diagnostic tests did not reveal other conditions that could explain the symptoms. Except for one patient, in whom parkinsonism was diagnosed. We conclude that not all patients with HACE recover within 1 week after descent. Post-HACE symptoms were long lasting. More research is needed to characterize post-HACE symptoms to support the development of a guideline for diagnosis and possible treatment.

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LONG-TERM RESIDENCE AT HIGH ALTITUDE ALTERS BRAIN FUNCTIONS IN A TIME-DEPENDENT MANNER IN LOWLANDERS

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High-altitude (HA) induction and residence impairs brain functions. However, there is hardly any information about the time-dependent effects of long-term residence at HA in lowlanders. This study aimed to evaluate the effect of 2 years residence at 14,500 ft altitude on brain functions. The study was conducted in normal healthy lowlanders of the Indian army in the age group 20–40 years. Sleep profile, event-related potentials, cerebral blood volume, and cognitive function tests were evaluated at sea level (Pathankot), within 7 days of induction at 14,500 ft (Loma), after 1, 6, 12, and 24 months of residence at 14,500 ft (Fukche) in the Western Himalayas. Results showed increase in sleep latency and number of awakenings and decrease in sleep efficiency at seventh day and after 1 month, but values recovered partly at 6, 12, and 24 months of residence. A reduction in mean

correct responses of choice reaction time and increased number of errors in spatial working memory and paired associate learning were observed at all time points up to 24 months of residence. Event-related potential P300 showed an increase in P3 latency and CNV showed an increased M1 peak latency at seventh day and after 6 months. There was an increase in cerebral blood volume at HA at all time points up to 24 months residence. High-altitude (14,500 ft) residence for 2 years altered neurocognitive functions and sleep architecture in a time-dependent manner in lowlanders.

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EFFECTS OF ACUTE NORMOBARIC VERSUS HYPOBARIC HYPOXIA ON REACTIVE OXYGEN SPECIES PRODUCTION ASSESSED BY ELECTRON PARAMAGNETIC RESONANCE AND OXIDATIVE DAMAGE

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Acute hypoxia induces reactive oxygen species (ROS) accumulation, generally associated with cell oxidative damage. The aim of this study was to (1) investigate in healthy lowlanders oxidative stress levels during acute exposure to normobaric hypoxia (NH, FIO₂ 12.5, 4500 msl; *n* = 57, 42.6 ± 13.7 years) and hypobaric hypoxia (HH, 3482 msl, *n* = 27, 37 ± 8.5 years; and at 3830 msl, *n* = 16, 39 ± 10.2 years); (2) evaluate the effects of (i) different passive ascending methods (cable/helicopter) and (ii) preacclimatization by NH (preacl-HH *n* = 16) on ROS production (EPR determined) and oxidative damage (lipids [TBARS, 8-iso], proteins [PC], antioxidant capacity [TAC], and DNA damage). In NH subjects, a fast ROS increase in capillary blood was observed (+44%; 3.21 ± 0.21 μmol·min⁻¹; *p* < 0.001) related to oxygen saturation (SaO₂) reduction (−17%), returning to prehypoxic levels at the end of NH (2.23 ± 0.20 μmol·min⁻¹). In HH, an oxidative damage was found (at 4 hours, TBARS +10, *p* < 0.05; PC +80%, *p* < 0.01) and up to 1 hour recovery (TBARS +28%, *p* < 0.01; PC +70%, *p* < 0.05), coming back to basal within 8 hours. In HH, ROS significantly increased peaking at 24 hours (range +90%–141%; 4.32 ± 0.68 μmol·min⁻¹; *p* < 0.01), according to the SaO₂ reduction (−14%), decreasing thereafter. At the same time PC, TBARS, 8-iso, and DNA increases were in the 50%–85% range, TAC decreased up to 40%. Passive HH exposure was associated with higher ROS production and related oxidative damage compared with NH (*p* < 0.01; *p* < 0.05 respectively). No differences were found for oxidative stress level according to ascending modality. One hour of simulated hypoxia a day

before HH exposure induced a significant reduction of ROS production (preacl-HH 70 vs. HH 110%; *p* < 0.01).

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TELECONSULTATION IN THE MOUNTAINS: THE ROLE OF NURSES EXPERT IN MOUNTAIN MEDICINE

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Introduction and Aim: From June 2017 to March 2018, five trained nurses were involved in the é-Res@mont project to develop a new model of teleconsultation in a remote area.

Methods: Nurses were trained in emergency setting and mountain medicine before starting the activity. The teleconsultation took place in five remote locations between 1500 and 3500 m, connected to the doctor through a telematic platform. Communication took place by data transmission, images, or through videoconference. Doctors and nurses chose the validated scales readjusted according to the altitude, defined tools, drugs, and identified a protocol to follow in case of lack of connection. On the basis of symptoms, patients were subjected to clinical evaluation (i.e., vital parameters, pulse oximetry, body mass index, and Lake Louise Score questionnaire); moreover a 12-lead electrocardiogram and lung echo could be performed. Based on the data received, the doctor made diagnosis and gave instructions to the nurse who provided the care.

Results: The activity was carried out for 7 months, with 702 visits (male 61%; average age 49 ± 17 years). The mean value for vital parameters was different according to altitude. The most treated pathologies were acute mountain sickness 8.0%, headache 4.0%, minor trauma 2.3%, and gastrointestinal disorders 1.3%. In 30 cases, the use of emergency rescue was avoided, specifically in 31% of cases the use of helicopter rescue. The average time of response to the nurse call was 20 minutes.

Conclusions: Trained nurses in mountain medicine and telemedicine are crucial: they are link between patients and doctors in the management of critical situation in a mountain environment.

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DEMOGRAPHIC PROFILE OF HELICOPTER-RESCUED PATIENTS VISITING CIWEC HOSPITAL

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Trekking and climbing are popular tourist activities in Nepal and sick travelers are often evacuated to Kathmandu by helicopter. We conducted a retrospective chart study from January 2016 to December 2017 to describe the prevalence and indication of helicopter-rescued patients from different regions of Nepal presenting at CIWEC Hospital.

Results: Among 1353 patients evacuated from the mountains and seen at our facility during the study period, 59% were male and the mean age was 41.8 years. Maximum number of

evacuations (almost two-third) was from the Everest region followed by Annapurna and Makalu trekking regions. Maximum evacuations were from the altitude of 2500 to 5000 m (usual trekking altitudes); however, significant number of evacuations was from altitudes of 5000 m or greater. Hospital diagnoses were extremely varied. Altitude illness with acute mountain sickness, high-altitude cerebral, and pulmonary edema was the most common diagnoses at 65% followed by musculoskeletal and gastrointestinal problems. Forty-four percent of the patients required hospitalization and two needed referral to other centers. The hospital stay ranged from 1 to 20 days, one-fourth of the patients requiring only one night of observation.

Conclusions: Easy accessibility of helicopter services has increased the number of rescues from the mountains as compared with a previous study. Helicopter rescues are occurring from higher altitudes, bringing sick travelers quicker to medical care in Kathmandu. This study provides better understanding of medical emergencies occurring on the mountains of Nepal and compares it with prior published work from CIWEC Hospital.

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THE EXPRESSION OF IMMUNOMOLECULES CD35, CD44, CD58, AND CD59 ON ERYTHROCYTES IN PERIPHERAL BLOOD OF PATIENTS IN CHRONIC MOUNTAIN SICKNESS

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Objective: To study the expression of immune molecules including CD35, CD44, CD58, and CD59 on erythrocytes in peripheral blood among patients in chronic mountain sickness (CMS), and to explore the changes of the immune function and clinical value in CMS.

Methods: The expression levels of CD35, CD44, CD58, and CD59 on the surface of mature erythrocytes in peripheral blood of CMS patients (30 cases) were detected by flow cytometry.

Results: The positive rates of CD35, CD44, and CD58 on erythrocyte surface in peripheral blood of patients in CMS were significantly lower than those of the normal control group with statistically significant difference ($p < 0.05$), and the expression of CD59 was not statistically significantly different ($p > 0.05$).

Conclusions: The immune function of erythrocyte in peripheral blood with patients in CMS decreases and provides the basis for the weakening of body resistance and the occurrence and prevention of infection in CMS.

Keywords: CD35; CD44; CD58; CD59; CMS; erythrocyte

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ABSTRACT WITHDRAWN

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LEVEL OF KNOWLEDGE ABOUT MOUNTAIN MEDICINE IN MOUNTAINEERS WHO TRIED TO ASCEND Mt. DHAULAGIRI DURING SPRING 2018

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Objective: Each season thousands of mountaineers try to ascend the 14 highest peaks of the planet, exposing themselves to the inherent medical conditions of the mountain. Identification and initial treatment are in the majority of cases in hands of them. To assess the general knowledge of mountain medicine, we conducted a field survey during the spring 2018 season in Mt. Dhaulagiri. We interviewed 17 mountaineers (informed consent) who anonymously answered a survey of eight questions (Have you received any formal mountain first aid course? Do you know how to identify acute mountain sickness [AMS], high-altitude cerebral edema [HACE], high-altitude pulmonary edema [HAPE]? Do you know the initial management of AMS, HACE, HAPE, Frostbite?).

Results: 23.5% reported having done some formal first aid course. Although 100% reported knowing how to recognize the AMS, none of them responded correctly to the symptoms described in the Lake Louise scale. Regarding HACE, 88% reported knowing how to recognize it, nevertheless 53% of them answered correctly. HAPE, 94% would know how to recognize it, nevertheless none of them answered correctly. AMS: 94% said they know how to treat it, but 18.7% of them answered correctly. HACE: 94% reported, with 87.5% correct answers. HAPE: 88.2% reported and 66% were correct. Frostbite: 88.2% reported, no one described a correct treatment.

Conclusions: Although the number of participants was low, the results were alarming. The level of general knowledge was unsatisfactory. It seems necessary to promote the training of mountaineers in this area.

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NUTRITIONAL STATUS DURING ACCLIMATIZATION AND STAY AT HIGH ALTITUDE

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The energy and nutrient requirements are more at high altitude than at sea level. Appetite and thirst perceptions are also inappropriate under cold and hypoxic environment and lead to inadequate food and water intake. The diet of humans differs in quantity and composition in different high-altitude regions. Although much of this variation may be due to availability of food in that area, there is a possibility of selection of certain classes of foods or adaptation to some dietary habits, which help in acclimatization process in that environment. Decreased food intake due to high-altitude anorexia causes negative energy balance, leading to loss of body mass in sojourners. Possible mechanism of anorexia could be changes in appetite regulatory peptides and proteins such as leptin, ghrelin, and CCK-8 observed under different studies on humans under field conditions and animals exposed to simulated environment. The digestibility and absorption of different nutrients are not adversely affected at heights up to 4500 m. High-carbohydrate diets are beneficial under hypoxic environment of high altitudes during early days of acclimatization. Requirement of B group of vitamins, antioxidants, and minerals is increased due to higher energy expenditure and oxidative stress. Maintenance of adequate hydration level is also important for work efficiency and proper acclimatization. The planning of ration for expeditions, military missions, and relief operations is a challenging task as balance between nutrient requirements for optimum health, palatability, and logistics of food preparation need to be ensured.

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EXPOSURE TO HIGH ALTITUDE: A POSSIBLE RISK FACTOR FOR VENOUS THROMBOEMBOLISM

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Introduction: Several reports from Indian Army have documented that Indian soldiers stationed at high-to-extreme altitudes for prolonged period suffer from various maladies related to extreme adverse conditions prevailing at high altitudes (HA). The increased incidences of both venous and arterial thrombotic episodes have been reported from HA regions. Although no exact epidemiological records are available for Indian Army, high incidences of venous thromboembolism (VTE) have been reported in Indian troops posted at HA. VTE has two major clinical implications that include deep vein thrombosis (DVT) and pulmonary embolism, the latter being potentially fatal. It is a complex multifactorial disease with unknown pathophysiological mechanism with several genetic and acquired risk factors. Our previous studies have shown that predisposing factors for VTE in Indians are different from those of Western counterparts.

Methodology: In compliance with our previous findings, an interdisciplinary approach addressing the genetic molecular proteomics is under investigation, to identify the known or novel biomarkers for VTE by using *in silico* analysis, real-time polymerase chain reaction, ITAQ analysis, and enzyme-linked immunosorbent assay in healthy volunteers and HA-DVT patients.

Results: By using this global approach, validation of novel targets as protein biomarkers and molecular signatures for

HA-induced DVT in the Indian population is under progress. Epigenetic modification, especially the role of methylation in HA-induced DVT, is also studied.

Conclusions: This comprehensive approach will help us to understand the molecular mechanism for HA-induced VTE to screen genetically susceptible individuals and formulate strategies for early prevention, diagnosis, and treatment.

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IMPACT OF CNVs UNDER HYPOBARIC HYPOXIA AT HIGH ALTITUDE

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Hypobaric hypoxia at high altitude (HA, 1500–3500 m) is the primary cause of stress concerning mountain diseases. In susceptible sojourners, hypobaric hypoxia stimulates oxidative stress, triggering endothelial damage and vascular wall remodeling leading to high-altitude pulmonary edema (HAPE); whereas genetic remodeling in HA natives stems their successful physiological adaptation. The literature attributes the role of various SNPs in HAPE and HA adaptation; however, the role of CNVs remains scarce. Hence, we aimed to decipher CNVs in HA physiology by conducting a genome-wide genotyping in three distinct study groups, namely HA natives (HLs), HAPE free (HAPE-f), and HAPE patients (HAPE-p). Extensive statistical and association analyses identified CNVs associating with HA health and disease. Dimensional analyses revealed that high- and low-altitude populations portray significantly higher deletion and duplication CNVs, respectively ($p = 0.001$). Furthermore, duplication and deletion CNVs associate with health and disorder of sojourners, respectively. Association analyses of CNVs revealed association of CNVs spanning (1) IKZF3, MEX3D, and MORF4L1 among others with HAPE protection, enriched for pathways such as serotonin receptors and HIF-1- α transcription factor network, (2) CREB1, HTR7, and CP among others with HAPE susceptibility, enriched for pathways such as T cell activation and oxidation by cytochrome-P450, and (3) TECRL, CSKN1E, and MTRR among others with HA adaptation, enriched for pathways such as aldosterone-regulated sodium reabsorption, vascular smooth muscle contraction, and iron metabolism. ($p = 0.001$). Intriguingly, these pathways are of physiological significance in HA disease and health. To conclude, this study reveals CNVs in possibly environmental sensor genes that assist us to perceive and adapt to environmental changes.

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CEREBROVASCULAR RESERVE: DIFFERENCES BETWEEN HEALTHY TIBETAN AND HAN ETHNICITIES AT DIFFERENT ALTITUDES REVEALED BY METHAZOLAMIDE TEST-BASED COMPUTED TOMOGRAPHY PERFUSION

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Purpose: To investigate the differences of cerebrovascular reserve capacity between healthy Tibetan and Han ethnicities and its relationship with different altitudes.

Methods: Forty cases of healthy Tibetan and Han ethnicities at the middle and high altitude underwent pre- and post-methazolamide test-based computed tomography perfusion (Revolution, GE). Data of cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT), and cerebrovascular reserve (CVR) were processed with SPSS 21.0 software, separately.

Results: Both CBF and CBV increased, with MTT decreased on postprovocation test. Compared with preprovocation test, there were statistical CBV differences in ROIs, except for in temporal and occipital lobes of Han at middle altitude, in thalamus of Han at high altitude, for MTT in frontal lobe of Tibetan at middle altitude, in temporal lobe and thalamus of Tibetan at high altitude, and in lenticular nucleus of Tibetan and Han at middle altitude. There were no CVR differences in frontal, temporal, and occipital lobes, and lenticular nucleus, and thalamus between Tibetan and Han at middle altitude; however, CVR in temporal lobe and lenticular nucleus of Tibetan were significant higher than those in Han at high altitude. In Tibetans, CVR measured at middle and high altitude, was shown to be significantly different in frontal, temporal, and occipital lobes, as well as the thalamus. Whereas, in Han, CVR was only shown to be significantly different in the frontal lobe and thalamus, where CVR at high altitude was found to be greater than when measured at middle altitude.

Conclusions: CVR capacity at high altitude is higher than that at middle altitude in both Tibetan and Han ethnicities. CVR capacity at high altitude in Tibetan is higher than that in Han ethnicity.

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OPTIMIZING HUMAN HEALTH IN HIGH ALTITUDE: DRDO'S INITIATIVES

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High-altitude research is important for India as a sizable population lives in the High Himalayan Region and many lowlanders visit and stay there for different time durations for occupational, sport activities, pilgrimage, etc. Cold and hypoxic environment has adverse effects on human health if appropriate preventive measures such as proper acclimatization, cold protection, and nutrition are not taken into consideration. We have taken initiatives on physiological process of acclimatization with the aim to prevent high-altitude maladies and optimization of performance of our soldiers deployed in high and extreme altitudes. Acclimatization schedule and tenure of stay are in use, and modalities for rapid induction and acclimatization to high altitude are being worked out. Nitric oxide therapy for treatment of high-altitude pulmonary edema (HAPE) and Alocal, an Aloe vera-based cream, for prevention and treatment of chilblains and frostbite have been found quite effective. Studies on the mechanism of appetite loss at high altitude have shown that complex interplay of different hormones and peptides results in negative energy balance with increased level of muscle protein degradation at heights >4300 m. Efforts are on for early detection of clotting disorder such as deep vein thrombosis. Our studies have revealed that HAPE-susceptible individuals (old HAPE cases) had elevated pulmonary artery pressure and BNP when subjected to hypoxia at sea level. DRDO's three establishments located in Western, Central, and Eastern Himalayas of India have developed a

large number of high-altitude agrotechnologies to augment fresh food availability for nutritional and health security in Trans-Himalayan regions.

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ASSOCIATION OF HIGH-ALTITUDE PULMONARY EDEMA RISK WITH TELOMERE LENGTH-RELATED GENES IN CHINESE HAN POPULATION

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High-altitude pulmonary edema (HAPE) is a potentially fatal form of severe high-altitude illness with the symptoms occurring at altitudes >2500 m in hypobaric hypoxia regions. In general, the environment and multiple genes contributed to the pathogenesis and progression of HAPE. Telomere length was significantly influenced by hypoxic exposure. We speculate that single nucleotide polymorphisms (SNPs) in the telomere-associated genes may contribute to the susceptibility of HAPE. A total of 43 SNPs within 13 telomere length-related genes (ACYP2, TERC, ARPM1, NAF1, TERT, TNIP1, OBFC1, MPHOSPH6, ZNF208, LOC105372327, STMN3, RTEL1, and TNFRSF6B) were genotyped using Sequenom's MassArray platform among 303 controls and 265 cases. Logistic regression adjusting for age and gender was carried out to estimate risk associations between specific genotype and haplotype frequencies and HAPE. The analysis revealed the most significant relationship between the presence of homozygotic genotype for ACYP2 rs6713088 G/G and increased risk of HAPE (codominant model, odds ratio [OR] = 1.84, 95% confidence interval [CI]: 1.10–3.07, $p = 0.020$; recessive model, OR = 1.85, 95% CI: 1.18–2.91, $p = 0.008$) after adjustment analysis for age and gender. The haplotype analysis revealed that strong linkage disequilibrium mapped in a 19kb LD haplotype block for SNPs rs6089953 and rs6010621, and the "GC" frequency was found to be associated with a decreased risk of HAPE (OR = 0.60, 95% CI: 0.45–0.81, $p < 0.001$). The results provided evidence that telomere length-related genes ACYP2, RTEL1, and TNFRSF6B polymorphisms are potentially implicated in HAPE susceptibility in Chinese Han population, which will provide useful information for screening, the early detection of HAPE, and shed new light on the length-related genes for HAPE susceptibility.

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"ITALY BIOMEDICAL RESEARCH—SHERPA PROJECT—NEPAL": PRELIMINARY RESULTS OF ENVIRONMENTALLY MODULATED METABOLIC ADAPTATION TO HYPOXIA IN ALTITUDE NATIVES AND SEA LEVEL DWELLERS

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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; determined 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. $0.16 \pm 0.01 \mu\text{mol} \cdot \text{min}^{-1}$) 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 ($0.16 \pm 0.02 \mu\text{mol} \cdot \text{min}^{-1}$, vs. $1.08 \pm 0.36 \text{ nmol} \cdot \text{mg}^{-1}$ 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.

3997

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).

3998

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 ($\text{FIO}_2 = 0.125$), 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·hour⁻¹ vs. 58.9 ± 34.4 events·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.

3999

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 (~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-1 β , 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

4000

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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Objective: To observe the nutrient status and clinical outcome before and after the efficacy of anti-infection in the treatment in hospitalized elderly chronic obstructive pulmonary disease (COPD) patients at high-altitude area.

Methods: Nutritional Risk Screening Scale (NRS2002) was used to perform nutritional risk screening for 60 elderly patients with COPD at high-altitude area. Body mass index, serum albumin, and prealbumin were measured before and after the efficacy of anti-infection in the treatment, and complications and length of hospitalization were observed after anti-infection.

Results: Patients with NRS2002 score = 3 points were 28 cases, and patients with NRS2002 < 3 points were 32 cases, the incidence rate of nutritional risk was 53.33%; there were significant differences of body mass index, serum albumin and prealbumin, complication, and length of hospitalization before and after anti-infection between patients with NRS2002 score = 3 points and patients with NRS2002 < 3 points ($p < 0.05$).

