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ABSTRACTS

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Abstracts

1.

TREATMENT WITH RHUEPO IN HUMANS IS ASSOCIATED WITH DOWN-REGULATIONS OF THE RENIN-ALDOSTERONE SYSTEM, PROXIMAL RENAL TUBULAR REABSORPTION AND GLOMERULAR FILTRATION RATE.

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Introduction: rHuEPO elevates hemoglobin concentration both by decreasing plasma volume and by an increase in red cell volume. This study delineated the association of rHuEPO-induced changes in blood volumes with changes in the renin-aldosterone system and renal function. **Methods:** 16 healthy males were given rHuEPO for 28 days in doses raising the hematocrit to 46–49%. Renal clearance studies with urine collections ($N = 8$) were done at baseline and at days 4, 11, 29 and 42. Glomerular filtration rate (GFR) was measured by 51Cr-EDTA. Renal clearance of lithium (CLi) was used as an index of proximal tubular outflow and to assess segmental renal tubular handling of sodium and water. **Results:** rHuEPO-induced increases in hematocrit occurred from day 10 onwards and was caused by both an increase in red cell volume and a fall in plasma volume. Well before that (from day 2 and throughout the treatment time), rHuEPO decreased plasma levels of renin and aldosterone ($N = 8$) by 21%–32% ($P < 0.05$) and 15 – 36 % ($P < 0.05$), respectively. After cessation of rHuEPO values returned to normal. rHuEPO on days 4, 11, 29 and 42 increased CLi indicating a significant 10 – 16 % decrease in absolute proximal reabsorption of sodium and water ($APR = GFR - -CLi$, $P < 0.05$). GFR decreased slightly, albeit significantly on days 4 and 11 ($P < 0.01$). **Conclusion:** In conclusion, rHuEPO promptly, and before any changes in blood volumes and hematocrit can be detected, causes a down-regulation of the renin-aldosterone system. In addition, proximal tubular reabsorption and GFR are decreased. The results are compatible with a rHuEPO-induced reduction in proximal reabsorption rate leading to activation of the tubulo-glomerular feedback mechanism and a fall in GFR. By this, treatment with rHuEPO may result in suppression of endogenous EPO secondary to a decrease in intrarenal oxygen consumption. **Acknowledgments:** This study received funding from Anti Doping Denmark; and the Scientific Board of Rigshospitalet, Copenhagen, Denmark.

2.

EXCESSIVE DAYTIME SLEEPINESS IN UNIVERSITY STUDENTS RESIDING AT HIGH ALTITUDE (PUNO 3827 M).

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Introduction: We are currently out with a study indicating the degree of daytime hypersomnolence in settlers from Puno (3827 m above sea level.), So we felt necessary to include this data for your reference. **Methods:** This study is a descriptive cross-sectional study.It took a simple probability sample finite population that consisted of a total of 393 students of the Universidad Nacional del Altiplano Puno (3827 m) in which the Epwoth test was applied and were processed PASW program in version 18. **Results:** 393 universities were surveyed, aged between 16 and 24 years, the average was 19.46 and a standard deviation of 2.034, of which 18.3% was cursed with excessive daytime sleepiness. **Conclusion:** These results indicate that a high percentage of excessive daytime somnolence in college. Further studies are needed for establishing the involvement of age, socioeconomic status and body mass index in the development of excessive daytime somnolence. **Acknowledgments:** to Dr. Oscar Vega Hinojosa for his valuable help.

3.

ARGINASE AND ORNITHINE TRANSCARBAMYLASE LIVER ACTIVITY AND PLASMA LEVELS OF UREA AND CITRULLINE OF GUINEA PIGS IN HIGH ALTITUDE (MOROCOCHA 4540 M).

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Introduction: We have studied the effect of chronic hypoxia of high altitude on the activity of two enzymes of the urea cycle: Arginase (EC 3.5.3.1.) and Ornithine transcarbamylase (EC 2.1.3.3.) present in liver of guinea pigs, and plasma levels of urea and citrulline. **Methods:** To this objetive we used a group of 10 adult male guinea pigs, born and raised at altitude (Morococha, 4540 m) and as control, another group of 10 adult male guinea pigs, born and raised at sea level (Lima, 153 m). Animals from both groups were put on fast 24 hours before slaughter. Plasma levels of Urea was determined by Wiener Lab. method, Citrulline by Archibald method. The specific activity of Arginase enzyme was determined by Berthelot method and Ornithine transcabamylase by Archibald method modified by Jones. **Results:** It was observed that chronic hypoxia increased the specific activity of Arginase and Ornithine transcarbamylase enzymes in liver tissue, observing a significant increase in their specific activities ($P < 0.001$). Moreover, plasma levels of urea and citrulline were higher in high altitude ($P < 0.05$ and $P < 0.001$, respectively), which is explained by the increased enzymatic activity of Arginase and Ornithine transcarbamylase found, which could be attributed to increased mobilization of amino acids. **Conclusion:** The chronic hypoxia increased the specific activity of Arginase and Ornithine transcarbamylase enzymes in liver tissue, observing a significant increase in their specific activities ($P < 0.001$). Plasma levels of urea and citrulline were