Conclusions: There is a high nutritional risk in elderly COPD patients at high-altitude area. Implementation of nutritional risk screening for such patients can detect the potential malnutrition and improve the clinical symptoms.

Keywords: COPD; high-altitude area; nutritional risk screening scale; nutritional screening

4002

SHERPA-EVEREST'2017 PROJECT: CARDIO-PULMONARY CHANGES BETWEEN CAUCASIANS AND SHERPAS AT Mt. EVEREST BASE CAMP (5364 m)

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Roughly 30,000 people trek yearly across the Khumbu valley until Everest base camp (EBC). Respiratory and cardiovascular systems experiment major functional adaptations at this high altitude. With the aim to explore some of these adaptations during a 9-day trekking from Luckla to EBC, we have compared 19 Caucasians trekkers (CT) with 15 Sherpa climbers (SC) at EBC (5634 m), by means of clinical measurements during resting conditions: heart rate (HR), arterial blood pressure, oxygen saturation (SpO₂), and forced vital capacity (FVC). A significant decrease in HR, SpO₂, and FVC was observed in all CT subjects compared with basal determinations ($p = 0.01$). The average SpO₂ at EBC was equal between CT and SC ($83\% \pm 5\%$ and $83\% \pm 4\%$, respectively, with $p = 0.873$), but HR presented significant differences between the CT and SC groups ($p = 0.004$). Paradoxically, our observation reflects that at EBC, the SC had higher basal HR with respect to CT, although there were no significant differences in SpO₂ between both ethnic groups. We do not have physiological explanation for this finding (although it could be justified by stressor factors associated with the medical procedures in SC). *The study is supported by Fundació La Caixa. Our gratitude goes to Ferran Latorre.

4004

SPLEEN VOLUME AND CONTRACTION DURING APNEA IN Mt. EVEREST CLIMBERS AND EVEREST BASE CAMP TREKKERS

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The factors determining individual tolerance to altitude are quite unknown. The spleen could be involved as it stores a reserve of red blood cells ejected into circulation during hypoxia. We previously found that the spleen contracts more during apnea after summiting Mt. Everest and that spleen volume increased after a trek to moderate altitude. We measured spleen volume and contraction in two groups each containing 12 European subjects (each three women): one planning to summit Mt. Everest (8848 m; "Climbers") and another trekking to Everest base camp (5300 m; "Trekking"). Tests were done in Kathmandu (1370 m) 1–3 days after arrival. Height, weight, and age of the subjects were similar (NS). After collecting anthropometrics and 15 minutes sitting rest, subjects performed a 1-minute apnea and, after 2 minutes rest, one maximal duration apnea. Three-axial spleen diameters were measured through ultrasonic imaging every minute for volume calculation. Mean (+SD) baseline spleen volume was larger in Climbers (367 + 181 mL) than in Trekkers (215 + 68 mL; $p = 0.013$), and lung volume tended to be larger in Climbers ($5.7 + 1.3$ vs. $4.7 + 1.3$ L; $p = 0.080$). Spleen contraction occurred during apneas in both groups, with the magnitude slightly larger in Climbers (266 vs. 169 mL; $p = 0.053$). Maximal apneic duration was longer in Climbers ($88 + 23$ vs. $63 + 22$ seconds; $p = 0.012$). One Climber and one Trekker turned early (7000 and 4400 m, respectively). Summiting 8000-m peaks requires considerable physiological preparation and most likely a favorable genetic predisposition and the differences between groups are probably due to both. Spleen and lung volumes were previously found to correlate with freediving ability, and may also characterize good climbers.

4005

CHOROIDAL THICKNESS CHANGES INDUCED BY HYPOXIA IN HIGH-ALTITUDE CONDITIONS: RESULTS FROM THE SHERPA-EVEREST'2017 PROJECT

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Ocular alterations induced by altitude include retinopathy, papilledema, and increased corneal thickness. Alterations in

the permeability of blood–brain–retinal barriers have a crucial role in the pathophysiology of the eye at high-altitude hypoxia. Eleven trekkers (9♂, 2♀) aged 22–58 years were studied using optical coherence tomography (OCT; swept-source domain). Measurements of the thickness of neurosensory retina, retinal nerve fiber layer, and choroidal vessel layers thickness (CVLT) were analyzed at sea level conditions, both before (A) and after (B) a 9-day trekking until Everest base camp (5364 m). A new control (C) was performed 1 month after withdraw altitude. As a preliminary analysis of ophthalmologic data, we present the results obtained of CVLT, where significant changes from high-altitude adaptation have been observed ($p = 0.006$). The CVLT decreased between measurements A and B by $6.84 \mu\text{m}$. It is a remarkable fact that 1 month after remaining at sea level (C), normal values have not yet recovered (although not significant at the global level). Cerebral hypoxia induces a predominance balance of arterial vasodilation, increased blood flow, venous drainage delay, and altered capillary permeability. A close anatomic correlation between vascular blood supply to the brain and the retina could explain changes observed in thickness of high-vascularized ocular structures, such as the case of retina and choroids. *This study is supported by Fundació La Caixa and the collaboration of TOPCON. Our gratitude goes to Ferran Latorre

4006

THE CHANGING DEMOGRAPHICS OF MOUNTAIN PORTERS IN THE GOKYO VALLEY OF NEPAL

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Commercial trekking companies are increasingly raising concerns at the lack of experienced porters to sustain the industry. Anecdotal reports suggest that a younger population is emerging that is less skilled at dealing with the challenges of the high-altitude environment. During a 3-week period in the postmonsoon season of 2017, 24 porters who stayed in Machermo village (4450 m) were interviewed by a native Nepali speaker to improve the care provided for porters at the IPPG-CAN Rescue Post in the village. Basic anonymized demographics were collected and the primary objective for portering and knowledge of altitude illness were discussed. All the porters interviewed were male with a median age of 21 (range 14–52 years) and, on average, only 1 year of portering experience (range 1–25 years). The commonest reason for portering was to help to support families and provide education for children, but six porters gave their primary objective as earning “pocket money” during school holidays. With one exception, all the responders described headache as a symptom of altitude illness but only one porter identified rapid ascent as a cause, whereas half of the porters thought that garlic prevented and treated altitude illness. Fifteen responders recognized descent as treatment for altitude illness. The commonest problems were finding safe accommodation (7/24) and the risk of illness (6/24). Only half of the porters knew about the rescue posts in the Gokyo Valley. Furthermore, formal work is needed to confirm these initial findings and improve care for trekking porters in Nepal.

4007

FAT MASS AND OBESITY-ASSOCIATED PROTEIN IN CHRONICALLY HYPOXIC MYOCARDIUM

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Adaptation to chronic hypoxia renders the heart more tolerant to ischemia/reperfusion injury. One of the adaptative changes is a shift in cellular energy metabolism. This alteration may be regulated by recently discovered fat mass and obesity-associated (FTO) protein, an RNA-based epigenetic regulator (N-6 methyladenosine demethylase), known to affect energy metabolism. This project aimed to study the role of FTO in the chronically hypoxic hearts. Adult male Sprague–Dawley rats were adapted to continuous normobaric hypoxia (CNH; 10% or 12% O₂; 3 weeks). CNH reduced the size of myocardial infarction by 20% in these animals. The FTO protein level was measured in the tissues of left (LV) and right (RV) heart ventricles and moreover in the liver and the cerebrum. Under the normoxic conditions, the level of FTO in the RV was 50% higher than in the LV. No circadian rhythmicity of FTO protein in the heart was observed. In the liver and the cerebrum, the levels of FTO were 6 times and 11 times higher than in the LV. CNH led to a significant increase of FTO protein level by 21% in the LV and by 27% in the RV. In the liver and the cerebrum, the levels were unaffected by CNH. Inhibition of FTO activity influenced levels of key regulatory metabolites (e.g., malonyl-CoA, regulator of fatty acid β oxidation) in isolated adult rat cardiomyocytes exposed to 24 hours hypoxia (2.5% O₂). Our results show that CNH increases level of the FTO in the heart, which may potentially participate in the ischemia-resistant phenotype.

4008

ASSOCIATION BETWEEN THE DIVING RESPONSE DURING APNEA AT SEA LEVEL AND THE ARTERIAL OXYGEN SATURATION AT SIMULATED HIGH ALTITUDE

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Acute mountain sickness (AMS) is caused by hypoxia and related to the lowered arterial oxygen saturation (SaO₂) occurring at high altitude. It is presently unknown what causes the great interindividual difference in susceptibility for AMS, and no simple predictive test exists. Apneic diving is another activity involving exposure to hypoxia, and the oxygen conserving “diving response,” consisting of selective vasoconstriction and heart rate (HR) reduction, is also known for great interindividual differences. We studied the individual diving response during voluntary apnea at sea level and SaO₂ at simulated high altitude in a normobaric hypoxic chamber. Fourteen healthy well-trained volunteers (three women) with mean (SD) age 24 (4) years participated. They performed three apneas spaced by 2 minutes rest, the first limited to 1 minute, the following of maximal duration. Twenty minutes after, apneas subjects were

exposed to simulated 5300 m altitude (10.7% O₂) for 30 minutes. HR and SaO₂ were measured using pulse oximetry. There was a positive correlation between the magnitude of the diving response (Δ HR during apnea) and the lowest SaO₂ at simulated altitude ($r = 0.605$; $p = 0.029$). There was also a positive correlation between minimum SaO₂ during 1 minute apnea and at 5300 m altitude ($r = 0.647$; $p = 0.017$). We concluded that there is an association between the apneic diving response and SaO₂ at high altitude, suggesting that the same defense system is involved in both situations. This association could help explain the interindividual differences in high-altitude susceptibility and be the first step in developing a predictive test for the individual risk of AMS.

4009

CROSS-SECTIONAL AND PROSPECTIVE STUDY OF THE ASSOCIATION BETWEEN LIFESTYLE, INDIVIDUAL RISK FACTORS, AND ACUTE MOUNTAIN SICKNESS

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In recent years, there has been an increase in the attendance of people at high altitudes for both tourism and work, so high-altitude diseases represent a non-negligible public health problem. This research examined cross-sectional and prospective associations of lifestyle, individual risk factors, and acute mountain sickness (AMS) in a community-based sample recruited in the cross-border area (Switzerland, Italy, and France Alps). Questionnaires were administered in the five mountain locations in Aosta Valley between 1500 and 3500 m. Data were analyzed from 1002 subjects (males 68.7%, females 31.3%; mean age 42 ± 14 years) in a cross-sectional study (session T0) and from 1112 interviews in a longitudinal study on three consecutive days (session T1-T2-T3), $n = 631$ in T1, $n = 300$ in T2, and $n = 181$ in T3. According to Lake Louise Score self-reported, at session T0, 35.9% of the subjects were classified as mild AMS and 17.5% as moderate-severe AMS. Among the subjects enrolled in the prospective study, 36.5% were classified as mild or moderate/severe AMS in at least one of the 3 days. Predisposing factors to AMS detected in the prospective study were gender (male; odds ratio [OR] = 1.4, confidence interval [CI]: 2.9–11.7; $p = 0.001$), history of strenuous physical activity (> 3 times per week) (OR = 3.1, CI: 2.1–8.7; $p = 0.001$), smoking > 5 cigarettes per day (OR = 2.4, CI: 2.0–6.5; $p = 0.001$), difficulty sleeping (≤ 6 hours), and previous AMS episode (OR = 1.4, CI: 1.2–1.6; $p = 0.001$). Life style could increase AMS risk. Further studies are needed to investigate whether interventions in life style behavior can modify the impact in high-altitude diseases.

4010

ANALYSIS OF RISK FACTORS ASSOCIATED WITH PROTEINURIA IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME IN HIGH-ALTITUDE AREA

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Objective: To analyze the prevalence and risk factors of proteinuria in obstructive sleep apnea-hypopnea syndrome (OSAHS) in Qinghai.

Methods: Data of patients diagnosed with OSAHS from November 2015 to November 2017 at the Affiliated Hospital of Qinghai University were continuously collected and patient's gender, nationality, age, lipids, HbA1c, and blood uric acid (UA), white blood cell count (WBC), hemoglobin (Hb), fasting blood glucose (GLU), smoking history, history of hypertension, history of coronary artery disease, body mass index (BMI), altitude, and 24-hour urine protein quantification were retrospectively reviewed. Inter-related and risk factors were analyzed.

Results: The detection rate of proteinuria in patients with OSAHS was 29.41% (35/119). There was no significant difference in age, nationality, gender, WBC, UA, Hb, GLU, smoking history, and coronary heart disease between OSAHS with proteinuria and uncombined proteinuria ($p > 0.05$); BMI with proteinuria HbA1c was higher than those without proteinuria ($p < 0.05$). The prevalence of hypertension and dyslipidemia in patients with proteinuria was significantly higher than those without albuminuria ($p < 0.05$). Whether or not the patients with OSAHS had proteinuria as the dependent variable and the univariate analysis as independent variables (hypertension, dyslipidemia, elevation, BMI, and HbA1c) was analyzed by multivariate logistic regression analysis, the results were retained at the $\alpha = 0.05$ level. The variables of the model are altitude and HbA1c. The OR values are 1.002 and 3.359.

Conclusions: The detection rate of proteinuria in patients with OSAHS in Qinghai is 29.41% (35/119). The detection rate increases with HbA1c and altitude. HbA1c has the greatest effect on the detection rate and is the main independent risk factor.

4012

PHYSIOLOGICAL PARAMETERS TO PREDICT ACUTE MOUNTAIN SICKNESS BASED ON LAKE LOUISE QUESTIONNAIRE SYMPTOMS: RESULTS FROM THE SHERPA-EVEREST'2017 PROJECT

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Lake Louise Scoring (LLS) uses a questionnaire to evaluate adults for symptoms of acute mountain sickness (AMS). With the aim of assessing the effect of cardiorespiratory function and the stage trail structure in the automatic prediction of LLS, measurements for 15 well-trained healthy trekkers were recorded along seven stages along the route from Lukla (2860 m) to Everest base camp (5364 m). These involve rest-

ing pulse oximetry (SpO₂), heart rate (HR), and arterial blood pressure, in addition to stage trail structure measurements, such as total vertical ascent and descent of each stage, and stage length, and individual parameters, such as age, gender, and body mass index are also taken into account. We predict binary LLS values at the end of each stage, distinguishing absence of symptoms (LLS < 3) against mild-severe AMS (LLS = 3) with $n = 100$ examples. We use a relaxed LASSO-like methodology for factor analysis. Confidence is assessed by means of 500 runs of a permutation test. The prediction power of the method is 72% with an area under the curve of 0.74 with $p = 0.036$. The average recall is 72.8% with $p = 0.016$. Despite the complexity of AMS and the fact that LLS is highly dependent on the individual, our results add more pieces of evidence on the importance of SpO₂ and HR as predictors of LLS as an evaluator of AMS. Stage length seems to have a small influence, probably due to this parameter being a proxy of fatigue. *The study is supported by Fundació La Caixa. Our gratitude goes to Ferran Latorre.

4013

EFFECTS OF 300 AND 1500 M ALTITUDE ON CARDIOVASCULAR RESPONSES DURING APNEA

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Aiming to develop a field test to predict acute mountain sickness susceptibility using an apnea protocol, we evaluated the effects of 1500 m altitude compared with sea level conditions (300 m) on apneic duration, SaO₂, and “diving response” heart rate (HR) reduction during apnea. Ten healthy participants (mean $\pm$ SD age 28 ± 3 years; six females) performed two tests in a weighted order at 300 m and simulated 1500 m altitude in a normobaric hypoxic chamber. Subjects performed one 1 minute apnea (A1) and two maximal apneas (A2; A3) separated by 2 minutes rest; 20 seconds of hyperventilation preceded A3. SaO₂ and HR were continuously measured using pulse oximetry. A2 duration was 86 ± 20 seconds at 300 m and 76 ± 20 seconds at 1500 m ($p < 0.01$). A3 duration was 109 ± 25 seconds at 300 m and 98 ± 23 seconds at 1500 m (NS). Mean HR dropped by 8%–10% during maximal apneas ($p < 0.05$) with no differences between conditions (NS). Individual diving bradycardia (Δ HR) during maximal apneas was correlated between the two conditions (A2: $r = 0.94$, $p < 0.01$; A3: $r = 0.68$, $p < 0.05$). Baseline SaO₂ was $99\% \pm 1\%$ at 300 m and $96\% \pm 2\%$ at 1500 m ($p < 0.01$). During A1 SaO₂ decreased by $3\% \pm 2\%$ at 300 m and $6\% \pm 3\%$ at 1500 m ($p < 0.01$). During A2 and A3, SaO₂ decreased by $6\% \pm 4\%$ and $9\% \pm 5\%$ at 300 m and by $7\% \pm 4\%$ and $11\% \pm 7\%$ at 1500 m (NS). We concluded that although apneic duration and SaO₂ after apnea are reduced at 1500 m compared with 300 m, the correlation between the diving bradycardia in both conditions shows that individual physiological responses remain consistent, suggesting that an apnea protocol may be used in both conditions for comparable results and without prior acclimatization.

4015

ACUTE MOUNTAIN SICKNESS PREVENTION WITH IBUPROFEN RELATIVE TO ACETAZOLAMIDE

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Acute mountain sickness (AMS) is a common occurrence with travel to high altitude. Although previous studies of ibuprofen have shown efficacy for AMS prevention, recommendations have been limited, as it has not been compared directly with acetazolamide, until this study. Adult volunteers were randomized to ibuprofen 600 mg, three times daily, 4 hours before ascent or acetazolamide 125 mg, twice daily, started the night before ascent to 3810 m in the White Mountains of California. The main outcome measure was AMS incidence, using the Lake Louise Questionnaire (LLQ), with a score of >3 with headache. Sleep quality and headache severity were measured with the Groningen Sleep Quality Survey (GSQS) and a modified visual analogue scale (mVAS). Ninety-two participants completed the study: 45 (49%) ibuprofen and 47 (51%) acetazolamide. The incidence of AMS was 56.5%, with ibuprofen 11% greater than acetazolamide, surpassing the predetermined 26% noninferiority margin (62.2% vs. 51.1%, 95% confidence interval [CI]: -11.1% to 33.5%). No difference was found in the total LLQ scores or subgroup symptoms between drugs ($p = 0.8$). The GSQS correlated with LLQ sleep ($r = 0.77$, 95% CI: 0.67 to 0.84) as was the mVAS with total LLQ severity ($r = 0.57$, 95% CI: 0.42 to 0.7). The acetazolamide group had higher SpO₂ than ibuprofen (88.5% vs. 85.6%, $p = 0.001$). Ibuprofen did not demonstrate noninferiority to acetazolamide for AMS prevention and should not be recommended over acetazolamide for rapid ascent. Average symptoms and severity were similar between drugs, suggesting prevention of disease.

4016

THE DIVING RESPONSE DURING APNEA CORRELATES WITH ACUTE MOUNTAIN SICKNESS SYMPTOMS IN EVEREST BASE CAMP TREKKERS

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The diving response, defined as the heart rate reduction (Δ HR) during apnea, reflects the body's ability to prioritize blood flow to selected organs to support vital functions during hypoxia. The response is pronounced in apneic divers and correlates with their performance. We hypothesized that this response may also characterize individuals able to cope well with high altitude. We tested 22 volunteers, planning to trek to Everest base camp, before the trek 1–2 days after arriving at Kathmandu. Tests consisted of three apneas separated by 2 minutes rest, the first apnea limited to 1 minute, the following two of maximal effort. The third apnea was preceded by 15 seconds hyperventilation. All trekkers followed the same altitude and time plan, and filled out a Lake Louise Questionnaire (LLQ) every morning and evening during the trek. The individual diving response (Δ HR during apneas) was compared with LLQ scores (total points) during ascent to

4400 m (Pearson correlation analysis). One subject was evacuated by helicopter from 4400 m due to acute mountain sickness (AMS), and about 50% had mild AMS symptoms. Most subjects responded with a diving response during apneas, with a large individual variation in magnitude. Δ HR during apneas was found to be correlated with LLQ points ($r = -0.44$; $p < 0.05$). Baseline HR did not correlate with LLQ points. We concluded that the diving response, known to characterize successful freedivers, may also define altitude tolerance. This is a novel finding and makes it a promising candidate for further studies aiming to develop a simple apnea-based test to predict AMS.

4017

OPPORTUNITIES AND CHALLENGES FACING THE USE OF DRONES BY MOUNTAIN RESCUE TEAMS IN THE UNITED KINGDOM

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Multirotor drones are a type of remotely driven aircraft available to the public, they are light weight and able to launch vertically. The UK government is in support of the use of such drones by emergency services, intuitively they would also have applications to mountain rescue teams (MRTs). This review aims to summarize the opportunities and challenges facing the use of drones by MRTs in the United Kingdom. Lochaber MRT currently uses a drone to search for missing persons. A simulation carried out by Donegal MRT showed that using a drone can reduce search time by $> 50\%$. A Norwegian study showed that a drone fitted with a transceiver was able to locate buried avalanche transceivers. Drones can also be used for supply drops; however, it is not currently legal to do so in the United Kingdom. No license is required for noncommercial flying; however, all drone users must comply with the Civil Aviation Authority's Drone Code. This would limit drone use by MRTs to daylight searches in sparsely populated environments where a helicopter is not also involved. A multirotor drone costs approximately £3000, typically such drones are not fully waterproof and limited to wind speeds under 20 knots. In 2016, MRTs in England and Wales spent 21,960 hours searching for casualties. Simulation testing suggests drones could significantly reduce this time and be used preferentially to search dangerous areas. However, high purchase costs, inability to fly in poor weather, and staying abreast of rapidly evolving legislation are significant challenges facing implementation of drone technology in UK MRTs.

4018

ANALYSIS OF THE AVALANCHE AT MOUNT EVEREST BASE CAMP DURING THE APRIL 2015 EARTHQUAKE IN NEPAL

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Introduction: An avalanche triggered by an earthquake on April 25, 2015, struck the Mount Everest base camp (EBC) resulting in 20 deaths and > 80 injuries. Despite the common occurrence of avalanches in this region, little is known about their intensity as well as the role that the region's warming is having on the stability of the glaciers that ring the Mount

Everest massif. In this study we present unique observations from a nearby automatic weather station (AWS) in the minutes immediately after the earthquake.

Methods: The AWS was situated at Kalla Patthar. It recorded temperature, relative humidity, pressure, solar radiation, as well as wind speed and direction at 1-minute intervals.

Results: The AWS recorded anomalies immediately after the earthquake. In particular, there was a rapid reduction in solar radiation that was attributed to the passage of a snow cloud. In addition, there were three distinct wind pulses observed at the AWS. We argue that these pulses are consistent with the triggering of multiple avalanches by the earthquake and suggest that the devastation, death, and injuries that occurred at EBC were the result of avalanche winds associated with this swarm.

Discussion: These results provide important data that can be used to improve our capability to forecast such events. In addition, the instability of the hanging glaciers that surround EBC may increase as the region continues to warm, suggesting that additional research into these glaciers needs to be undertaken to reduce the risk to those who work at or visit the region.

4019

TIBETANS WITH EGLN1 C12G/G380C HAPLOTYPE EXHIBIT DIMINISHED INFLAMMATORY RESPONSE BY MONOCYTES

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We previously identified a Tibetan-specific polymorphism (c.[12C>G: D4E]) in the EGLN1 gene (encoding prolyl hydroxylase 2 [PHD2]), the principal negative regulator of hypoxia sensing. This polymorphism is present at a high gene frequency ($\sim 80\%$) in Tibetans that contribute to their high-altitude adaptation. It is always present in *cis* with another missense polymorphism (c.[380G>C]) and PHD2D4E/C127S has a higher affinity for oxygen than PHD2wt, thus degrading HIF-1 α and HIF-2 α more efficiently under hypoxia. This haplotype is the first identified mechanism that functionally contributes to the protection of Tibetans against polycythemia. However, HIFs in addition to regulation of erythropoiesis also regulate immune function and other hypoxia-mediated essential physiological functions. We now report that the monocytes, the integral part of the first line of immune defense, elutriated from genetically adapted Tibetans expressing PHD2D4E/C127S from Leh (altitude ~ 3600 m) and Srinagar (altitude ~ 1800 m), have diminished secretion of inflammatory cytokines, including IL-1 β (PHD2D4E/C127S: 6.24 ± 2.63 pg/mL, PHD2wt: 40.01 ± 12.78 pg/mL), TNF- α (PHD2D4E/C127S: 3.63 ± 1.5 pg/mL, PHD2wt: 7.25 ± 0.78 pg/mL), and IL-6 (PHD2D4E/C127S: 51.6 ± 24 pg/mL, PHD2wt: 157 ± 29 pg/mL) in response to bacterial lipopolysaccharide. The PHD2D4E/C127S monocytes exhibit abrogated induction of the costimulatory molecule CD80 (PHD2D4E/C127S: 4706 ± 640 , PHD2wt: 7785 ± 981 MFI arbitrary units) in comparison with wild-type monocytes. These data suggest that the coding variant PHD2D4E/C127S may provide a heretofore unreported evolutionary advantage to Tibetans to combat hypoxia-mediated inflammatory responses.

4020

THE EMS MOBILE APP

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The EMS mobile app's ability in an emergency to verify the patient's exact location is key to success. Patients often are not able to provide this, especially if they are in shock, seriously injured, or their surroundings are unfamiliar, especially in remote or mountain areas. Present state providing these vital coordinates and other important data can be done through the mobile app, which uses GPS to confirm and send the caller's exact position and other important data directly to the EMS. Through the app, EMS crews can reach the patient in a far shorter period of time. Methodology statistical data are collected from all EMS providers in Czech Republic and mountain rescue operators.

Results: Within 2 years in the Czech Republic, the app has gained 600,000 users and initiated 15,000 rescue callouts. The first abroad provider to join is 144 Notruf Niederösterreich in Austria – "Rettung." The overall concept is for a universal platform, the app works not only in the user's homeland. Most significant here are the local points of interest—the nearest 24/7 pharmacy, dentist, ER, or AEDs. We plan to present data from distribution of emergency calls through the app between regions with/without mountains, age distribution of users, accuracy of the determination of the location, use of other medical info, and the number of missions by mountain rescue in Czech Republic. The Záchranka app became both the official Czech EMS and mountain rescue app and also Rettung became an official emergency app of Austria.

4021

4022

COMPARING METHOXYFLURANE WITH NON-ORAL OPIOID ANALGESICS: WHERE DOES METHOXYFLURANE FIT ON THE PAIN TREATMENT PYRAMID?

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Methoxyflurane is an inhaled analgesic agent that is used as an alternative to opioid analgesia. The Wilderness Medical Society (WMS) guidelines describe a pain treatment pyramid that escalates analgesia based on severity of pain. Intravenous opioid is the gold standard for managing moderate-to-severe pain in the wilderness and mountain rescue setting. However, intranasal, intramuscular, and buccal opioids are commonly used alternatives when the intravenous route is unavailable. This review, which critically appraises the literature, aims to summarize the evidence comparing methoxyflurane with intranasal, intramuscular, or buccal opioids in treating moderate-to-severe pain in the prehospital setting. A literature review was carried out using a journals and databases search available through NICE using HDAS as the interface to search Medline, PubMed, and EMBASE. The Cochrane library was searched directly. The literature search found three articles to be relevant. Johnston (2010) found that intranasal fentanyl was more effective than methoxyflurane. Middleton (2010) found that in adults, methoxyflurane was inferior to intravenous morphine, intranasal fentanyl, and combination analgesia. Bendall (2011) found that in children, methoxyflurane was inferior to morphine, fentanyl, and combination analgesia. It can be concluded that in adults and children in the prehospital environment with moderate and severe pain, intravenous and intranasal opioids are better than methoxyflurane at providing effective pain relief. However, when strong opioids are not available, methoxyflurane provides effective analgesia. Given that weak opioids have been shown to be ineffective in this environment, methoxyflurane is, therefore, likely to sit between weak opioids and strong opioids on the WMS pain pyramid.

4023

OCCUPATIONAL INJURIES IN MOUNTAIN RESCUE VOLUNTEERSJohn Baldy,¹ Michael Greene,² and Karen Greene²¹West Cumberland Hospital, United Kingdom; ²Mountain Rescue England and Wales, United Kingdom

Mountain rescue involves strenuous physical activity in hazardous environments. The incidence and type of injuries sustained by rescue volunteers have not been extensively reported. This study describes the injuries sustained by Mountain Rescue England and Wales volunteers during active duty >10 years. An electronic survey was sent to volunteers. The anonymous data included demographics, rescue experience, injury characteristics, mechanism of injury,

ABSTRACT WITHDRAWN

treatment, and recovery. A total of 447 volunteers completed the survey in 2018. One-third (148, 33.1%) declared at least one injury. Injuries occurred on average after 6 years of experience (6.29, 95%) with peaks within the first 5 years of experience (74, 50.0%) and after >10 years of experience (44, 29.7%). Sprains accounted for most injuries (77, 52.0%) and were caused by stumbles (61, 44.2%) or carrying the casualty (44, 31.9%). The limbs (94, 63.5%) and the back (43, 29.1%) were most often injured. Rock fall, technical climbing, and interactions with helicopters caused small number of injuries. One-third (47, 31.7%) of injured volunteers required medical attention and 30 (20%) failed to make a full recovery. Volunteers (43, 29.1%) lost time from employment and were absent from rescue duties (42, 28.4%) for >15 days. There were 43 (9.6%) reports of mental health or stress-related problems due to mountain rescue activity. This survey demonstrates that there are physical and mental injuries related to rescue activity with potential serious consequence to volunteers. More research is required and injury prevention should focus on reducing stress during lifts and carries.

4025 DIFFERENTIAL EFFECTS ON SLEEP AND AUTONOMIC BALANCE BETWEEN LOWLANDER AND HIGHLANDER CHILDREN DWELLING AT HIGH ALTITUDE

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Colombia has an internal migration rate of 36.2%, only surpassed by that of Syria. Those population movements in a geographical territory with abrupt changes in altitude determine the acute and chronic exposition of lowlanders to high altitude, being the children the most vulnerable of those migrants. This study aimed to assess the impact of such exposition in children dwelling at Bogotá (2660 m a.s.l.) on sleep and neurocardiac activity. Demographic (especially the time dwelling at Bogotá = DWE) and clinical features of 10 male children (age = 10.6 years, SD = 2.4) were collected and contrasted with polysomnographic measurements, sleep and behavior scales, and electrocardiographic analysis during a vigilant test. We found a positive correlation between sleep efficiency and HR, the low-frequency band in the HRV analysis, SD2/SD1 ratio, alpha 1, QRS, and Tpeak-Tend HR. In contrast, the efficiency was negatively correlated with RR, RMSSD, HF, SD1, and sample entropy. Most of the sleep stages have significant correlations; however, the most consistent finding was with N3. In this study, there was a positive correlation between N3 and approximate entropy, JT, p amplitude, and importantly with DWE. For this reason, we performed one exploratory analysis splitting the group according to DWE (highlander natives vs. lowlander natives). Such an approach gave us in a *t*-test a statistical significant difference in N2 ($p = 0.03$) and N3 ($p = 0.02$). The same group divided by Apnea-Hypopnea Index does not present divergences. Taken together, our findings reveal a long-term adaptive effect due to an early and continuous exposition to high altitude in children.

4026 ACETAZOLAMIDE TOXICITY MASQUERADING AS ACUTE MOUNTAIN SICKNESS

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Acetazolamide is long established as prophylaxis and treatment for acute mountain sickness (AMS). Although common dose-dependent side effects are well recognized, the ability of acetazolamide to mimic the very disease it is prescribed to prevent is less well known. We report five cases of acetazolamide toxicity whose presentation mimicked AMS. The cases all presented to the Mountain Medicine Institute in Namche Bazaar, Nepal (3500 m) within a 12-month period. The age range of the patients was 33–73 years. Two were female. The dose of acetazolamide taken varied from 125 mg twice daily to 750 mg daily. Two of the patients had taken additional acetazolamide up to 1 g extra in the 48 hours before presentation. One patient was dehydrated from diarrhea. All patients had a modified Lake Louise Score = 3, with headache. Four had respiratory rates >20/min at rest and all had oxygen saturations of 90%–95%, in excess of what would be expected on arrival in Namche. Four patients complained of nausea and two complained of significant limb paraesthesia. All symptoms resolved completely within 1.5 to 3 days of stopping acetazolamide. Some trekkers appear unaware of the safe dosage of acetazolamide for prophylaxis of AMS and the danger of taking supplementary doses beyond this. Acetazolamide toxicity should be considered as a differential diagnosis in all patients taking the drug who present with the clinical features of AMS, but with higher-than-expected oxygen saturations and/or paraesthesia.

4027 DEMOGRAPHICS OF PATIENTS ATTENDING TWO HIGH-ALTITUDE RESCUE POSTS IN THE NEPALESE HIMALAYA BETWEEN 2012 AND 2017

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The International Porter Protection Group operates two rescue posts in Machermo (4450 m) and Gokyo (4800 m) villages, Nepal, which are open during the spring and autumn trekking seasons. We report the demographics of 1977 cases seen during the 5 years from 2012. The autumn season is busier than the spring with an average of 217 and 134 patients, respectively. The 49.4% of patients seen were Nepalese (24.5% porters, 19.9% locals, and 5% trekking guides). The 50.6% of patients who were trekkers came from a total of 58 countries with almost half (47.9%) from 5 countries (Australia, United Kingdom, United States, France, and Germany). The median age of patients seen was 32 years (range 4 months–85 years). The most common age range for porters/locals/guides was 15–25 years (43% of this group) and 25–35 years for trekkers (29% of trekkers). A total of 32% of patients had altitude illness as their primary diagnosis—the majority being mild-moderate acute mountain sickness. Upper respiratory tract infection was the second most common diagnosis (18% of cases). A total of 32.3% of patients were troubled by cough, either as a primary or sec-

ondary diagnosis. Twelve percent of patients (of which 40% had high-altitude pulmonary edema or high-altitude cerebral oedema or both) were evacuated or advised to descend. Of those evacuated, 64% were by helicopter, 21% walked, and 2% descended by horse or porter carry. The remaining 13% were advised to descend. These data are a rich source of information regarding the patients and pathologies encountered at high altitude. To our knowledge, data of this size have not been presented previously.

4028

HYPOXIA ADAPTATION OF TIBETAN MOUNTAINEERING ATHLETES

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As one special group of the native inhabitants living on Qinghai-Tibetan Plateau, Tibetan mountaineering athletes appear to be the best adapted as shown by their high-intensity exercises at extremely high altitudes. In this study we performed genome-wide scans utilizing the whole-genome genotyping data and the echocardiographic and hematologic-related phenotypes in 36 Tibetan mountaineers. Genes showing the strongest evidence of selection, including EPAS1, EDAR, and PRKCE, appear to be associated with cardiopulmonary function that may contribute to Tibetan's hypoxia tolerance at altitude. Based on the linear regression model, we calculated the living altitude of populations with 68 loci of candidate genes. Such an estimation proposed Tibetan mountaineers to thrive at 5055 m altitude, which is much higher than their birth place of 4200 m. In addition, results from population differentiation and association analyses indicated that various genes involved in calcium signaling pathway may prompt the complex mechanism of the high-altitude adaptation in Tibetans. Furthermore, we found that the major alleles of certain loci in PRKCE were associated with lower heart rate in Tibetans, which reflects a better cardiac function. Especially these loci have hypoxia-induced interactions to EPAS1 as demonstrated in the 4C (Circularized Chromosome Conformation Capture) study, suggesting compound heterozygosity effects on cardiovascular phenotypes. Our results showed that the genetic adaption to high altitude in these highlanders is the synergistic effect of multiple genes involved in cardiopulmonary and erythropoietic functions that help to maintain adequate oxygen supply at high altitude.

4029

THE IODINE STATUS OF PATIENTS WITH THYROID NODULES IN THE DIFFERENT REGIONS OF QINGHAI PROVINCE

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Objective: To investigate iodine nutritional status of thyroid nodules in different areas of Qinghai province and analyze its characteristics.

Methods: In 2014–2016, from the selected 553 cases of thyroid nodules in nine regions of Qinghai province (traditional Tibetan areas: Xie Wu, Kao Qian, Jiegu, and Guo Luo; nontraditional Tibetan areas: Xining, Huzhu, Menyuan, Ledu, and Minhe), serum TSH and urine iodine were mea-

sured. Waist circumference and weight were measured and body mass index was calculated.

Results: From the thyroid nodules in Qinghai, the median of urinary iodine was 160.8 µg/L, the median of TSH was 2.97 IU/L, and iodine nutritional status was at the appropriate level. In the cases < 30 years old from nontraditional Tibetan areas, MUIC was 233.4 µg/L, which was in excess of iodine, and the difference was statistically significant ($\chi^2 = 8.900$, $p < 0.05$) compared with those in the traditional Tibetan area (200.4 µg/L). MUIC (281.1 µg/L) of male thyroid nodules in the Tibetan area < 30 years old was significantly higher than that of women (185.0 µg/L), and the difference was statistically significant ($p < 0.05$).

Conclusions: We should strengthen the monitoring of iodine nutritional status in the key population of thyroid nodules in the mentioned areas of Qinghai province.

4030

MORBIDITY AMONG RUNNERS PRESENTING FOR MEDICAL CARE DURING THREE EDITIONS OF AN ULTRA TRAIL RACE IN THE HIMALAYAS

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Purpose: This study aimed to describe the injuries and illnesses befalling the participants of the seven-stage 212 km trail races at high altitude.

Methods: All medical encounters of the 101 participants competing in the Manaslu Trail Race in Nepal from 2014 to 2016 were retrospectively analyzed and classified into various categories.

Results: Acute diarrhea was the most common ailment reported among the participants (17.82%), followed closely by musculoskeletal problems (16.83%). Altitude illness made up 6.19% of service provided with around 35% runners using acetazolamide for prophylaxis. The one case needing evacuation was that of high-altitude pulmonary edema.

Conclusions: Ultra trail races at high altitude pose a challenge in terms of provision of medical care in a remote setting with limited resources. However, most of the illnesses are minor in nature and easily managed by the race doctor. Knowledge of common illnesses among travelers to the area can help aid in preparation and provision of proper care.

4031

STRANGERS IN PARADISE: TOURISTS PRESENTING TO A MOUNTAIN HOSPITAL IN NEPAL

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The majority of trekkers coming to the Khumbu region plan to ascend to an altitude between 4860 m above sea level (Gokyo) and 5380 m (Everest base camp). As they often arrive badly acclimatized and experience important altitude differences, they are more susceptible to altitude-related ill-

nesses than the local population. When suffering from medical problems, they rely on local healthcare facilities such as the HRA healthposts in Pheriche and Manang and the hospitals in Khunde, Lukla, or Namche Bazaar. The hospital in Khunde and the Pasang Lhamu Nicole Niquille (PLNN) hospital in Lukla are the only hospitals that are open year-round providing basic healthcare for the local community and tourists alike. In this retrospective cohort analysis, we wanted to assess the prevailing medical problems of all non-Nepalese patients seeking medical help in PLNN hospital between spring 2016 and 2017. A total of 227 foreign patients presented to PLNN hospital in the study period and 43.2% arrived by helicopter. Almost 20% of patients suffered from serious medical problems. A total of 11.1% were admitted to the hospital ward, whereas 15.1% were transferred to Kathmandu for further management. A total of 43.1% of patients presented with high-altitude illnesses, making this the most common diagnosis of all. Our data indicate that altitude-related health problems largely contribute to the burden of disease of tourists in the Nepal Himalayas. Further education of tourists and guides is necessary to prevent this main cause of morbidity among trekkers in the region.

4032

ASSOCIATIONS BETWEEN ARTERIAL OXYGEN SATURATION, HEART RATE, AND ACUTE MOUNTAIN SICKNESS IN A POPULATION OF 17–21-YEAR OLD HAN CHINESE STUDENTS TRAVELING FROM LOW ALTITUDE TO LHASA AT 3658 M ABOVE SEA LEVEL

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Objectives: The aim of this study was to evaluate associations between acute mountain sickness (AMS) and resting arterial oxygen saturation (SaO₂) and heart rate (HR) measured at low altitude and three consecutive days after an ascent to high altitude in a population that had previously not been at high altitude.

Methods: A cohort of 801 Han Chinese students (413 male and 388 female) aged 17 to 21 years were followed from low to high altitude during August and September 2014. The symptoms of AMS were assessed by questionnaire before leaving the lowland and on the third day after arrival at the high altitude city of Lhasa at 3658 m. AMS was defined by the Lake Louise Scoring System (LLSS) (headache and a cumulative Lake Louise Score = 4).

Results: The risk of AMS increased by decreasing SaO₂ levels measured both in the lowland (risk ratio [RR]: 1.16, 95% confidence interval [CI]: 1.13–1.20) and on the first day in the highland (RR: 1.19, 95% CI: 1.15–1.22) per a 1% reduction in SaO₂ level. Heart rate and AMS were only weakly associated at any given point in time. Other potential AMS risk factors such as gender, height, weight, use of prophylactics, health condition, and diseases did not affect the results if they were added into the regression models.

Conclusions: SaO₂ at both low and high altitude were independent predictors of AMS. As a predictor for AMS, SaO₂ has its limitations, although individuals with a clear reduction in SaO₂ were at an increased risk of AMS.

4033

A REPORT OF RESCUE WORK IN 2014 VOLCANIC ERUPTION IN JAPAN

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Mt. Ontake (3067 m), the second highest volcano in Japan, erupted without apparent warning and led to a heavy loss of life on September 26, 2014. I collected the data personally from Military, National Police, and Fire Defense Agency sources, in addition to publicly available data from the cabinet office. Fifty-six deaths and 7 losses and at least 26 survivors rescued were reported. The water vapor explosion spewed out huge rocks and blocks. The primary cause of death was trauma by abrupt fallen rocks. The location of dead bodies was concentrated on the mountain trails of 1-km radius from the craters. Also most of the survivors rescued had trauma. More than 20,000 rescuers engaged in a search and rescue for 20 days till winter had come to the mountain. Many rescuers with less mountain skills, equipment, and rescue experiences had to carry out their missions. There were no deaths of rescuers but some had acute mountain sickness and hypothermia on missions. The volcano erupted violently and rapidly, leaving little or no time for people to escape or take shelter. Emergency medical care played a small role in severe volcanic eruptions. But, in contrast, medical care to rescuers must be necessary and helpful. This report will help to develop medical and rescue planning for not only emergency casualties but also rescuers.