higher in high altitude ($P < 0.05$ and $P < 0.001$, respectively). It could be explained by the increased enzymatic activity of Arginase and Ornithine transcarbamylase found, which could be attributed to increased mobilization of amino acids. **Acknowledgments:** To the personal of the Instituto Nacional de Biología Andina de la Universidad Nacional Mayor de San Marcos, sedes Lima y Morococha.

4.

PERFUSION CHARACTERISTICS OF KIDNEYS IN DIFFERENT HIGH ALTITUDE AREAS USING COMPUTED TOMOGRAPHY.

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Introduction: To investigate the kidney perfusion of the normal adult in different high altitude areas by the multi-slice computed tomography. **Methods:** 35 high altitude residents were selected from healthy individuals of different ages from 23 to 50 years (23 males, 12 females), mean ages 38.67 ± 10.76. From them, 20 were high altitude residents living at an elevation of 2,260 m—3,000 m (A group), 7 were high altitude residents living at an elevation of 3000 m-4000 m (B group), and 8 were high altitude residents living at an elevation of above 4000 m (C group). All selected residents had no conscious symptom and had no positive test results --such as in urine routine test, in Bun, Cr and uric acid test that showed all to be normal. Renal tissue perfusion was performed in 35 cases of normal kidneys in high altitude areas by applying Philips CT and perfusion software with 50 mL Ultravist (300 mgI/mL) and 4 mL/s injection flow. Data post-processing was performed on Philips work-station by using kidney analyzing software in the package of general perfusion. All the cortex and medulla perfusion param of the normal kidney were measured. **Results:** (1)The time-density curves of bilateral normal renal cortex and medulla are symmetric, even coincident, and the mean blood flow of renal cortex and medulla were 171.09 ± 48.39 mL/100 mL/min and 57.70 ± 28.25 mL/100 mL/min, respectively. The time-density curve (TDC) of the abdominal aorta on the level of renal hilum began at 12.47 ± 2.69 s after the injection of contrast material, and the time to peak (TTP) was 22.48 ± 2.72 s. The rising time of TDC refer to the renal cortex and medulla were 15.76 ± 2.77 s and 18.33 ± 3.24 s, respectively. The blood flow condition and the separation of the renal cortex and medulla were clearly displayed on the perfusion CT color maps. The Perfusion values were from low to high flow and the color-code were from black to blue, green, yellow and red. The peak enhancement (PEI), time to peak (TTP), blood flow (BV) of the renal cortex and medulla were 96.54 ± 24.92 Hu, 16.61 ± 3.85 s, 55.45 ± 11.46 mL/100 g and 43.88 ± 17.15 Hu, 22.67 ± 5.54 s, 22.53 ± 6.9 mL/100 g. (2) Perfusion values in the cortex or medulla of bilateral kidneys of the 35 cases were not obviously different significance respectively ($P > 0.05$) but in the same kidneys, the perfusion values in the cortex showed great difference from those in the medulla ($P < 0.05$). (3) Using analysis of variance, there were no differences between right and left side in the perfusion param; but the perfusion param of cortex and medulla appeared significantly in different altitude ($P < 0.05$). **Conclusion:** (1) MSCT perfusion imaging can measure the cortex and medulla perfusion param of the normal kidney and quantitatively evaluate the haemodynamic changes in normal renal tissue. It provides quantitative information about renal blood flowing. (2) There is a certain correlation between attitude and all the perfusion param. but there are no differences between right and left side in all the perfusion param of the normal kidney.

5.

THE STUDY ON BRAIN CT IN PATIENTS WITH CHRONIC MOUNTAIN SICKNESS.