4034

PATHOLOGICAL CHARACTERISTICS OF GASTRIC MUCOSAL LESION IN PATIENTS WITH EXCESSIVE POLYCYTHEMIA AT HIGH ALTITUDE

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High-altitude polycythemia (HAPC) is characterized by severe symptomatic excessive erythrocytosis (EE; Hb ≥ 19 g/dL for women and Hb ≥ 21 g/dL for men) and accentuated hypoxemia, which are frequently associated with pulmonary hypertension. However, there are limited data available on the effects of hypoxia-ischemia on HAPC-related gastric mucosal lesion. This study aimed to evaluate the pathological changes of gastroduodenal mucosa in patients with HAPC. 183 cases of gastric mucosal lesion in patients with HAPC were studied at a hospital of Haixi Mongolian and Tibetan Autonomous Prefecture (3200 m above the sea level) between January 2013 and December 2016. All the patients underwent upper endoscopy and gastric biopsies. Most of them were male Han Chinese (90%) and age between 3 and 49 years. Hemoglobin levels were > 21 g/dL in all patients. The most frequent diagnosis by endoscopy was gastric ulcer (19.67%), atrophic gastritis with erosion (43.17%), non-atrophic gastritis (16.56%), duodenal ulcer (12.02%), and duodenal globulitis (8.20%). Histopathological analysis revealed that HAPC induced severe congestion, edema, and multiple hemorrhagic erosions in the gastric mucosa. A dilation and distortion accompanied by hyperemia and bleeding were also observed in vessels within gastroduodenal mucosa. Therefore, the present findings suggested that severe

chronic hypoxemia and consequent excessive polycythemia in patients with HAPC may induce to impair gastric mucosal barrier and lead to develop chronic gastroduodenal disorder.

4035

STUDY ON THE CORRELATION BETWEEN VASCULAR LESIONS AND COGNITIVE FUNCTION IN NATIVE TIBETAN WITH H-TYPE HYPERTENSION IN PLATEAU

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Objective: To explore characteristics of vascular lesions and the correlation between vascular lesions and cognitive function in native Tibetan patients with H-type hypertension in Qinghai-Tibetan Plateau of China.

Methods: Sixty-two cases with H-type hypertension and 178 cases with non-H-type hypertension were enrolled in native Tibetan patients at high altitude (Yushu city, Qinghai Province, China; 3800 m). All the subjects detected carotid artery atherosclerotic plaques and carotid intima-media thickness (CMT) with the color Doppler ultrasound, examined the cognitive function with the minimal state examination (MMSE), and measured the brachial-ankle pulse wave velocity (BaPWV), and ankle brachial index (ABI) with the Colin-VP1000 type artery stiff diagnosis apparatus.

Results: Comparing with non-H-type hypertension, the incidence of carotid artery atherosclerotic plaques, CMT, and BaPWV was significantly higher in the native Tibetan with H-type hypertension ($p < 0.05$), whereas MMSE and ABI were significantly decreased ($p < 0.05$). MMSE were positively correlated with BaPWV, CMT, and plaques, MMSE was negatively correlated with ABI and plaques.

Conclusions: The patients with H-type hypertension are more likely to have the peripheral artery structure and function impairments and more severe the cognition impaired, which closely correlate with high altitude and hypoxia. Hypoxia and special national diet (less vegetables and more meat) affect the metabolism of homocysteine. Elevated plasma Hcy level may aggravate vascular lesions and cognitive impairment in native Tibetan patients with high blood pressure in the plateau.

Keywords: cognitive function; high altitude; H-type hypertension; native Tibetan patients; vascular lesions

4036

ADAPTOGENS FOR INCREASING PHYSICAL AND MENTAL PERFORMANCE AT HIGH MOUNTAINS

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Several oriental systems of medicine including Ayurveda described natural products, derived largely from plant sources, to possess stress-relieving and endurance-promoting properties. Such preparations are likely to be of immense use and importance where endurance promotion is required and desirable such as during recuperation, among aging personnel, and in adverse environmental conditions. The experimental evidence in favor of such products, called adaptogens and Rasayan, was meager. To fulfill this lacuna, several studies were performed on experimental animals and clinical trials on human volunteers in severe adverse environmental conditions. A comprehensive new experimental model was needed and developed to evaluate the antistress and endurance-

promoting substances. The model was based on the maintenance of thermoregulation under severe conditions of cold (5°C), hypoxia (428 mmHg), and restraint. With this model, the efficacy of several single plant preparations and some composite Indian herbal preparations (CIHPs) was evaluated and found effective as adaptogen. The mechanism of action of CIHPs consisted of strengthening of oxygen delivery system, improved cellular permeability restricting other stress-induced changes. There was a shift from carbohydrate metabolism to utilization of free fatty acids for maintenance of body temperature under cold-hypoxic exposure.

The double-blind placebo-controlled clinical trials of CIHP1 and CIHP2 on soldiers operating in cold-hypoxic high mountains indicated that these mineral-herbal preparations increased the high altitude and cold tolerance and relieved the debilitating effect of high altitudes. Furthermore, on return from high-altitude areas, the CIHPs accelerated the recovery process.

4037

UNUSUAL PRESENTATIONS AT THE EVEREST ER

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Working at Everest ER (altitude 5340 m), the temporary clinic at the Everest base camp for the spring climbing season of 2018, we treated some intriguing medical problems against the background of cold, hypoxia, and often unforgettable human behavior at that altitude. Some of these were rare diagnoses in themselves, whereas the rest represented a deviation from the regular presentations. These cases range from an unusual intersection syndrome of the wrist and another uncommon friction burn by the harness to a severe allergic contact dermatitis and a mystifying case of high-altitude pulmonary edema (HAPE) that seemed to worsen with descent. Also included is a case of a determined climber who amazingly returned to the base camp on a helicopter within a short period of being evacuated to a lower altitude after the diagnosis of HAPE, which he had acquired after a rapid ascent. He went on to summit two 8000 m peaks and complete the Everest marathon! And finally, a case of a climber with multiple medical problems is described. These patients remind us that besides proper scientific knowledge, a great degree of presence of mind and an understanding of human behavior at that altitude are warranted in competently managing problems in the Everest ER.

4038

CARDIORESPIRATORY EXERCISE RESPONSES IN NORMOBARIC AND HYPOBARIC HYPOXIA

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There is an ongoing discussion about physiological differences between normobaric hypoxia (NH) and hypobaric hypoxia (HH). This study aimed to compare submaximal exercise responses during acute exposure to NH and HH. Eight healthy male study participants performed a graded submaximal exercise test in NH and HH in a cross-over study design. NH

testing was conducted in a hypoxic chamber in Bad Aibling (Germany, 490 m) with an inspiratory fraction of oxygen of 15.0% corresponding to a simulated altitude of ~3150 m. HH testing took place at real high altitude after ascent by cable car to 3150 m. After 30 minutes at rest, a submaximal cycle ergometer test with three intensity stages (50, 100, and 150 watts), each lasting 5 minutes, was performed. Heart rate, arterial oxygen saturation (finger pulse oximetry), ventilatory, and gas exchange parameter were continuously measured during the test. Blood lactate concentrations were determined at the end of each intensity stage. Minute ventilation did not differ between conditions across all intensities, whereas breathing frequency tended to be higher ($p = 0.06$) and tidal volume tended to be lower ($p = 0.09$) in HH than in NH. No differences in heart rate and arterial oxygen saturation were observed. Blood lactate concentration tended to be higher in HH than in NH ($p = 0.05$). The results suggest that small differences in the ventilatory pattern seem to be present between NH and HH even at the beginning of an exposure. However, these differences did not result in condition-specific cardiorespiratory responses during submaximal exercise.

4040

EFFECT OF ALTITUDE ON HOSPITALIZATIONS FOR BRONCHIOLITIS IN THE FRENCH ALPS

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This study reports hospitalizations at Albertville hospital for bronchiolitis among visitors to ski resorts during the past winters. Albertville (altitude 300 m) is the local hospital for the Three Valleys, the biggest ski domain in the world, with the highest ski resorts in the French Alps (maximum 2300 m). Cases were defined as infants and young children with diagnosis of bronchiolitis and identified as visitors. Medical files were reviewed, collecting altitude of home residence and ski resort, SaO₂ at ski resort and on arrival at the hospital, oxygen need, and length of hospitalization. About 20 patients filled the criteria for inclusion every winter season. All originated from low altitude. Most of them arrived at the ski resort with upper respiratory tract infection and were sent down to Albertville by local GP with severe symptoms of bronchiolitis and/or hypoxemia, usually in the first 24 hours of stay at altitude. SaO₂ was often in the range 80%–85% at the ski resort but usually correct on arrival at the hospital. Most nasal samples were positive for respiratory syncytial virus. Some children needed oxygen during hospitalization but not all. However, it was not possible to allow them to go back quickly to altitude. According to the usual definition of high altitude (2500 m), our cases were staying at moderate altitudes. However, these moderate altitudes are high enough to precipitate worsening of symptoms just after arrival. Doctors and families need information about the risk of bringing infants at the highest resorts during bronchiolitis epidemics.

4041

CLINICAL OBSERVATION OF CHINESE HERB JIEYU HOHUA IN TREATMENT OF INSOMNIA AT HIGH ALTITUDE

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Objective: Insomnia or sleep disorder at high altitude is more common than at sea level. In this study, we compare the efficiency and safety of Chinese traditional herbs Jieyu hehuan decoction and western medicine Alprazolam in the treatment of insomnia.

Method: We selected 200 patients with insomnia at 2300 m: those patients were randomly divided into the traditional medicine ($n = 100$) and Western medicine (Alprazolam) groups ($n = 100$). The Western medicine group was orally taking Alprazolam, and the traditional medicine group was orally taking Jieyu Hohuan decoction. Both groups were treated for 1, 2, and 3 months, and sleep quality was assessed using Pittsburgh sleep quality index (PSQI).

Result: There were no significant differences ($p > 0.05$) found among PSQI taken at three time points between Alprazolam and Jieyu Hohuan groups. However, after treatment, when compared with baseline, the PSQI was significantly reduced in both groups ($p < 0.01$), but the total effective rate of the Jieyu Hohuan group was 98%, that of the Alprazolam group was 82% (< 0.01). Also we found that about 50% patients experienced side effects after 3 months treatment using alprazolam, but it was absent in the Jieyu Hohuan group.

Conclusions: When compared with Western medicine, the Traditional Chinese medicine for treatment of sleep disorder is more effective and has less side effect. We, therefore, encourage people to use traditional medicine to treat disturbed sleep at high altitude.

4042

TRAVELER'S DIARRHEA

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Traveler's diarrhea (TD) continues to be one of the most common health problems facing travelers. Resistance is increasing to mainstay therapy for TD in many regions of the world. Travel to South Asia and antibiotic treatment have strongly been associated with colonization by extended spectrum beta-lactamase-producing enterobacteriaceae in returning travelers. Changing etiology of TD and resistance to antibiotics in Nepal are discussed during this session. New guidelines for TD treatment that is hoped to decrease gut colonization by resistant bacteria in travelers are also addressed.

4043

WHAT IS NOT DUE TO HIGH ALTITUDE: CASE-BASED PRESENTATION

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During each trekking/climbing season in the mountains of Nepal, CIWEC hospital sees patients with emergencies that turn out not to be due to high-altitude illness. Various emergencies that might at first present as high-altitude illness are discussed in a case-based scenario. A broad range of cases are presented.

4044

ACUTE HYPOXIA DECREASES SYSTEMIC BLOOD PRESSURE AT EXERCISE, AT CONSTANT HEART RATE, AND IN HYPERTENSIVE AND NORMOTENSIVE SUBJECTS

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This study aimed to determine whether acute hypoxia associated with exercise induces an increase in systemic blood pressure (SBP) in normotensive and hypertensive subjects, and whether hypertensive subjects are more prone to develop severe high-altitude illnesses (SHAI). Finally, to determine whether SBP and electrocardiogram (ECG) changes at exercise in hypoxia in hypertensive subjects are predictive factors for SHAI. From 2012 to 2015, 1113 sea level natives went through a hypoxia exercise test before a sojourn at high altitude, allowing the calculation of an SHAI prediction score. A total of 958 subjects were enrolled in the study, including 106 hypertensive subjects. From 272 subjects who sent back a questionnaire evaluating their tolerance to high altitude, 52 suffered from SHAI. When compared with normoxia, for the same heart rate, acute hypoxia induced a decrease in SBP at exercise in normotensive and hypertensive subjects. Hypertensive subjects treated by beta blockers showed a lower arterial oxygen saturation (vs. other treatments) and blunted cardiac and ventilatory responses to hypoxia at exercise. Hypertensive subjects were not more prone than normotensive subjects to develop SHAI. Hypertensive subjects suffering from SHAI although taking acetazolamide showed similar SBP and ECG characteristics to hypertensive subjects without SHAI and without acetazolamide. In conclusion, hypoxia induces a peripheral vasodilation that balances vasoconstriction and tachycardia centrally induced through the adrenergic system. Hypertensive and normotensive subjects behave similarly during exercise in acute hypoxia. Hypoxia does not exacerbate the exercise-induced increase in SBP. Systemic arterial pressure is not a useful predictor of intolerance to high altitude.

4045

REVISITING THE LAKE LOUISE SCORE AND ITS 2018 VERSION

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The Lake Louise AMS Score (LLS) is widely used in field studies for the diagnosis of acute mountain sickness (AMS). This score aggregates symptoms that are unspecific: headache, digestive symptoms, fatigue, dizziness, and sleep disturbances can be due to a variety of causes unrelated to altitude hypoxia. It was recently suggested to remove sleep disturbances from the score. We analyzed LLS from 317 trekkers at high altitude. Among them, 119 suffered from mild AMS (mAMS: $3 = \text{LLS} < 6$) and 64 from moderate to severe AMS (sAMS: $\text{LLS} = 6$). The objective was to (1) re-evaluate the need for a headache score >0 for the diagnosis of AMS, (2) evaluate the role of sleep disturbances, in relation to other symptoms, and (3) evaluate the significance of dizziness. mAMS was related to sleep, fatigue, headache, digestive, and dizziness, and sAMS to headache, dizziness, fatigue, digestive, and sleep, by decreasing order of importance. Cluster analysis of AMS evidenced two main groups: (1) associating fatigue, headache, and dizziness; (2) associating sleep, fatigue, and headache. A total of 27% of mAMS and 9.4% of sAMS subjects had 0 headache. Only absence of headache associated with absence of fatigue or sleep disturbances was specific of sAMS. In subjects presenting a dizziness score >1 , end tidal PCO_2 during hypoxic exercise was slightly lower. Subjects with very high ventilatory response to hypoxia may develop dizziness during high-altitude exposure. In conclu-

sion, (1) an isolated headache score >0 should not be mandatory to define AMS, (2) sleep is important in the diagnosis of sAMS, and (3) dizziness might be confused with headache or be linked to an hyper-response to hypoxia.

4046

VENTILATORY RESPONSE TO HYPOXIA AND TOLERANCE TO HIGH ALTITUDE IN WOMEN: INFLUENCE OF MENSTRUAL CYCLE, ORAL CONTRACEPTION, AND MENOPAUSE

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Tolerance to high altitude in women might be influenced by hormonal status since female hormones are known to modulate ventilation. We explored the influence of (1) the phase of menstrual cycle, (2) oral contraception, and (3) menopause with or without hormonal treatment, on ventilatory (HVRe) and cardiac (HCRE) responses to hypoxia at exercise in 1060 women before exposure at high altitude. HCRE and HVRe were measured during a routine hypoxia exercise test. Prevalence of severe high-altitude illness (SHAI) was assessed in a subgroup of 260 women. Four groups of women were defined: nonmenopausal with or without oral contraception and menopausal with or without hormonal treatment. In nonmenopausal women without contraception, HVRe was higher in the early luteal phase than in the early follicular phase (0.89 ± 0.37 vs. 0.75 ± 0.27 mL/min/kg, $p = 0.03$). HVRe was higher ($p = 0.016$) and HCRE lower ($p < 0.001$) in menopausal vs. nonmenopausal women. Independently of hormonal status, HVRe decreased from second to fourth decade of age and increased from fourth to eighth decade, whereas HCRE consistently decreased with aging. Oral contraception or hormonal treatment had no effect on responses to hypoxia. The prevalence of SHAI was similar in all groups. SHAI prediction score was higher and HVRe lower in women with SHAI, without taking acetazolamide. In conclusion, (1) physiological responses to hypoxia depend on the ovarian cycle phase and on menopause status, (2) oral contraception and hormonal treatments have no influence on response to hypoxia and tolerance to high altitude, and (3) independently of hormonal status, aging modulates physiological responses to hypoxia.

4047

EVALUATION OF MAIN PULMONARY ARTERY CHANGES WITH CHRONIC MOUNTAIN SICKNESS USING PHASE CONTRAST MAGNETIC RESONANCE IMAGING

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Objective: According to research, due to hypoxia and cold in the Qinghai-Tibet Plateau, pulmonary circulation structure and function of patients with chronic mountain sickness (CMS) often change at advanced stages. The objective was to evaluate the clinical application value of changes of main pulmonary artery (MPA) in CMS patients by using phase contrast magnetic resonance imaging (PC-MRI).

Materials and Methods: Twenty-eight male adult CMS patients (CMS group) and 25 healthy male adult volunteers (control group) from the same altitude were recruited. The

2D/QF sequence of Philips 1.5T magnetic resonance scanner was used for MPA.

Results: (1) Structure parameters: the cross-sectional area (CSA) and relative dilatation degree (RDD) of CMS group were $(8.32 \pm 0.62) \text{ cm}^2$ and $(39.41 \pm 9.25)\%$, respectively, and those of the control group were $(5.44 \pm 1.08) \text{ cm}^2$ and $(55.72 \pm 8.45)\%$, respectively. CSA increased by ($p < 0.01$) compared with the control group, and RDD decreased by ($p < 0.01$). (2) Hemodynamics parameters: the peak positive velocity (PPV), peak negative velocity (PNV), and regurgitant fraction (RF) of the CMS group were $(77.89 \pm 8.32) \text{ cm/s}$, $(29.41 \pm 5.12) \text{ cm/s}$, and $(6.02 \pm 1.05)\%$, respectively, and those of the control group were $(84.52 \pm 10.25) \text{ cm/s}$, $(19.22 \pm 5.21) \text{ cm/s}$, and $(3.98 \pm 0.32)\%$, respectively. The PPV decreased by ($p < 0.05$) compared with the control group, the PNV increased by ($p < 0.01$) and the RF increased by ($p < 0.01$). (3) MPA pressure $(40.91\text{--}10.25) \text{ mmHg}$ in the CMS group was significantly higher than that of $(17.32 \pm 6.83) \text{ mmHg}$ in the control group by ($p < 0.01$).

Conclusions: PC-MRI can noninvasively and accurately provide the information of the MPA structure, hemodynamics, and pressure.

4048

PRELIMINARY STUDY IN RIGHT VENTRICULAR REMODELING IN PATIENTS WITH CHRONIC MOUNTAIN SICKNESS WITH CARDIAC MAGNETIC RESONANCE

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Objective: According to estimates, the number of patients suffering from chronic mountain sickness (CMS) in Qinghai-Tibet Plateau is $\sim 250,000$. The objective of this study was to investigate the changes of right ventricle structure and function in CMS patients by using cardiac magnetic resonance (CMR), Black Blood Sequences, and Movie Sequences.

Method: Twenty-four patients clinically diagnosed with CMS and 20 healthy volunteers whose gender, age, and altitude matched were recruited for cardiac MRI scan to obtain their right ventricular structure and function-related parameters by using heart-specific postprocessing analysis software.

Results: (1) Pulmonary artery diameter (PAD): CMS group: $30.7 \pm 4.5 \text{ mm}$, normal control group: $22.3 \pm 4.2 \text{ mm}$. (2) Right ventricular structure: CMS group: End-diastolic right ventricular wall thickness (RVT) $6.6 \pm 1.8 \text{ mm}$, interventricular septum (IVS) $10.9 \pm 2.6 \text{ mm}$, right ventricular mass (RVM) $34.7 \pm 15.8 \text{ g}$, right ventricular papillary muscle mass (RVPM) $30.4 \pm 13.6 \text{ g}$, right ventricular end diastolic transverse diameter (RVEDTD) $40.8 \pm 5.6 \text{ mm}$; normal control group corresponding results: $3.6 \pm 0.8 \text{ mm}$, $7.7 \pm 1.7 \text{ mm}$, $24.7 \pm 11.1 \text{ g}$, $23.3 \pm 8.3 \text{ g}$, $36.1 \pm 5.1 \text{ mm}$. (3) Right heart function measurement result: CMS group: cardiac output (CO) $2.4 \pm 1.2 \text{ L}/(\text{min}/\text{m}^2)$, end diastolic volume (EDV) $95.2 \pm 29.2 \text{ mL}$, end systolic volume (ESV) $62.4 \pm 21.8 \text{ mL}$; normal control group corresponding results: $1.7 \pm 7.5 \text{ L}/(\text{min}/\text{m}^2)$, $72.0 \pm 21.3 \text{ mL}$, $46.2 \pm 14.1 \text{ mL}$. Compared with normal control group, the difference between RVT, PAD, IVS, RVM, RVPM, EDV, ESV, CO, and RVEDTD of CMS group is significant.

Conclusions: CMR can accurately assess the structure and function of right ventricle in patients with chronic mountain

sickness. It also has the advantage of providing early detection and intervention for heart failure through the modeling of the right ventricular structure.

4049

CARDIAC MAGNETIC RESONANCE EVALUATES THE EFFECT OF MAIN PULMONARY ARTERY DILATATION ON RIGHT HEART STRUCTURE AND FUNCTION WITH CHRONIC MOUNTAIN SICKNESS

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Objective: In some patients with chronic mountain sickness (CMS), the main pulmonary artery (MPA) is dilated. To a certain extent, MPA dilation can reflect the pulmonary hypertension. This program uses cardiac magnetic resonance (CMR) to explore changes of right ventricular structure and function in patients with CMS.

Methods: Forty male volunteers who were clinically diagnosed as CMS were collected. CMR scans were performed on all subjects using the Philips Achieva 1.5T superconducting nuclear magnetic resonance scanner and the acquired images were postprocessed and analyzed. The patients (dMPA $> 30 \text{ mm}$) were included in the MPA-dilated group ($n = 21$), the rest of the patients (dMPA $= 30 \text{ mm}$) were in the control group ($n = 19$).

Results: (1) Right heart structure: The values of right ventricle lateral wall (RVLW), right ventricle anterior wall (RVAW), right ventricular end systolic transverse diameter (RVESD), and right ventricular end diastolic mass (RVESD) in the MPA-dilated group were $5.45 \pm 0.97 \text{ mm}$, $4.90 \pm 0.99 \text{ mm}$, $33.23 \pm 6.48 \text{ mm}$, and $47.91 \pm 14.42 \text{ g}$, respectively. The values of those in the control group were $3.56 \pm 0.71 \text{ mm}$, $3.24 \pm 0.61 \text{ mm}$, $25.71 \pm 4.43 \text{ mm}$, and $35.92 \pm 6.08 \text{ g}$, respectively. (2) Right heart function: The value of tricuspid annular systolic displacement (TASD) in the MPA-dilated group was $16.95 \pm 6.88 \text{ mm}$. The value of that in the control group was $25.98 \pm 4.21 \text{ mm}$. Compared with those in the control group, RVLW, RVAW, RVESD, and RVESD in MPA-dilated group were higher, TASD was significantly lower ($p < 0.05$).

Conclusions: Some CMS patients' MPA was dilated, and the structure of right heart changes obviously and the function changes slightly.

4050

CTA EVALUATION OF CEREBROVASCULAR COLLATERALS IN NORMAL ADULTS AT ALTITUDE

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Objective: Willis circle plays an important role in the occurrence, development, and prognosis of ischemic cerebrovascular disease, and the mechanism of vascular compensatory mechanisms in high altitude due to its special hypoxic environment changes. This study investigated the effect of long-term high-altitude lifestyles on adults with Willis circle mutations, along with related studies, to provide an anatomical basis for high-altitude cerebrovascular disease.

Methods: The collected 536 patients (average age 43.47 ± 9.62 years old) were examined by 256 slice spiral CTA from the attached hospital who lived in high-altitude areas (2500–4000 m and above) for > 10 years. They have headaches, dizziness, poor

sleep quality, and other symptoms. But there were no tumor and inflammatory and other diseases. Willis circle multifaceted form of observation and classification by postprocessing techniques was used to capture images.

Results: The 536 patients were classified into four types according to international classification, of which the detection rate of type III (abnormality in posterior circulation) was the highest; increase in subtypes according to actual work, in which the detection rate of type IIIa (unilateral dysplasia) is the highest; lack of A1 segment leads to more ipsilateral PCoA thickening; and changes in altitude affect of the Willis circle.

Conclusions: The completeness of the Willis circle is lower in the high-altitude area than in the low-altitude area. Changes in altitude will affect the type of variation in the Willis circle. Hypoxic environment can promote the opening of posterior communicating artery for adaptive compensation.

4051

RESTING STATE FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY OF BRAIN WITH OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME IN TIBETANS

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Objective: Tibetans are an important ethnic population in China Qinghai-Tibet Plateau. Owing to their high-altitude hypoxia condition, sleep disorder and OSAHS are more prone to happen. This study explores the brain changes in structure and function of Tibetan OSAHS patients.

Methods: Sixteen Tibetan OSAHS patients and 15 Tibetan healthy adults were recruited. The two groups were matched by age, education, and altitude; all subjects were male and right handed. T1-3D structure and resting-state functional magnetic resonance imaging (rs-fMRI) examinations were performed in this study. We used VBM, ReHo, and ALFF methods to study the differences in brain structure and function between the two groups.

Results: There is no significant difference in GMV between the two groups ($p < 0.05$, Alphasim corrected). In the Tibetan OSAHS patients, reduced ReHo value was found in the left cerebellum lobule 6. Higher ReHo values were found in the superior frontal gyrus and the left middle frontal gyrus ($p < 0.05$, Alphasim corrected). Decreased ALFF was found in the left cuneus. Increased ALFF values were found in the right inferior frontal gyrus and the right insula ($p < 0.05$, Alphasim corrected).

Conclusions: There were no significant changes in brain structure of Tibetan OSAHS patients, which may be due to their adaption to the hypoxia environment. ReHo values and ALFF values changes in multiple brain areas in Tibetan OSAHS patients indicated brain functional impairment in multiple brain regions.

4052

MAGNETIC RESONANCE IMAGING STUDY OF NORMAL TIBETAN AND HAN PEOPLE'S SKULL BONE MARROW IN HIGH-ALTITUDE AREA

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High-altitude hypoxic environment stimulates red bone marrow hematopoiesis at physiological angle. This study

explores the sensitivity of the hematopoietic system to the hypoxic environment in Tibetan and Han people.

Objective: To investigate the differences in skull bone marrow of normal Tibetan and Han people in high-altitude regions based on conventional magnetic resonance imaging and DWI techniques.

Method: A total of 200 Han people and 200 Tibetan people in normal Tibetan areas ranging from 3000 to 4000 m above sea level and 30–50 years old were selected. We measured the axial T1 WI sequence signal intensity, ADC value, and average barrier thickness of frontal, parietal, occipital, and temporal at the same scan layer, and compared the measured data using statistical methods.

Results: There was no significant difference in signal strength and ADC of frontal and parietal bone marrow and average barrier thickness between Tibetan and Han residents ($p > 0.05$). However, the signal intensity of occipital bone and temporal bone marrow of Tibetan residents was lower than that of the Han nationality. The ADC values of occipital bone and temporal bone marrow of Tibetan residents were slightly higher than those of Han nationality residents, and the statistical results were significantly different ($p < 0.05$).

Conclusions: Considering the long-term hypoxic environment during the skull bone marrow transformation, occipital bone and temporal bone marrow of the normal Tibetan people may be related to the red medullary of the skull bone marrow or delayed conversion.

4053

VBM AND ReHo WITHIN BRAIN GRAY MATTER AND NEURAL ACTIVITY HOMOGENEITY IN OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME

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Objective: OSAHS is characterized by intermittent hypoxia, which can lead to cognitive, memory, and executive function impairments due to multiple brain regions. The aim of this study is to explore the brain gray matter structure subtle changes and function spontaneous activity alterations of OSAHS patients from a neuroimaging perspective.

Methods: A total of 29 cases of OSAHS patients and 27 cases of healthy adults were recruited. The two groups were matched by ages, education, and altitude, all subjects were Hans male and right handed. T1-3D and rs-fMRI examinations were performed in this study. We used VBM with ReHo methods to study the differences in gray matter volume (GMV) and function between the two groups. The ReHo values and the differences in brain area's GMV can be related to the apnea-hypopnea index (AHI) for OSAHS.

Results: Lower GMV in OSAHS patients occurs in the parahippocampal gyrus, the fusiform gyrus, the surrounding cortex, and the left hippocampus ($p < 0.05$, Alphasim corrected). The brain areas with lower ReHo values are the inferior temporal gyrus, the left superior temporal gyrus, and the left lingual gyrus. Higher ReHo values occur in the superior frontal gyrus, the precuneus, the postcentral gyrus, and the right cingulate gyrus ($p < 0.05$, Alphasim corrected). The patient's AHI index was negatively correlated with the ReHo value of the left superior frontal gyrus and positively correlated with the right inferior temporal gyrus.

Conclusions: There are many brain regions in OSAHS patients with GMV reduction and functional changes, which are independent of each other. ReHo value changes in some brain areas are related to the OSAHS condition.

4054

STUDY ON CEREBRAL HEMODYNAMICS OF CHRONIC MOUNTAIN SICKNESS WITH MR PERFUSION

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Objective: Chronic mountain sickness (CMS) is a common disease in high-altitude areas. Owing to the increase of hemoglobin, blood viscosity increases, which causes many clinical symptoms, among which headache is the most common. In this study, MR perfusion (MRP) was used to investigate the changes of cerebral hemodynamics in patients with chronic altitude sickness.

Methods: Sixteen CMS patients and 14 healthy volunteers were examined using PWI scan after no abnormalities were seen on conventional MRI scans. An independent sample *t* test was used to compare differences in cerebral hemodynamic parameters between the two groups.

Results: Compared with that of the volunteer group, the relative cerebral blood flow decreased in CMS patients ($p < 0.05$). The mean transit time (MTT) and time to peak (TTP) were increased ($p < 0.05$).

Conclusions: The changes in MTT and TTP suggest that there may be collateral circulation compensation in the brain of patients with chronic mountain sickness. Cerebral hemodynamics changes in patients with chronic altitude sickness. MRP is significant in the medical treatment and further study of CMS brain changes.

4055

EMERGENCE OF SALMONELLA PARATYPHI A IN FRENCH TRAVELERS RETURNING FROM NEPAL

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Salmonella Paratyphi A has emerged in the Indian subcontinent at the end of the 90s. In Nepal it represents more than one-third of positive blood cultures in enteric fever. We report a cluster of three cases in a group of seven persons after trekking in Nepal during monsoon season. As people lived in different areas in France, the first author, who was also the mountain leader, contacted the national reference center for Salmonella (CNR) to mention the cluster, and began an epidemiological investigation. The first case was a teenager hospitalized with fever, blood cultures were positive for Salmonella Paratyphi A, and she was treated with ceftriaxone. The two other cases were adults presenting with the same symptoms shortly after the first case. They received ambulatory treatment of azithromycin before receiving blood culture results, as the bacterial resistance to nalidixic acid was previously discovered. A probable specific place of contamination was identified in Kathmandu valley (after trekking). Two more cases returning from Nepal were reported to the CNR on the same year, compared with less than one case per year usually. The CNR could analyze four

strains: they were susceptible to ampicillin, chloramphenicol, cotrimoxazole, and azithromycin, but resistant to nalidixic acid with decreased susceptibility to ciprofloxacin. All had unique DNA restriction profile on pulsed field gel electrophoresis (before the time of whole-genome sequencing). Emergence of Salmonella Paratyphi A in Nepal sets travelers three problems: potential severity of infection, increasing resistance to antibiotics, and lack of an efficient vaccine. Prevention is mainly based on universal hygiene recommendations.

4056

TRANSCRIPTION FACTORS REGULATION IN HUMAN PERIPHERAL WHITE BLOOD CELLS DURING HYPOBARIC HYPOXIA EXPOSURE: AN IN VIVO EXPERIMENTAL STUDY

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High altitude is a natural laboratory, within which the clinical study of human physiological response to hypoxia is possible. An inadequate response to hypoxia may lead to cardiovascular and respiratory diseases. Thus, investigating temporal changes in key transcription factors (TFs) HIF-1a, HIF-2a, NF- κ B, and NRF2 mRNA levels, relative to oxidative stress (OxS) and inflammatory markers, may reveal molecular targets that contrast deleterious effects of hypoxia. Biological samples and clinical data from 15 healthy participants were collected at baseline and after rapid passive ascent to 3830 m (24 and 72 hours). RNA was extracted by PAXgene Blood RNA method, gene expression was assessed by qPCR, and reactive oxygen species (ROS) generation was determined by EPR spectroscopy. Oxidative damage and cytokine levels were estimated by immuno or enzymatic methods. Hypoxia transiently enhanced HIF-1a mRNA levels over time, reaching a peak after 24 hours. Whereas HIF-2a and NRF2 mRNA levels increased consistently over time. In contrast, NF- κ B mRNA levels remained unchanged. Plasma levels of IL-1 β and IL-6 also remained within normal ranges. Whereas ROS production rate and markers of OxS damage were significantly increased over time. The analysis of TF gene expression suggests that HIF-1a is a lead TF during hypobaric hypoxia exposure. The prolongation of HH exposure led to a switch between HIF-1a and HIF-2a/NRF2, suggesting the activation of new pathways. These results provide new insights regarding the temporal regulation of key TFs, inflammatory state, and ROS homeostasis involved in human hypoxic response, potentially also relevant to the mediation of diseases that induce a hypoxic state.

4057

CANOE ACCIDENT WITH THREE ADOLESCENT BOYS WITH SUBMERSION AND PROFOUND ACIDENTAL HYPOTHERMIA IN THE SWEDISH MOUNTAINS

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Submersion and accidental hypothermia with cardiac arrest represent a challenge for mountain rescue as well as for medical prehospital personnel, especially when it happens in remote areas under harsh weather and water conditions. Three adolescent boys were canoeing on a mountain lake in June when their canoe capsized and they all fell into the cold water. The immersion time spanned from 59 to 80 minutes. Two of the victims showed no vital signs after being pulled out of the water. The third victim had vital signs although he was unconscious. Two of the victims had extremely low body temperature and were brought to the Trondheim University Hospital in Norway, where they were successfully resuscitated with extracorporeal rewarming. After 1 day, they were transported to Karolinska University Hospital in Stockholm, Sweden, by their ECMO team. The third victim with moderate-to-severe hypothermia was brought to the regional hospital in Östersund, Sweden. The challenges for the mountain rescuers were the windy weather and rough water conditions, to do the rescue maneuvers from the water, to make a decision, and start the cardiopulmonary resuscitation (CPR) during transportation directly on the small boat. For the medical prehospital personnel, the challenge was to maintain a high qualitative intermittent CPR in tough terrain and to heavily carry the patients to the helicopter, and then to focus on the very important triage and getting the patient to the right destination without any delay.

4059

IMPLEMENTATION OF A MECHANICAL CARDIOPULMONARY RESUSCITATION DEVICE IN A PHYSICIAN-STAFFED HELICOPTER EMERGENCY MEDICAL SERVICE: A PROSPECTIVE OBSERVATIONAL STUDY

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In this prospective observational study, we describe the incidence and characteristics of out-of-hospital cardiac arrest (OHCA) cases who received mechanical cardiopulmonary resuscitation (CPR) after the implementation of a mechanical CPR device (LUCAS 2; Physio Control, Redmond, WA) in a physician-staffed helicopter emergency medical service (HEMS) in South Tyrol, Italy. During the study period (June 2013–April 2016), 525 OHCA cases were registered by the dispatch center and 271 (51.6%) were assisted by HEMS. LUCAS 2 was applied in 18 (6.6%) of all HEMS-assisted OHCA patients: 10 were treated with LUCAS 2 at the scene only and 8 were transported to hospital with ongoing CPR. Two (11.1%) of the 18 patients survived long term with full neurological recovery. In seven of eight patients transferred

to hospital with ongoing CPR, CPR was ceased in the emergency room without further intervention. Retrospectively, all HEMS-assisted OHCA cases were screened for proposed indication criteria for prolonged CPR. Thirteen patients fulfilled these criteria, but only two of them were transported to hospital. Based on these results, we propose a standard operating procedure for HEMS-assisted patients with refractory OHCA in a region without hospitals with ECLS capacity.

4060

PREHOSPITAL TIMES AND CLINICAL CHARACTERISTICS OF SEVERE TRAUMA PATIENTS: A COMPARISON BETWEEN MOUNTAIN AND URBAN/SUBURBAN AREAS

Airway, Circulation and Trauma Management

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We investigated prehospital times, clinical characteristics, and therapeutic interventions in multisystem trauma patients injured in mountainous areas in comparison with both urban and suburban trauma patient admissions.

Methods: Prehospital and in-hospital data collected from trauma patients included in the International Alpine Trauma Register (IATR) hosted in Bolzano, Italy (aged 16–80 years with an ISS = 16) were compared with trauma patient data published from those urban and suburban areas included in the Trauma Register DGU[®] (TR-DGU) of the German Trauma Society. A total of 94 patients from the IATR and 11,020 patients from the TR-DGU met the inclusion criteria. Due to longer treatment-free intervals (mean 59.1 vs. 19.7 minutes), total out-of-hospital time was reportedly longer in individuals injured in mountainous areas than in urban/suburban areas (117.4 ± 142.9 vs. 68.7 ± 28.6 minutes, $p = 0.002$), despite the more frequent helicopter rescue (93% vs. 40%, $p < 0.001$). A total of 57% of IATR patients were hypothermic at hospital arrival, mean ISS was higher (38.5 ± 15.8 vs. 28.6 ± 12.2 , $p = 0.001$), and patients with a systolic blood pressure (SBP) = 90 mmHg were more frequent (27% vs. 15%, $p = 0.005$), yet less patients had received volume therapy (82% vs. 93%, $p = 0.001$). However, overall no difference in hospital mortality rate was observed (11% vs. 17%, $p = 0.159$). Trauma incidents in mountainous areas commonly feature significantly increased out-of-hospital time, which is associated with a more severe ISS, higher risk of accidental hypothermia, and more frequent hypotension, than urban/suburban trauma. Nonetheless, the mortality rate of IATR patients is comparable with that of urban/suburban trauma patients.

4061

SUSPENSION SYNDROME: A POTENTIALLY FATAL VAGALLY MEDIATED CIRCULATORY COLLAPSE: AN EXPERIMENTAL RANDOMIZED CROSSOVER TRIAL

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Suspension syndrome describes a potentially life-threatening event during passive suspension on a rope. The pathophysiological mechanisms are not fully understood and the treatment is unknown. We aimed to elucidate the pathophysiology and to give treatment recommendations. In this experimental randomized crossover trial, 20 healthy volunteers were passively suspended in a harness for a maximum of 60 minutes, with and without prior climbing. During the tests, heart rate (HR), blood pressure (BP), and stroke volume were monitored and left ventricular diameters were determined by transthoracic echocardiography. Venous pooling was assessed by measuring the diameter of the superficial femoral vein (SFV) with ultrasound and lower leg tissue oxygenation (StO₂) with near infrared spectroscopy (NIRS) and localized bioelectrical impedance. Signs and symptoms of presyncope were recorded. Twelve (30%) out of 40 tests were prematurely interrupted due to presyncopal symptoms after a mean time of 44.7 minutes (minimum 13.4, maximum 59.7). An increase in SFV diameter and a decrease in StO₂ indicate venous pooling during suspension. In addition, the capacitive resistance (Xc) of the cells decreased. However, HR and BP did not change in participants without presyncope, but suddenly decreased in participants with presyncope. All symptoms resolved and values returned to normal within 5 minutes with participants in supine position. During passive suspension in a harness, venous pooling takes place in lower legs. Yet, no effect on macrocirculation was observed and a vagal mechanism seems to lead to a presyncope. Persons suspended on a rope should be rescued and put into a supine position as soon as possible.

4062

DECISIONS AT HIGH ALTITUDE: PSYCHOLOGICAL TECHNIQUES OF MOTIVATION IN HIGH-RISK SITUATIONS

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The aim of this study was to explore the decision-making process of a selected group of Bulgarian climbers during high-mountain expeditions. The study is a part of a larger research project on decision-making psychology. The participants were expert male climbers with an experience in high-altitude mountaineering in the Himalaya, with ascents of 8000 m peaks, first ascents in Antarctica and Karakoram, as well as climbing route development in the Andes. The research method chosen was an in-depth semistructured interview consisting of 10 questions. The climbers provide concrete examples of critical situations and individual decision-making strategies. The analysis shows how decision-making is influenced by factors such as inner speech, visual imagery, experience, and intuition. It is anticipated that the study results will contribute to better understanding of climbers' individual decision-making patterns under the challenging conditions of high-altitude mountaineering. The study may help extreme athletes in overcoming critical situations in pursuit of new heights of performance.

Keywords: climbing; decision-making; inner speech; risk; visual imagery

4063

A USER FRIENDLY MOTHER AND CHILD HEALTH HAND BOOK CAN EMPOWER PREGNANT MOTHERS TO IMPROVE PREGNANCY OUTCOME AND CHILD CARE: A CROSS-SECTIONAL STUDY IN A SECONDARY LEVEL CARE HOSPITAL IN LADAKH (ALT. 2800–4500 M) 2015–2018

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Institutional delivery is the norm in Ladakh (altitude 2800–4500 m). Present day mothers are predominantly literate. Ninety percent of the deliveries in Ladakh take place in SNM Hospital, Leh. Capitalizing on these facts, we developed a user-friendly mother and child health hand book to follow 3778 consecutive deliveries for their pregnancy outcome from April 2015 to February 2018. In Leh district, 2342 (75.82%) were born by normal vaginal deliveries and 738 (23.8%) by C-section. In Kargil district, 525 (78.01%) were by normal vaginal deliveries and 146 (21.6%) by C-section. Rate of C-section subdivision wise was Leh (27.2%), Kargil (24.4%), Nubra (23.9%), Sham (21%), Zaskar (19.2%), and Changthang (17%). Of 3101 babies of Leh district, 1442 (46.50%) were female and 1659 were male. Of 677 babies from Kargil, 313 (46.23%) were female and 364 were male. There were 28 intrauterine deaths (IUDs) and 20 postnatal deaths, making it an overall mortality rate of 1.53% in Leh district. In Kargil district, there were five IUDs and five postnatal deaths with an overall mortality rate of 1.45%. Division wise, Leh with 11 expired and 12 IUDs was unsatisfactory followed by Nubra subdivision with 4 expired and 7 IUDs. The findings vindicate our strong conviction that there is a strong case for adoption of the user-friendly single-tool mother and child health handbook to improve the pregnancy outcome. The risk factors highlighted in this handbook at the beginning of antenatal check up will certainly draw the attention of the obstetrician to pay special attention to high-risk subjects and thus reduce mortality.

4064

GROWTH PATTERN IN NEWBORN AT HIGH ALTITUDE (ALT. 2700–4500 M): A CROSS-SECTIONAL STUDY OF NEW BORN THROUGH EARLY CHILDHOOD IN LADAKH, NORTHERN INDIA 2015–2018

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Children born and living at high altitude are known to be small at birth and have delayed growth. Ladakh in northern India (2700–4500 m) is one such high-altitude region. SNM Hospital at the district headquarter Leh with good gynae/obs services and a well-equipped sick baby unit is favored by pregnant mothers of five subdivisions of the district for delivery. From April 2015 to February 2018, we assessed and followed up 3778 newborns representative of the whole

district. Within 24 hours of birth, weight, length, and head and chest circumferences were measured according to WHO multicenter growth reference study (MCGR). Median birth length of male term babies born normally and by C-section ($n = 1901$) and similarly that of born female ($n = 1641$) were comparable with MCGR norm of 50.0 cm and 49.0 cm, respectively. However, the median birth weight was marginally low at 3.180 kg and 3.000 kg, respectively, for male and female. Median head circumference of similarly born group of male and female at birth was 36.00 and 35.00 cm, respectively. Interestingly, comparison between infants of two extreme altitudes in our cohort, Changthang at highest ($= 3700$ m) and Kargil at lowest (2700 m) depicts slightly higher BMI with infants of Changthang recording 12.8 ($n = 264$) versus 12.6 ($n = 170$) for males and 12.32 ($n = 227$) versus 11.26 ($n = 147$) for females. The detailed follow-up will reveal not only the trend or catch up for these anthropometric measurements but also address the role of altitude in child development in this genetically heterogeneous population.

Keywords: growth pattern; high altitude

4065

CHRONIC MOUNTAIN SICKNESS IN RUBSHO VALLEY OF LADAKH (ALTITUDE 4500–4900 M): COMPARATIVE STUDY OF TWO DIFFERENT ETHNIC POPULATIONS WITH DIFFERENT CHRONIC MOUNTAIN SICKNESS SCORING SYSTEM

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Rubsho valley in Ladakh (4500–5000 m) on the Trans-Himalaya range is one of the world's highest inhabited places. People's whole existence depends on rearing cattle and livestock including yak, the best adapted animal, and goats, the source of finest pashmina wool of Cashmere shawl, and are in constant movement with their flocks in search of pasture. In May 2017, we studied two different nomadic population in Rubsho: Tibetan and Ladakhi living at similar altitude, but belonging to different ancestry. For screening of chronic mountain sickness, we applied the two internationally accepted chronic mountain sickness (CMS) scoring systems, one before Xining and one after Xining world congress. Sixty subjects, 32 male and 28 female, with an average age of 48.36 and 48.68 years were studied. Applying the two scoring systems, none of the subjects were in the severe category of CMS. Five percent and 10% were in moderate category of CMS by international scoring before Xining and after Xining, respectively, whereas 35% and 28.3% were in mild category of CMS. A total of 31.2% of Tibetan men were suffering from CMS as against 44% of the Tibetan women. A total of 12.5% of Ladakhi men suffered from CMS as against 31.5% of Ladakhi women. Breathlessness (69.23% vs. 48.3%), dizziness (61.5% vs. 48.3%), headache (55.7% vs. 50.0%) and sleep disturbance (40.38%

vs. 16.6%) formed the predominant symptoms, with injected conjunctiva (36.6% vs. 31.6%) and cyanosis (31.6% vs. 36.6%) the predominant signs in the respective scoring system. CMS is more prevalent in women as the condition occurs around the menopause age. Tibetan men are more vulnerable than Ladakhi men.

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ABSTRACT WITHDRAWN

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ALTITUDE CHANGES OF HYPOXIA-INDUCIBLE FACTOR-1A, INDUCIBLE NITRIC OXIDE SYNTHASE, AND NITRIC OXIDE IN HEALTHY SUBJECTS AND THE INFLUENCE ON ERYTHROCYTE DEFORMABILITY

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Objective: To observe the altitude changes of hypoxia-inducible factor-1a (HIF-1a), inducible nitric oxide synthase (iNOS), and nitric oxide (NO), as well as to explore the influence on erythrocyte deformability (ED) in healthy subjects.

Methods: HIF-1a, iNOS, NO, and erythrocyte filtration index (EFI) were measured in 320 healthy subjects at different altitudes (2260 meters group A, 3300 meters group B, and 4080 meters group C).

Results: The level of HIF-1a in group C (7.65 ± 1.36) $\mu\text{g/L}$ was higher than that in group B (5.39 ± 1.02) $\mu\text{g/L}$ and group A (4.18 ± 1.14) $\mu\text{g/L}$ ($p < 0.01$), the level of HIF-1a in group B was also higher than that in group A ($p < 0.01$), serum content of iNOS in group C (5.86 ± 1.43) $\mu\text{mol/L}$ was significantly lower than that in group B (9.44 ± 2.13) $\mu\text{mol/L}$ and group A (12.23 ± 2.07) $\mu\text{mol/L}$ ($p < 0.01$), and the

content of serum nNOS in group B was lower than that in group A ($p < 0.01$). The serum concentration of NO in group C (38.53 ± 4.23) $\mu\text{mol/L}$ was lower than that in group B (47.85 ± 3.77) $\mu\text{mol/L}$ and group A (59.23 ± 4.01) $\mu\text{mol/L}$ ($p < 0.01$), and the content of serum NO in group B was lower than that in group A ($p < 0.01$). EFI increased with increasing altitudes (group A: 4.67 ± 0.49 , group B: 7.05 ± 1.51 , group C: 11.45 ± 1.78), there were significant differences at different altitudes ($p < 0.01$). Correlative analyses showed that EFI was negatively correlated with iNOS and NO concentrations, and positively correlated with the level of HIF-1 α .

Conclusions: The formation of the different concentrations of HIF-1 α , iNOS, and NO plays core roles in the pathophysiological mechanism of abnormalities of ED in healthy subjects at different altitudes, and altitude changes on ED were closely correlated with altitude difference of biological effects of iNOS and NO.

4069

EVALUATION OF 90-DAY OUTCOME AND SLEEP QUALITY IN PATIENTS WITH NONDISABLING ISCHEMIC CEREBROVASCULAR EVENTS AT HIGH ALTITUDE

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Objective: To investigate the incidence of sleep disorders and poor outcome and identify the relevant factors for sleep disorders in patients with nondisabling ischemic cerebrovascular events in Qinghai.

Methods: The consecutive patients with NICE in Qinghai admitted to hospital within 7 days after onset were enrolled prospectively and followed for 90 days face to face. Poor outcome was assessed by modified Rankin scale. Pittsburgh sleep quality index (PSQI) and Epworth sleepiness scale were used to evaluate the sleep disorder. The sleep disorder in patients with NICE was defined as PSQI scores that were > 11 . Multivariate logistic regression and further stratification analysis were used to identify the risk factors for the sleep disorder in patients with NICE.

Results: A total of 132 patients were recruited. Forty-two patients (31.8%) had poor outcomes. According to the results of follow-up, the proportion of sleep disorder and excessive daytime sleepiness was 45.5% and 31.8%, respectively. In multivariate logistic regression, obesity (odds ratio [OR] = 4.550, 95% confidence interval [CI]: 2.374–11.451, $p = 0.009$), poor outcome (OR = 8.545, 95% CI: 1.869–49.978, $p = 0.002$), excessive daytime sleepiness (OR = 1.129, 95% CI: 1.069–2.978, $p = 0.048$), posterior circulation stroke (OR = 1.223, 95% CI: 1.029–3.547, $p = 0.042$), high-altitude residence (OR = 1.345, 95% CI: 1.063–4.978, $p = 0.039$), and high-altitude polycythemia (OR = 2.374, 95% CI: 1.679–5.263, $p = 0.023$) were the important predictors of sleep disorder in patients with NICE. Stratification analysis showed that high-altitude residence and high-altitude polycythemia were positively related with sleep disorder in patients with the obesity–poor outcome–excessive daytime sleepiness and posterior circulation stroke.

Conclusions: Nearly one-third of patients with NICE had poor outcome. According to the results of follow-up, the proportion of sleep disorder and excessive daytime sleepiness

was 45.5% and 31.8%, respectively. High-altitude residence and high-altitude polycythemia are independently related with sleep disorders of NICE patients in Qinghai.

4070

CLINICAL RESEARCH ON INTRAVENOUS HYDRATION AND ORAL HYDRATION OF PLATEAU AREA PATIENTS IN PREVENTION OF POST-OPERATIVE CONTRAST AGENT NEPHROPATHY WITH CORONARY INTERVENTION

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Objective: To investigate the effect of venous and oral hydration on the prevention of cardiac insufficiency in patients with contrast agent nephropathy after percutaneous coronary intervention from plateau areas.

Methods: The clinical data of 250 patients with cardiac insufficiency requiring coronary intervention were collected and randomly divided into observation group with venous hydration ($n = 127$) and control group with oral hydration ($n = 123$). The occurrence rate of contrast agent nephropathy was recorded and compared in-between two groups.

Results: The incidence of contrast agent nephropathy was significantly lower in patients from the observation group than in those in the control group (14.17% vs. 24.39%, $\chi^2 = 4.204$, $p < 0.05$). The serum creatinine levels of patients from both groups reached peak values at the third day after application of the contrast agents. Whereas at the first day after application, the value of serum creatinine was significantly lower in observation group than that in the control group ($p < 0.05$). Furthermore, the cystatin C level of patients for both groups reached the peak value at the third day after application of contrast agent, afterward, the level of which was degraded greatly in the observation group than that in the control group ($p < 0.05$).

Conclusions: The occurrence of chronic cardiac insufficiency and the occurrence of contrast agent nephropathy after percutaneous coronary intervention in plateau areas are higher than those in plain areas. This study suggested that venous hydration could more effectively prevent the occurrence of contrast agent nephropathy after percutaneous coronary intervention in patients with cardiac insufficiency in plateau areas than oral hydration.

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NEUROPROTECTIVE EFFECTS AND EXPRESSION OF TLR4 OF INTERMITTENT HYPOBARIC HYPOXIA PRECONDITIONING ON MIDDLE CEREBRAL ARTERY OCCLUSION RATS

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Objective: To investigate the neuroprotective effect of intermittent hypobaric hypoxia preconditioning (HP) on rats' unilateral middle cerebral artery occlusion (MCAO) model, and the effects of Toll-like receptor 4 and nuclear factor kappa B expression change on brain tissue.

Methods: A total of 171 male Sprague–Dawley rats were randomly divided into normal control group (C) with 30 rats, sham operation group (S) with 26 rats, hypoxia treatment group (H) with 35 rats that receive intermittent hypobaric

hypoxia treatment, middle cerebral artery occlusion group (M) with 43 rats, and hypobaric hypoxia preconditioning and MCAO (HM) group with 37 rats; hypobaric hypoxia preconditioning was performed for 7 days a week, 3 hours per day, then make MCAO model; Longa scores were recorded and analyzed statistically, TTC staining to calculate the infarction volume and rate determination analysis to observe the degree of brain edema, immunohistochemistry staining method to observe the TLR4 expression on cells, enzyme-linked immunosorbent assay (ELISA) and Westernblot method for the determination of expression of TLR4 and NF- κ B on brain tissue.

Results: The neurological deficits in HM group rats were improved and the volume of cerebral infarction was decreased; the brain water content in group HM was significantly lower than that in group M; immunohistochemistry, ELISA, and Westernblot results showed that preconditioning could downregulate the expression of TLR4 and NF- κ B.

Conclusions: Appropriate HP can effectively relieve nerve injury of MCAO rats and decrease the expression of TLR4 and NF- κ B. Both HP and cerebral ischemia can increase the expression of TLR4.

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ABSTRACT REMOVED

4073

CEREBRAL VENOUS OUTFLOW AT HIGH ALTITUDE: A DESCRIPTIVE PROSPECTIVE STUDY

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One of the possible causes of acute mountain sickness (AMS) is an abnormal venous drainage of the cephalic district, which might lead to intracranial fluid accumulation and extravasation within the interstitial and intracellular spaces, determining cerebral parenchyma edema. The combination of morphological and hemodynamic parameters of the echocolor-Doppler (ECD) represents an ideal direct and real-time method for the study of cerebral venous outflow. A group of 11 healthy male volunteers was recruited (mean age 37.6 years). They were all not acclimatized to high altitude. They received no treatment to prevent AMS. The subjects underwent different clinical and ECD measurements at sea level and at high altitude (Mosso Institute 2901 m) after a 12-hour stay. The clinical part provided Lake Louise Score (LLS) assessment. The following parameters were assessed with ECD: flow direction, flow velocity, presence and competence of the IJV valve, IJV cross-sectional area (CSA) in relation to change in posture, duplex derived flowmetry, and anomalous morphology of the endoluminal venous space. In our small sample, no severe AMS was registered. In this preliminary study, data showed three issues of statistical relevance that can support our hypothesis: the increase of CSA at sitting position at altitude, the increase of IJV flow at altitude, and the correlation between the latter and the absence of jugular valves. In the near future, it will be possible to synchronize the electrocardiogram with brain inflow and outflow to have a noninvasive ultrasound picture of the brain-heart axis.

4074

EFFECTS OF TIBETAN HERB, RHODIOLA ALGIDA, ON PROLIFERATION AND HIF-1 α AND HIF-2 α EXPRESSION IN MCF-7 CELLS UNDER HYPOXIA *IN VITRO*

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Object: Rhodiola algida is used in traditional Tibetan medicine to stimulate the immune system, and widely used in prevention and treatment of both acute and chronic mountain sickness in Qinghai-Tibetan plateau. This study attempted to identify the potential effect of Rhodiola algida extract on hypoxic MCF-7 breast cancer cells and the underlying mechanisms.

Methods: The antiproliferative effects of *Rhodiola algida* on MCF-7 breast cancer cells were compared *in vitro* under hypoxic and normal conditions by using MTT analysis. The influence of *R. algida* on cancer cell apoptosis was determined by flow cytometry. The expression levels of hypoxia-inducible factor (HIF)-1 α and HIF-2 α were evaluated by Western blot analysis.

Results: *R. algida* inhibited the proliferation of MCF-7 breast cancer cells in a dose- and time-dependent manner. The results of flow cytometry indicated that the antiproliferative effect of *R. algida* was mediated by apoptosis induction. Pretreatment with *R. algida* significantly sup-

pressed the hypoxia-induced proliferation and expression of HIF-1 α and HIF-2 α in MCF-7 breast cancer cells.

Conclusions: *R. algida* might exert an anticarcinogenic effect on MCF-7 breast cancer cells by decreasing the protein levels of HIF-1 α and HIF-2 α , which are overexpressed under hypoxic conditions. This effect might be elicited by inhibiting the hypoxia-induced proliferation of MCF-7 breast cancer cells.

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EFFECTS OF HYPOXIA, HYPERCAPNIA, AND HYPOTHERMIA ON CEREBRAL OXYGENATION: A PROSPECTIVE PORCINE STUDY

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Limited data are available regarding the combined effects of hypoxia, hypercapnia, and hypothermia on cerebral oxygenation, a clinical condition called triple H syndrome in avalanche victims. The aim of this study was to evaluate the influence of hypothermia, hypoxia, and hypercapnia on brain oxygenation in a porcine model. Nine anesthetized pigs were surface cooled to a core temperature of 28°C and underwent a period (20 minutes) of hypoxia (FiO₂: 17%) before hypercapnia was induced. Endpoint was considered onset of hemodynamic instability (30% decrease in MAP) or 60 minutes posthypercapnia induction. Pigs were ventilated volume controlled; brain oxygenation measurements included intracranial pressure (ICP), cerebral perfusion pressure (CPP), and cerebral venous oxygen saturation (ScvO₂). Analysis of variance for repeated measures was used to compare values across phases for ICP, CPP, and ScvO₂. Pairwise comparisons were analyzed by means of Student's *t*-test with Bonferroni correction. ICP did not show significant changes during the hypothermia ($p > 0.05$) and hypoxia phases ($p > 0.05$), but significantly increased during hypercapnia ($p < 0.05$). Despite a progressive and significant decrease of CPP in all three phases ($p < 0.05$), the decrease in CPP had clinically relevant modification only during the hypothermia and hypercapnia phases. ScvO₂ increased significantly during the hypothermia induction ($p < 0.05$), did not show significant changes during the hypoxia phase ($p > 0.05$), and decreased significantly during the hypercapnia phase ($p < 0.05$). Our results demonstrate that hypercapnia increases ICP in a hypothermic hypoxic pig to such a degree that CPP is impaired causing cerebral hypoxia, despite a reduced oxygen demand due to a severe hypothermic status.

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INTERNATIONAL COMMISSION FOR MOUNTAIN EMERGENCY MEDICINE (ICAR MEDCOM) CONSENSUS GUIDELINES FOR ON-SITE MANAGEMENT AND TRANSPORT OF PATIENTS IN CANYONEERING INCIDENTS

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Canyoneering is a recreational activity that has increased in popularity in the past decade in Europe and North America, resulting in up to 40% of the total search and rescue costs in some geographic locations. The International Commission for Mountain Emergency Medicine (ICAR Medcom) convened an expert panel to develop recommendations for on-site management and transport of patients in canyoneering incidents. Guidance to healthcare providers and canyoneering rescue professionals is provided about best practices for rescue and medical treatment through the evaluation of the existing best evidence, focusing on the unique combination of remoteness, water exposure, limited on-site patient management options, and technically challenging terrain. Recommendations are graded on the basis of quality of supporting evidence according to the classification scheme of the American College of Chest Physicians.

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HEMOGLOBIN CONCENTRATION, PULSE, AND LIFETIME REPRODUCTIVE SUCCESS AMONG ETHNIC TIBETANS AT HIGH ALTITUDES IN NEPAL

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Since the 1970s, Tibetan and Sherpas, mainly from Nepal, transformed the study of high-altitude adaptation. In particular, the distinctively unelevated hemoglobin of Tibetans and Sherpas, compared with that of Andean highlanders and acclimatized lowlanders, has drawn attention and led to the hypothesis that it represents an adaptation resulting from natural selection. This presentation reports a test of the hypothesis that genetic variants in the oxygen homeostasis pathway associate with hemoglobin concentration and reproductive success. A sample of 1006 postreproductive Tibetan women residing at altitudes from 3000 to 4100 m in Nepal provided reproductive histories by interviews in native dialects, physiological measurements, and DNA from saliva samples. Regression analyses selected influential covariates of the number of pregnancies, livebirths, and children surviving to 15 years. Genomic analyses tested for associations with physiological and reproductive success variables. Beneficial alleles with signals of selection at EPAS1 SNP sites (but not EGLN1) associated with unelevated hemoglobin concentration. Unelevated hemoglobin concentration associated with greater lifetime reproductive success measured as the probability a pregnancy progressed to a livebirth. Yet the

EPAS1 variants did not associate with pregnancy outcome, likely due to insufficient statistical power. EPAS1 did not associate with pulse although lower pulse associated with more pregnancies and live births. A genome-wide polygenic model of adaptation identified genes unrelated to hypoxia, favoring lower pulse, more livebirths, and fewer child deaths. The findings illustrate the complexity of identifying adaptations. They support the hypothesis that selection is acting against elevated hemoglobin concentration, pulse, or another correlated trait among Tibetans at high altitude.

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ABSTRACT WITHDRAWN

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HYPOXIA-INDUCED VESSEL WALL INJURY AND ACTIVATION OF NLRP3 INFLAMMASOME CONTRIBUTE TOWARD PROTHROMBOTIC PHENOTYPE

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Exposure to hypobaric hypoxia during high-altitude (HA) expedition, mountain climbing, or air travel serves as a risk

factor for thromboembolism. Despite the recently reported role of NLRP3 inflammasome in thrombus development, investigations are still required to understand the pathophysiology of HA-induced thromboembolism. Using localized hypoxia-induced thrombosis and simulated HH animal model systems, effect of hypoxia on hemostasis was observed. Samples were collected from normoxia/hypoxia-exposed prothrombotic animals and subjected to polymerase chain reaction-based hypoxia signaling pathways array. Data showed that thrombus formed under hypoxic environments is an aggravated form of thrombus developed under normoxic conditions. Using whole transcriptome analysis, we reported the novel role of NLRP3-caspase-1-IL-1 β signaling in hypoxia-induced thrombogenesis. We extended our investigations to find an explanation for origin of inflammatory response (inflammasome activation). Bioinformatics-based ingenuity pathway analysis predicted that endothelial barrier dysfunction and leukocyte rolling were the key events occurring before inflammasome activation. These predictions were confirmed by observing vascular perturbations using Evans blue extravasation approach.

Results: The results demonstrated that hypoxia induces endothelial injury at the site of origin of thrombus formation. Nonetheless, immunofluorescence staining of vein wall with markers of monocytes/macrophage (mac387), neutrophils (neutrophil elastase), and platelet ($\alpha 2\beta 3$) revealed that leukocytes and platelets adhere to vein wall under hypoxic milieu. Our findings clearly indicate that hypoxia-induced vessel wall injury accompanied with leukocyte adhesion is an early event associated with inflammasome activation and precedes the development of prothrombotic phenotype. *Part of this work has been published in PNAS 2017 May 2; 114(18):4763–4768.

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EXPANSION OF VECTOR-BORNE DISEASES TO HIGHER ALTITUDES: RISK FOR LOCAL POPULATIONS AND TRAVELERS

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There is growing evidence of expansion of vectors to higher altitudes with global warming. WHO published altitude limits for malaria in different countries in 1995, still used for counseling travelers, but these data have never been updated. In some East African countries, a shift in distribution of malaria vectors toward altitude has been recently observed, for example, in Kilimanjaro region, threatening local native populations and perhaps travelers. Malaria burden has globally decreased in the past decade, but other risks have increased or emerged: *Aedes* sp, vectors for yellow fever, dengue, Zika, chikungunya, are present as high as 2000 m in Central and South America, with some epidemics reported at altitude. Evidence of Japanese encephalitis virus transmission has been found at 2900 m in Tibet and in mountain districts of Nepal. Activity of *Ixodes ricinus*, vector of Lyme disease and tick-borne encephalitis in Europe, is increasing in altitude and latitude. These are only a few examples in popular trekking regions. Risk assessment is complex, depending on environmental parameters (temperature, precipitation, deforestation, etc), vectors and pathogens biology, animal and human hosts, and multiple socioeconomic factors (demography, migrations, urbanization, agricultural prac-

tices, health system etc.). Geographic information systems are used in specific studies, but data are scarce and need to be collected for a better knowledge of vector-borne diseases risk in mountainous areas.

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HYPOXIC VENTILATORY RESPONSE IN RELATION TO HYPOBARIC HYPOXIA AMONG THE TAWANG MONPA FROM EASTERN HIMALAYAN MOUNTAIN

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An increase in ventilation with low ambient oxygen pressure is a physiological response to high-altitude hypoxia to deal with the decline of arterial blood oxygen saturation (SaO₂). Such an adaptive measure to maintain the required level of arterial blood oxygen saturation at high altitude is known as hypoxic ventilatory response (HVR). In general, on acute exposure to hypobaric hypoxia, new comers reveal high level of HVR. However, one might expect somewhat a different adaptive mechanism for those who have been living at high altitude for generations, that is, high-altitude native people who are chronically exposed to hypobaric hypoxia. Interestingly, previous studies suggest that Andean high-altitude natives have a low (blunted) HVR and low ventilation as compared with the new comers. Therefore, it might be academically informative and interesting to know whether Indian high-altitude native populations follow the same trend or whether they have a complete different pathway of maintaining required level of arterial blood oxygen saturation under hypobaric hypoxia. Unfortunately, such data from Indian high-altitude native populations are hugely lacking for comparison with other high-altitude native populations. With this information in mind, this is an exploratory study in nature in exploring the hypoxic ventilatory responses among the Tawang Monpa from Eastern Himalayan Mountain of Arunachal Pradesh with special emphasis on the factors influencing such physiological adaptive measures of this population. Interestingly, unlike Andean high-altitude natives (0.71 ± 0.05 L/min/%SaO₂) Monpa show high level of HVR (3.097 ± 1.79 L/min/%SaO₂) and resting ventilation.

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TERRA X CUBE: THE NEXT HI-TECH RESEARCH PLATFORM FOR EXTREME HIGH-ALTITUDE CLIMATE SIMULATION

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Field-based scientific investigations in extreme environments represent a major research challenge. Complex combinations of multiple environmental parameters can prove highly difficult to mitigate against, thus making it difficult to standardize the logistics necessary to enable assessment of individual physiological or biological response. In an effort to resolve these research concerns, plus remain reactive to technological advancements, institutions have developed specific simulation chambers and accessible facilities in extreme earth habitats. In conjunction with the ongoing development of next-generation simulation-tech research plat-

forms, environmental simulation and interest in investigating climate combinations at a high-altitude equivalent are becoming an international hot topic. The design and realization of the TerraXcube, powered by EURAC Research, are a unique example of the latest in technological advancement. A newly emergent EU research infrastructure, the TerraXcube, is complete with two hypobaric climate-enabled chambers (large and small cube), medical support services, and research expertise. The large cube (137 m²) will enable the synchronous control of multiple climatic parameters: barometric pressure (= 300 mbar), temperature (−40°C–+60°C), humidity (10%–95%), wind (= 30 m/s), precipitation (rain and snowfall), and light (day and night cycles). In total, 15 individuals can be accommodated. Test protocols in the Large Cube test chamber may be inclusive of the adjacent hypobaric ambulatory room, airlock, and toilet facilities, thus enabling investigation of long-term exposure at low barometric pressures, specific ascent/descent use cases, O₂ and CO₂ enrichment considerations, and controlled investigation of potentially invasive measures. TerraXcube will be officially opened on November 30, 2018.

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BASIC LIFE SUPPORT RESUSCITATION IN AVALANCHE VICTIMS IS RELATED TO BODY POSITION: A RANDOMIZED SINGLE BLINDED MANNEQUIN STUDY

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Time-related asphyxia is the leading cause of death in completely buried avalanche victims. Time needed to extricate and to bring a buried victim into a position that allows basic life support (BLS) is unknown. The aim of this study was to investigate the duration of extrication and the possibility to perform BLS in relation to the victim's body position under snow. A randomized single-blinded mannequin study was performed with 18 participants with either BLS or ALS certification in April 2017. Each participant completed three test series. Resuscitation mannequins were buried in an artificial avalanche (1 m depth) and placed in three different burial positions (head downhill, prone position; head uphill, prone position; and head uphill, supine position). During extrication, the times to extricate the mannequin, free its airways, and to start cardiopulmonary resuscitation (CPR) in the supine standard position were evaluated; data were analyzed with Students *t*-test, Fisher-exact test, and one-way analysis of variance. Thirty-six tests were done. Median time to extricate the victim was 2.51 minutes (0.60–8.58), to free airways 7.22 minutes (2.28–20.43), and to bring them into standard CPR position 10.06 minutes (2.97–24.93). Overall, there was a significant difference between body position and time to free the airway ($p = 0.03$). The shortest time was found in head-uphill supine positions compared with uphill prone and downhill positions ($p < 0.05$). Overall, there was no difference in time between single and double rescuer teams ($p > 0.05$). The study suggests the need to specify education and resuscitation strategy for BLS of avalanche victims.

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ISOLATED PSYCHOSIS DURING EXPOSURE TO VERY HIGH AND EXTREME ALTITUDE: CHARACTERIZATION OF A NEW MEDICAL ENTITYKatharina Hüfner,¹ Hermann Brugger,² Eva Kuster,¹ Franziska Dünsser,¹ Agnieszka Stawingoa,² Rachel Turner,² Iztok Tomazin,³ and Barbara Sperner-Unterweger¹¹Department of Psychiatry, Psychotherapy and Psychosomatics, University Clinic for Psychosomatic Medicine, Medical University of Innsbruck, Italy; ²Institute of Mountain Emergency Medicine, EURAC Research, Bolzano, Italy; ³Department of Family Medicine, Faculty of Medicine, University of Ljubljana, Slovenia

Psychotic episodes during very high or extreme altitude exposure have been frequently reported in mountain literature, but not systematically analyzed and acknowledged as a distinct clinical entity. Episodes reported for >3500 m altitude with possible psychosis were collected from the lay literature and provide the basis for this observational study. Dimensional criteria of the *Diagnostic and Statistical Manual of Mental Disorders* were used for psychosis, and the Lake Louise Scoring criteria for acute mountain sickness and high-altitude cerebral edema (HACE). Eighty-three of the episodes collected underwent a cluster analysis to identify similar groups. Ratings were completed by two independent trained researchers (κ values 0.6–1). Cluster 1 included 51% (42/83) episodes without psychosis; cluster 2 included 22% (18/83) cases with psychosis, plus symptoms of HACE or mental status change from other origins; and cluster 3 included 28% (23/83) episodes with isolated psychosis. Possible risk factors of psychosis and associated somatic symptoms were analyzed between the three clusters and revealed differences regarding the factors “starvation” (χ^2 test, $p = 0.002$), “frostbite” ($p = 0.024$), and “supplemental oxygen” ($p = 0.046$). Episodes with psychosis were reversible but associated with near accidents and accidents ($p = 0.007$, odds ratio 4.44). Episodes of psychosis during exposure to high altitude are frequently reported, but have not been specifically examined or assigned to medical diagnoses. In addition to the risk of suffering from somatic mountain illnesses, climbers and workers at high altitude should be aware of the potential occurrence of psychotic episodes, the associated risks, and the respective coping strategies.

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MOUNTAIN ULTRAMARATHON RUNNING: PERFORMANCE DETERMINANTS AND BIOCHEMICAL ALTERATIONSKai Schenk,^{1,2} Hannes Gatterer,¹ Simon Rauch,^{1,3} Emily Procter,^{1,2} Rachel Turner,¹ Katharina Grasegger,¹ Markus Herrmann,^{4,5} Giacomo Strapazzon,¹ and Hermann Brugger¹¹Institute of Mountain Emergency Medicine, EURAC Research, Bolzano, Italy; ²Department of Sport Science, University Innsbruck, Innsbruck, Austria; ³Department of Anaesthesiology, University Hospital, LMU Munich, Munich, Germany; ⁴Department of Clinical Pathology, Bolzano Hospital, Italy; ⁵Clinical Institute for Medical and Chemical Laboratory Diagnostics, Medical University of Graz, Austria

In recent years, mountain ultramarathons have become increasingly popular and are considered a model to investigate physiological responses to extreme exercise load. This

study aimed to investigate cardiorespiratory fitness of amateur mountain ultramarathon runners and to characterize biochemical changes during the single-stage ultrasky-race South-Tyrol, which comprised a short (68 km, 4260 m elevation gain) and a long (121 km, 7554 m elevation gain) competition. Eleven male finishers (age: 42.4 ± 8.8 years) of the short and seven male finishers (age: 41.0 ± 10.2 years) of the long race were studied. One week before the race, athletes performed a treadmill-running test to exhaustion. Before and after the race, venous blood was collected and fluid intake was registered during the race. Athletes' maximal oxygen uptake (VO_2max) was 57.9 ± 5.8 mL/min per kg. Overall race time was 686 ± 124 and 1649 ± 203 minutes for the short and long competitions, respectively. VO_2max and the ventilator threshold were inversely related to race time of the short race ($r = -0.764$ and $r = -0.782$, $p < 0.05$) but showed no correlation with the long race ($r = -0.179$ and $r = -0.357$, $p > 0.05$). Fluid intake per hour was 612.4 ± 187.6 (short) and 422.3 ± 198 mL/h (long). Body weight decreased during both competitions (-2.3 ± 1.0 and -2.1 ± 1.6 kg, for the short and long races, respectively). Increased WBC ($+9.8 \pm 3.2$ and $+9.3 \pm 1.5 \cdot 10^3/\mu\text{L}$), CK ($+1562 \pm 1250$ and $+4933 \pm 3760$ U/L), IL6 ($+49.1 \pm 19.7$ and 59.5 ± 57.3 pg/mL), and ROS ($+0.034 \pm 0.010$ and $+0.032 \pm 0.013$, for short and long, respectively) were found after both competitions. Results outline the high physiological stress imposed by both contests. Interestingly, VO_2max and the ventilator threshold were related to competition time only during the short race, indicating that with increasing competition length, other factors (e.g., pain threshold, pacing, and nutrition) determine race outcome.

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CONSIDERATIONS FOR ENHANCED DELINEATION OF THE PHYSIOLOGICAL IMPACT OF HIGH-ALTITUDE STRESSORSGiacomo Strapazzon,¹ Rachel Turner,¹ Sandro Malacrida,¹ Marika Falla,² Hannes Gatterer,¹ Nikolaus Netzer,¹ Tomas Dal Cappello,¹ and Hermann Brugger¹¹Institute of Mountain Emergency Medicine, EURAC Research, Bolzano, Italy; ²Department of Neurology, General Hospital of Bolzano, Bolzano, Italy

Acute hypobaric hypoxic (HH) exposure in healthy subjects is commonly associated with complex pathophysiological acute mountain sickness (AMS) symptomology. Specifically, failure to adequately adapt to HH during rapid ascent to high altitude can result in hypoxemia and tissue oxidative stress (OxS). However, the validity of potential surrogate measures for accurate definition of adaptive or maladaptive response to hypoxia remains under investigation. A prospective study to monitor human physiological parameters on acute HH exposure of 16 healthy individuals to 3830 m was conducted through direct helicopter ascent to Mount Ortles glacier. Neurological signs and symptoms of AMS, high-altitude cerebral edema, clinical parameters, ultrasonography of ONSD, and biological samples were prospectively assessed at baseline (262 m) and after ascent (9, 24, and 72 hours). Reactive oxygen species (ROS) production rate was determined by means of an electron paramagnetic resonance method. OxS biomarkers were assessed by immune and/or enzymatic methods. ONSD increased with

exposure to altitude in all participants ($p = 0.003$), more so in those with AMS ($p < 0.001$). After 24 hours, the imbalance between ROS production (+141%) and scavenging (-41%) reflected an increase in OxS-related damages by 50%–85% ($p < 0.05$). Despite the concurrent increase of ONSD, regression analysis did not infer a causal relationship between OxS biomarkers and changes in ONSD. These results provide new insight regarding ROS homeostasis and potential pathophysiological mechanisms of acute exposure to HH. However, further validation is recommended, as there remain limitations to the applicable diagnostic utility of such relatively noninvasive measures, within such challenging high-altitude environments.

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HUMAN PHYSIOLOGY DURING EXPOSURE TO CAVE ENVIRONMENT: A SYSTEMATIC REVIEW AND POTENTIAL FUTURE IMPLICATIONS FOR HYPOBARIC CHAMBER RESEARCH

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Caves are characterized by absence of light and day/night cycles, specific environmental conditions, confinement, isolation, and unique three-dimensional human movement. Since 1938, studies in caves have been conducted on human behavior, physiology, and neuroscience. In the 1970s, isolation studies of Siffre and Montalbini first attracted the interest of space agencies worldwide as the pertinence of this unique environment was realized as a potential space analogue, and parallels were drawn between explorative climbing and mountaineering. However, still little is known about human physiological responses during either short or prolonged isolations/explorations. The aim of this systematic review was to identify human studies associated with permanence in caves, with a view to extend the results to implications for aerospace medicine, including identifying potential confounders for analogue research in chambers and challenging remote habitats. A systematic search was conducted following the structured PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) in five electronic databases (Google Scholar, MEDLINE, NASA Technical Reports Server, OPAC, and WorldCat). This systematic search retrieved 2097 articles. A total of 156 articles were considered for further review under seven differing categories: atmospheric science (24), emergency medicine (61), human factors (0), human physiology (23), neuroscience (29), psychological aspects (4), and radiation (15). Methodological analysis revealed wide discrepancies with respect to the selection and number of participants, the nature of the experimental protocols, and degree of scientific rigor. This review provides the first comprehensive overview of factors that may affect human physiology during isolated cave

exploration, with implications for altered circadian rhythm and immunological considerations.

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CUT-OFF VALUES FOR SERUM POTASSIUM AND CORE TEMPERATURE AT HOSPITAL ADMISSION FOR EXTRACORPOREAL REWARMING OF AVALANCHE VICTIMS IN CARDIAC ARREST

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Identification of hypothermic avalanche victims with reversible out-of-hospital cardiac arrest (OHCA) is still difficult, as many will die despite achieving return of spontaneous circulation. Algorithms with prehospital cut-off values have been proposed since 1996, but evidence is low and the adherence to the guidelines has remained suboptimal. Aim of the study was the definition of reliable cut-off values at hospital admission to improve allocation of extracorporeal life support (ECLS) resources. All avalanche victims with OHCA admitted to the following ECLS centers from 1995 to 2016 were retrospectively included: Bern (Switzerland), Grenoble (France), Innsbruck (Austria), Krakow (Poland), Lausanne and Sion (Switzerland), and Tromsø (Norway). Out-of-hospital and in-hospital patient data were collected and all cases were included. Cut-off values for each parameter, identified by logistic regression, were assessed as upper limits of the respective 95% confidence intervals for percentiles, calculated by means of bootstrapping and exact binomial distribution. Receiver operating characteristic curves were calculated. In total, 103 avalanche victims with OHCA have been included into this study. Of the 103 patients, 61 (58%) have been rewarmed by ECLS. Six (9.8%; 95% confidence interval: 4% to 19%) of rewarmed patients survived and 55 (90%) died. Vital signs at extrication are strongly associated with survival. For an in-hospital triage of avalanche victims admitted with OHCA, the serum potassium accurately predicts survival. The combination of the cut-offs 7 mmol/L for serum potassium with 30°C for core temperature achieved the lowest overtriage rate (47.3%) and highest

positive predictive value (18.8%), with a sensitivity of 100% for survivors.

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CHALLENGES AND APPLICATIONS FOR ADVANCED MEDICAL MONITORING IN EXTREME ENVIRONMENTS

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Monitoring vital parameters in extreme environments can provide a means to dynamically manage aspects of health, safety, and energy expenditure throughout a given activity, avoiding unnecessary fatigue or increased risk. Equally, this technology could allow insight into physiological responses in a continuous manner, steeping away from “spot check” data sampling. With the advent of the biosensewear revolution, recent reviews have compared emerging wearable technologies, highlighting the potential for noninvasive and continuous monitoring of core physiological parameters (electrocardiogram, SpO₂, ventilatory rate, and skin and core temperature) and related environmental parameters (barometric pressure and ambient temperature) under extreme exercise or working conditions. Herein, we review the challenges associated with monitoring these parameters continuously during challenging activities in isolated environments, as both a tool for careful remote management of personal safety, plus a requirement for future development of clinically relevant predictive algorithms. However, the measurement of health and performance in locations such as terrestrial high altitude, remote areas, subterranean space analogues, hypobaric climate-enabled chambers, or even the stratosphere requires a unique approach. It is essential for a functional biosensewear solution to be small, lightweight, robust, and able to continuously collect accurate data without movement artifact. Equally, continuous remote acquisition and visualization under even the most challenging of climate combinations (i.e., high humidity and temperature changes [+60°C to -40°C], hypobaria and precipitation) is required. To ensure efficient data acquisition for scientific or clinical interrogation, operational validity must be established and existing challenges (e.g., robust data acquisition and telemetry, battery life, and accurate under all environmental conditions) overcome.

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URINARY PHYSIOLOGY AT ALTITUDE: EFFECT OF A MODERATE HYPOXIA ON SYMPATHOVAGAL BALANCE AND URODYNAMIC PARAMETERS
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Reacting adaptively to chronic hypoxic states, the bladder responds to different ultrastructural and physiological changes with bladder noncompliance, detrusor instability, nocturia, and increased spontaneous contraction. The autonomic nervous system is known to be a key player in urinary physiology, since neurological control of the bladder–urethral unit is governed by somatic and autonomic (both parasympathetic and sympathetic) fibers. Exposure to hypoxic environments influences the sympathetic activation and, simultaneously, the urinary physiology. Therefore, in this pilot study, we investigated the adaptive response of urodynamic variables and sympathovagal balance in subjects who live at sea level participating in 7 days of trekking at moderate altitude. The study was carried out during a lightweight expedition to Namche Bazar, Nepal, by four healthy subjects (two females and two males). Measurements were taken at three different times: (1) Kathmandu before (KB) (1300 m a.s.l.), (2) Namche Bazar (NB) (3500 m a.s.l.), (3) and again Kathmandu after (KA) (1300 m a.s.l.). The small population does not allow us to draw reliable conclusions, but it seems large enough for us to detect some interesting trends. At NB, both the heart rate (HR) and the low-to-high frequency power ratio increased with respect to KB and to (KA), showing a clear sympathetic dominance, agreeing with literature evidence on nonnative subjects. At the same time, we noted that permanence, even if only for a few days at (NB), generated interesting movements of the urodynamic profile, which suggests a correlation between hypoxic state, sympathetic dominance, and urinary physiology.

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SUCCESSFUL USE OF AMLODIPINE FOR HIGH-ALTITUDE PULMONARY EDEMA IN PATIENTS WITH LOW SYSTOLIC BLOOD PRESSURE

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Nifedipine, a calcium channel blocker (CCB), is recommended for treating high-altitude pulmonary edema (HAPE). At the Mountain Medicine Institute (MMI) in Namche Bazaar, Nepal (3500 m), amlodipine, a related CCB, is used because nifedipine is not available. Most patients with HAPE have increased SBP, but those who have low SBP are at risk for systemic hypotension with use of a CCB. Amlodipine has slower time to peak effect after oral administration that may be advantageous in patients with HAPE who are at risk of systemic hypotension. We report two cases of patients with HAPE and SBP about 100 mmHg who were treated at the MMI with bed rest, oxygen, oral rehydration, and amlodipine 10 mg orally on day 1 followed by 5 mg every 12 hours for two more days. Both patients recovered without further decrease in SBP. At discharge, both patients had normal SBP about 120. Patient 1 was a 34-year old male who had vomiting for 2 days. Vital signs were heart rate (HR) 125, BP 98/54, and oxygen saturation (SpO₂) 34%. Normal SpO₂ at 3500 m is 85%–90%. Patient 2 was a 43-year old male who had decreased oral intake for 2 days. Vital signs were HR 118, BP 102/66, and SpO₂ 60%. Amlodipine may be an ef-

fective alternative to nifedipine for the treatment of HAPE with decreased risk of hypotension in patients with low SBP.

4093

UPDATE OF SLEEP DISORDER AND CHRONIC MOUNTAIN SICKNESS

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The pathogenesis of chronic mountain sickness (CMS) is not totally clear. People believe that sleep disorder and obesity are the risk factors of CMS. However, the type of sleep disorder of CMS patients versus the type of sleep disorder of obese CMS patients is not clear. We collected 82 patients who lived at high altitude (>3000 m) and suspected as CMS (the hemoglobin all >21 g/L, CMS score >5). We divided them into two groups according to the body mass index (BMI <24 kg/m² and BMI >25 kg/m²) and did the polysomnography (PSG) for them. The hemoglobin concentration was significantly higher in obese group than in nonobese group (243.7 ± 8.1 vs. 220.3 ± 4.9 g/L, *p* < 0.01). The apnea/hypopnea index (AHI) was significantly higher in obese group than in nonobese group (46.7 [33.5, 57.2] vs. 14.7 [11.4, 21.8], *p* < 0.01). The main type of apnea was obstructive apnea in obese group. Central apnea, mixture apnea, periodic breathing, and hypopnea were also observed in obese group. The hypopnea was the main type of sleep disorder in the nonobese group. The mean and lowest sleep oxygen saturation (SaO₂) were significantly lower in the obese group than in the nonobese group (all *p* < 0.01). We concluded that obese patients with polycythemia at high altitude should perform the PSG and if the type of sleep disorder showed as obstructive sleep apnea, these patients should be diagnosed as obstructive sleep apnea/hypopnea syndrome. So we can give these people the continuous positive airway pressure. These patients suffered from hypoxia due to OSAHS and high altitude, so the situations of these patients were even more severe than pure OSAHS patients and CMS patients.

4094

HOMEOSTASIS OF MOLECULES OF HYPOXIA-SENSING PATHWAY IN ADAPTATION TO HYPOBARIC HYPOXIA

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Hypobaric hypoxia at high altitude (HA, >2500 m) is responsible for low partial pressure, causing reduced blood arterial oxygen saturation (SaO₂) in the body. It regulates adaptive physiological processes such as hypoxia sensing, pulmonary vasoconstriction, and endothelial dysfunction in sojourners (lowland natives) and HA permanent residents. Among the mountain disorders, HA pulmonary edema (HAPE) afflicts sojourners. Susceptibility may be attributed to the selective genome remodeling, epigenetic responses, and DNA methylation. Hence, the aim of our research has been to identify genetic and biological markers that may predispose individuals to adaptation and or maladaptation. HIF-prolyl hydroxylase (EGLN1), Apelin (APLN), and endothelial nitric oxide synthase (NOS3) were investigated for allelic variants, epigenetic regulation, and association with clinical

and biochemical parameters in a comparative study of healthy highlanders (HLs) and sojourners, that is, HAPE-free controls (HAPE-f) and HAPE patients (HAPE-p). HAPE-p had significantly lower level of SaO₂ and elevated pulmonary arterial systolic pressure (PASP) than HLs and HAPE-f (*p* < 0.01). The higher PASP in HAPE indicates higher pulmonary hypertension that leads to alveoli leakage and edema. Several EGLN1 risk variants and respective haplotypes correlated with decreased SaO₂ level and increased EGLN1 expression (*p* < 0.05). The 4.55-fold upregulated EGLN1 expression in HAPE-p (*p* < 0.01) suggested the dysfunction of HIF-1α. This prohibits the downstream genes from maintaining cellular O₂ homeostasis. APLN and NOS3 expression levels were downregulated two—fivefold and plasma APLN and nitric oxide levels decreased significantly in HAPE-p (*p* < 0.05). Hypoxia-signaling pathway is affected at HA contributing to adaptation/HAPE.

4095

ABSTRACT WITHDRAWN

4096

MULTIPLE HORNET STINGS AND ACUTE RENAL FAILURE: A CASE SERIES

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Multiple hornet sting can lead to life-threatening condition such as anaphylactic shock, acute renal failure, and multiple

organ failure. The hornet stings happen in austere environments of remote areas among farmers. Traditionally, farmers in remote Nepal harvest the hornet nest for food risking life to multiple stings. First case, a 35-year old male was stung by a swarm of hornets (~200 stings) when he was attempting to destroy hornet nest for food at night. The case presented with severe swelling and multiple hyperemic stings all over the body more prominently in scalp, face, and shoulder region. Serum creatinine (143 $\mu\text{mol/L}$), creatine phosphokinase (4179 U/L), and lactate (4.5 mmol/L) were raised. The case was managed for anaphylactic reaction to hornet sting and subsequent acute renal failure. Second case was a 30-year male from Western hills of Nepal who was bitten by multiple hornets when he tried to harvest the nest for food. The Patient had extreme pain, tingling sensation over the whole body, and was passing red colored urine. The urinary output decreased subsequently. The serum urea (42.7 mmol/L), creatinine (634 $\mu\text{mol/L}$), and creatine phosphokinase (1115 U/L) were elevated. Similarly, serum amylase (246 U/L) and lipase (349 U/L) were also elevated. The patient was managed for hornet sting-induced acute renal failure with pancreatitis. Hornet sting in Nepal usually happens in far remote areas among farmers who attempt to harvest hornet nest for food. The multiple stings can lead to anaphylactic shock and subsequently life-threatening complications. Immediate hospitalization, treatment, and monitoring are key steps of saving life.

4097

FENTANYL SUBLINGUAL VERSUS FENTANYL INTRAVENOUS FOR ACUTE TRAUMATIC PAIN: A PROSPECTIVE RANDOMIZED DOUBLE-BLIND CLINICAL SINGLE-CENTER NONINFERIORITY TRIAL

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Introduction: Acute traumatic extremity pain is one of the most important complaints in the emergency department (ED). We hypothesized that fentanyl sublingual (FSL) is not inferior to fentanyl intravenously (FIV) regarding efficacy and safety in the management of acute pain (4 on the 11 points numeric rating scale [NRS]) without gender differences.

Methods: This is a prospective randomized double-blind clinical single-center noninferiority trial (NCT03080324) with 108 adult patients (54 females and 54 males) enrolled in ED for acute traumatic extremity pain; if pain was NRS = 4/10, they received either FIV (1 $\mu\text{g/kg}$) or FSL (100 μg) and the correspondent placebo intravenously or sublingually. Pain measurements followed 5, 10, 20, 30, and 60 minutes.

Results: Baseline pain intensity was high: mean NRS was 7.1 (SD ± 1.9) in the FSL group and 6.8 (SD ± 1.7) in the FIV group and did not differ between intervention ($p = 0.377$) nor in gender groups (female 7.1 [SD ± 1.9], male 6.9 [SD ± 1.8], $p = 0.377$). Pain reduction in the FSL and FIV groups was not significantly different at any time point within 60 minutes. Pain reduction of 33% was reached in 42 of 46 in the FSL group and in 44 of 51 in the FIV group ($p = 0.743$). Dizziness was more present in the FIV group (33/51 vs. 8/46). There were no gender differences regarding pain reduction, need for rescue dose, side effects, and patients' satisfaction.

Conclusions: FSL may be—for trained healthcare providers—a noninferior efficient and safe-alternative to FIV in the ED for treatment of traumatic extremity pain. More studies are needed to investigate FSL in a larger population and with repeated doses.

4098

DIABETES MELLITUS AND MOUNTAINEERING: THE NEW RECOMMENDATION OF UIAA MEDICAL COMMISSION

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With an aging population and a more and more active population in general, the number of persons who go to the mountains although they suffer from pre-existing diseases is increasing significantly. This causes a complex task for physicians who give pretravel advice to trekkers or climbers. UIAA Medical Commission (UIAA MedCom) has published several recommendation articles addressing a couple of diagnoses. Recently the topic “diabetes” has been updated. The lecture will give an overview of how to advise diabetic mountaineers and how to continue with modern strategies of diabetes therapy in the field. The most important take-home message is: Except for very rare situations, diabetes is not a contraindication for hiking, climbing, or mountaineering when some marginal conditions are known and followed by the athlete.

4099

NOCTURNAL PERIPHERAL PERFUSION IS NOT AFFECTED BY HYPOXIA

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According to the equivalent air altitude (EAA) theory, the physiological responses observed during exposure to normobaric and hypobaric hypoxia are similar. Confirmation of this theory for different physiological systems is necessary to ensure that the responses observed in the latter can be studied in the former. This study evaluated the EAA theory on the basis of the circadian rhythm of proximal–distal skin temperature gradient. Data from two studies were used for this analysis. In one study, subjects (11 males) were confined to normobaric hypoxia at the Olympic Sport Centre Planica (Rateče, Slovenia) for 21 days (simulated altitude 4000 m). In the other study, personnel (16 males and 2 females) at the Antarctic Research Station Concordia situated at 3233 m above sea level participated in the study. Owing to the geographical location of the facility, the ambient pressure is actually lower than at an equal altitude at the equator, thus the partial pressure of inspired oxygen was equivalent to that at an altitude of 3800. In both studies, at regular intervals, we monitored the proximal–distal skin temperature gradient between the calf and the toe ($\Delta T_{\text{c-t}}$), an index of peripheral perfusion, of all participants from 17:00 to 06:00 hours the following morning. Hypoxia, whether normobaric or hypobaric, did not affect nocturnal vasodilation. Sleep onset is highly dependent on peripheral skin temperature, and as there

was no difference in $\Delta Tc-t$ between the groups at any time point for the night-time measurement, increasing the time spent in hypoxia has no effect on any peripheral mechanisms contributing to sleep onset.

4100

DEVELOPMENT OF A QUESTIONNAIRE TO DETECT HIGH-ALTITUDE PSYCHOSIS: THE HAPSY QUESTIONNAIRE

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Psychotic episodes during exposure to very high or extreme altitude have been related to accidents or near accidents in the mountains. It is thus of great importance to identify individuals with psychotic symptoms quickly and reliably directly on the mountain even in the absence of experienced medical personnel. Psychotic episodes are characterized by symptoms such as hallucinations (e.g., seeing people who are not really there, feeling the presence of another being who is not really present), delusions, disorganized thinking/speech, or abnormal psychomotor behavior. The aim of this study was to develop a questionnaire (HAPSY questionnaire) to assess psychotic symptoms through a self-rating directly on the mountain. We used two existing self-rating questionnaires for psychotic symptoms (the psychotomimetic states inventory and the Cardiff Anomalous Perception Scale) as a basis for a two-round Delphi process. Additional statements were proposed by the Delphi participants. The Delphi experts were 14 climbers, who had previously experienced psychosis at altitude, and 26 psychiatrists with expertise in psychosis research and/or treatment. Through the Delphi process, eleven questions – all of them related to perceptual distortion – were finally identified to be most useful for the detection of psychotic symptoms at altitude via self-rating. The next step will be to validate the HAPSY questionnaire in a field study, where the self-ratings will be compared with physicians' ratings.

0001

UTILIZING DRONES IN HIGH-ALTITUDE SEARCH AND RESCUE OPERATIONS: A CASE STUDY

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Unmanned aerial vehicles, or drones, are becoming increasingly common consumer products; their potential application to search and rescue (SAR) operations are becoming ever more apparent. A consumer drone was used to locate a mountaineer after he became separated from his partner while summiting Broad Peak, the world's 12th tallest summit situated in the Karakoram Mountains of Northeastern Pakistan. The use of the drone allowed for a quick rescue mission and eliminated the need for the mobilization of a rescue party. The rescue party would have been faced with immense challenges, including a vast search area and altitudes near the

limits of viable human physiological function. With real-time imagery and GPS capabilities, drones may be a vital tool in SAR operations to help reduce response time while maintaining the safety of responders, especially at high altitude.

0002

ETHICAL ISSUES IN MOUNTAIN AND HIGH-ALTITUDE MEDICINE: RESULTS FROM AN INTERVIEW STUDY WITH PHYSICIANS IN THE FIELD

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Background: Physicians in mountain and high-altitude medicine face different ethical issues compared with routine clinical care because they practice under specifically challenging conditions regarding the medical situation, external circumstances, available medical resources, and personal risks. Although several ethical issues have been mentioned in the literature, they have—to our knowledge—never been studied systematically.

Methods: We, therefore, conducted a qualitative interview study with 10 physicians with year-long experience in mountain and/or high-altitude medicine in varying circumstances (maximum variation sampling) to answer the following research questions: (1) What ethical issues do the interviewees encounter in their practice? (2) How do they deal with the ethical issues? The interviews were recorded, transcribed verbatim, and analyzed by means of a qualitative content analysis.

Results: The interviewees described the various specific conditions of their practice, like limited medical resources, limited diagnostic and prognostic information, difficult external conditions, risks for the rescuers, and “irresponsible” mountaineers. In one cluster, the interviewees reported ethical issues arising in mountain rescue, which relate, for example, to balancing the obligations toward the injured mountaineer versus the risks for the rescuers, the mountaineer's individual responsibility, triage situations, and the allocation of resources into rescue infrastructures. In the second cluster, the interviewees reported ethical issues in high-altitude medicine, especially the ethical acceptability of prescribing prophylactic or performance-enhancing drugs. In most cases, the physicians solve the ethical issues case by case by carefully balancing the conflicting ethical obligations as there is usually no general ethical guidance available.

0003

EFFECT OF ALTITUDE VARIATIONS ON CARDIO-RESPIRATORY PARAMETERS AMONG TREKKERS TO THE INDIAN HIMALAYAS

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Introduction: High-altitude trekking among unacclimatized trekkers is on the rise with limited research among Indians on physiological changes directly or indirectly related to lower oxygen saturation at varying altitudes. Thus, this study aims to understand the effect of altitude variations on cardiorespiratory parameters (oxygen saturation and heart rate) across

age groups, nationality (Indian and non-Indian), and season among trekkers in the Indian Himalayas.

Methods: Secondary data analysis was carried out using heart rate (HR) and oxygen saturation of 5023 trekkers in the Indian Himalayas, collected by the trekking organization, Indiahikes. The differences across altitudes (initial < 1500 m, intermediate 1500–3500 m, and high 3500–5000 m), age groups, and seasons (January–March, April–June, July–August, and September–December) were analyzed using the mixed-model analysis of variance.

Results: Oxygen saturation decreased with increase in altitude, whereas heart rate showed an increase up to 3500 m, beyond which it showed a decrease. The youngest age group (6–17-year old), irrespective of gender, exhibited highest adaptability in heart rate across altitude. Female trekkers showed no significant difference in heart rate from intermediate to high altitude irrespective of age groups; however, males aged 18–35 years showed a significant decrease from intermediate to high altitude. Non-Indian trekkers showed a significantly lower HR and diastolic blood pressure. Across seasons, January to March (winter) exhibited the highest oxygen saturation with increased HR seen at high altitude.

Conclusions: Higher oxygen saturation and lower heart rate at high altitude were observed among the younger trekkers, and the non-Indian trekkers showed better acclimatization. Therefore, appropriate fitness regimens should be followed by Indians trekking to higher altitudes, especially in the age group of 18–35 years, for better acclimatization.

0004

Garlic consumption habits among the high altitude pilgrims and its effect in prevention of acute mountain sickness: A review

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Introduction: Garlic is regarded as an important dietary and medicinal plant since long back in history. Different studies have shown beneficial effects of garlic in cardiovascular diseases, diabetes along with antitumor and antimicrobial properties. There is a tradition of consuming garlic among Nepalese pilgrims ascending to high altitude for prevention of Acute Mountain Sickness (AMS). This review was done with the objective to find out the outcomes of garlic consumption in prevention of AMS among the high altitude pilgrims.

Methods: The literature search was done in Pubmed and Google Scholar with keywords including “garlic,” “altitude sickness,” “mountain sickness,” and “high altitude pilgrims.” The relevant articles were screened and reviewed for the effects of garlic on the pilgrims ascending to high altitude.

Results: A total of five articles have been analyzed and they have shown no beneficiary effect of garlic on prevention of AMS. Instead, some studies have demonstrated the higher incidence of AMS in those taking garlic as a remedy to prevent from AMS. Rather, acclimatization and acetazolamide prophylaxis in susceptible ones have shown the better outcomes for the prevention of AMS.

Conclusion: The traditional belief of garlic preventing from AMS has no established scientific evidence and such practices should be discouraged. It is necessary to educate and aware the pilgrims regarding better practices like slow as-

cending and pharmacological prophylaxis instead of such traditional methods.

0005

Losartan has no effect on the hypoxic diuretic response to altitude

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Background: An early onset naturesis occurs on ascent to high altitude. We postulated that losartan, an angiotensin 2 receptor antagonist, taken during ascent would reduce aldosterone activity thereby enhancing this early adaptive diuresis.

Methods: Twenty participants (paired for age, gender and ACE genotype) were randomised, on a double-blind basis, to either daily losartan, 100 mgs. or placebo. Trial medication was commenced following sea-level urine and blood collections and 7 days before a motorised ascent over 6 days to 5035m. Daily 24-hour urine collections were measured for volume during ascent and aliquots frozen at –80deg C for subsequent measurement of electrolytes. Blood samples were obtained at baseline and at the high point on day 6 for subsequent measurement of aldosterone and copeptin levels.

Results: During the period of main ascent days 2–6 (2850–5035 m) there was a significant progressive increase in daily urine volume in both the losartan and placebo groups (losartan 2165–3002 mls $p < 0.003$; placebo 1768–3062 ml; $p < 0.001$) accompanied by an increase in daily urinary sodium in both groups (losartan 102–170 mmols/24hrs $p < 0.002$; Placebo 101–168 mmols/24hrs $p < 0.004$). No significant differences were observed between the trial groups in daily urine volume or sodium excretion or in Aldosterone and Copeptin levels.

Conclusion: The early naturesis accompanying ascent to high altitude is not influenced by angiotensin 2 blockade ruling out the renin angiotensin aldosterone system in its genesis.

0006

Hypoxia is not the mechanism for exercise-induced proteinuria

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Introduction: Using alpha-1 acid glycoprotein as a sensitive marker of proteinuria, the objective of this study was to examine how changes in relative hypoxia might contribute to exercise proteinuria, and whether losartan (an angiotensin-receptor blocker) would lower exercise-induced proteinuria due to reductions in blood pressure.

Methods: Twenty pair-matched individuals (sex, age, and ACE genotype) completed maximal exercise tests once at sea-level (SL) and twice at altitude (5035m), with losartan (100 mg/day) randomly assigned to one individual in each pair (21-days pre-

altitude exposure). The first altitude test was completed within 24–48 hours after arrival (each pair within ~1 hr), immediately after which acetazolamide (Az) (250 mg twice daily) was administered for 48 hrs prior to their 2nd altitude exercise test.

Results: Exercise associated increases in α 1-AGP trended towards being lower at altitude in the losartan group (58%; $p = 0.098$), whereas there was no difference between altitude and SL exercise-induced proteinuria for the placebo group, despite similar maximal-exercise SpO_2 in both groups at altitude ($70.0 \pm 5.4\%$; $p = 0.95$). In the placebo group ($n = 8$), Az reduced exercise-induced increases in proteinuria by approximately 3-fold (pre-Az $9.3 \pm 9.7 \mu\text{g}/\text{min}$ and Az $3.6 \pm 6.0 \mu\text{g}/\text{min}$; $p = 0.029$); however, these changes were not correlated ($r = -0.10$) with the improvements in SpO_2 ($69.1 \pm 4.5\%$ vs. $75.8 \pm 3.8\%$; $p = 0.001$).

Conclusion: A greater hypoxic stimulus does not result in increased proteinuria nor do improvements in SpO_2 appear to be related to proteinuria with hypoxic exercise. These findings indicate that the mechanism for exercise-induced proteinuria is not directly related to hypoxia.

0007

Official Master in Mountain and Wilderness Emergency Medicine (Master MUMMI)

Maria A. Nerin Rotger

CUEMUM-Asociación de Medicina de Montaña José Ramón Morandeira

Dr. José Ramón Morandeira, mountaineer and himalayist, surgeon and specialist in frostbites, carried out the Specialisation Courses in Mountain Emergency Medicine (CUEMUM) in Spain since 1996. From these CUEMUM was born the first Master's Degree in Mountain Emergency Medicine. The purpose was to train physicians and nurses who would take charge of the medical aspects of rescue and wilderness medicine, offering them a university degree which guaranteed their full professional abilities within the normative context of the European Union and ICAR. These physicians and nurses can provide the medical component of mountain rescue teams, and participate effectively as public health workers in humanitarian efforts anywhere in the world, extreme outlying regions or remote areas. Dr. Morandeira died in November 2012. In order to preserve his heritage in mountain medicine knowledge and to continue working for healthy and safety mountain activities, a Mountain Medicine Association was created with his name and spirit in 2015 to work in: mountain medicine and rescue, health of highlanders, prevention of mountain casualties, risk management, health education and sports training of mountaineers and alpinists, to improve the safety of mountaineering and health of mountaineers and mountain people. An Official Master in Mountain and Wilderness Emergency Medicine (60 ECTS credits) was started in 2016 in order to give coverage to these needs, the Europa's unique Official Master in this area, in collaboration with Camilo José Cela University, TASSICA, CUEMUM, FEMAD, Spanish Army and Guardia Civil.

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