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Introduction: To investigate the cerebral appearance and cerebral hemodynamics of chronic mountain sickness (CMS) using Multi-Detector Computed Tomography. **Methods:** We selected 10 patients with CMS at admission and used plain brain CT scanning and computed tomography perfusion (CTP). In order to compare the study, we collected the same relevant data of 15 normal adults. The hemoglobin level of all subjects was estimated within 72 hours. The images of plain brain CT scanning were observed and studied. The param of the brain perfusion were including cerebral blood flow (CBF), cerebral blood volume (CBV), time to peak enhancement (TTP), and mean transit time (MTT) levels. They were measured in grey matter and white matter of interest manually outlined on the CT scan. **Results:** The density of cerebral vessels were differently strengthened (10 cases), especially the density of middle cerebral artery and superior sagittal sinus. An obvious parallel correlation existed between the CT value of cerebral vessels (bilateral middle cerebral artery and superior sagittal sinus) and the hemoglobin level. ($r = 0.522$ and $r = 0.714$, both $P < 0.01$). The CT value of bilateral middle cerebral artery and superior sagittal sinus were significantly higher in CMS group than that in normal group ($t = 6.834$, $P < 0.01$ and $t = 7.153$, $P < 0.01$). 6 cases of CMS show diffuse cerebral edema. CBF change was greater in grey matter than in white matter. In grey matter CBF was obviously reduces more in CMS group than in normal group ($P < 0.01$). The TTP in grey matter was obviously prolonged in CMS group ($P < 0.05$). The MTT in grey matter and white matter are both obviously prolonged in CMS group ($P < 0.01$). **Conclusion:** The plain brain CT scans of the CMS has its own characteristic: the density of blood vessels were augmented, especially the density of bilateral middle cerebral artery and superior sagittal sinus., meanwhile the sign of increased middle cerebral artery density and superior sagittal sinus density, the possibility to judge the hemoglobin level for roughly. Some patient show diffuse cerebral edema. Multi-slice CT perfusion is a valuable tool to study the cerebral hemodynamics in chronic mountain sickness. **Acknowledgments:** This work was supported by a grant from the National Basic Research Program of China (No. 2006CB504100).

6.

PERINATAL VARIABLES AND MTDNA HAPLOGROUPS IN AYMARA POPULATIONS FROM THE REGION OF ARICA PARINACOTA, CHILE.

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Introduction: High altitude ecosystems are extreme environments which in theory can exercise selective pressures on populations inhabiting them. The Aymara are among the first tribal populations colonizing high altitude Andean ter-

ritories and several studies have shown that Caucasian admixture of this ethnic group is one of the lowest in the Andes, being therefore a group of interest for the study of adaptation to altitude. One of the variables that has been linked to altitude is low weight of newborns, which as known is the result of a complex interaction of genetic and environmental factors. This work aims to study the association of perinatal variables with heigh altitude and mtDNA haplogroups in the Chilean Aymara population. **Methods:** As part of this research the largest perinatal database available for this ethnic group in Chile was developed, including information of all births occurred between December 2007 and February 2009, in the region of Arica. During the study, 6981 live births were recorded, being 26.47% Aymara. **Results:** In the group living above 3000 m altitude, the average birth weight was 3280 g, ds + / - 403 g, the mtDNA haplogroups shows a gradient of distribution according to altitude, with predominance of haplogroup B at high altitudes. **Conclusion:** Results fail to indicate a reduction in birth weight and other perinatal variables in high altitude Aymara new borns, a result that is at variance with previous findings reported in Aymara populations from neighbouring countries. We suggest that our results could be due to recent health and nutritional improvements experienced by the Chilean Aymara.These last results must be considered preliminary.

7.

FREE RADICAL FORMATION IN THE HYPOXIC HUMAN BRAIN.

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Introduction: Molecular oxygen (O_2) exists in air as a free radical revealing a more nebulous side to a gas traditionally considered the "elixir of life". It is a double-edged sword, capable of sustaining life yet fatal in excess or indeed when limited. **Methods:** The current presentation will focus on the factors that regulate O_2 transport to the exercising human brain with a specific focus on inspiratory hypoxia and its impact on reactive oxygen-nitrogen species (ROS-RNS) metabolism; in essence, how we provide what is provocatively considered the most important "organ" in the Body with the most important "molecule" in the World! Recent advances have been made through the combined application of state-of-the art measurement techniques for the regional detection and characterization of free radicals across the cerebral circulation and diffusion-weighted magnetic resonance imaging. **Results:** This presentation will integrate and translate the adventures of high-altitude expeditioning with the rigors of laboratory experimentation to reveal how the exercised-hypoxic brain becomes oxidatively-nitrosatively stressed-out, sore and swollen. The notion that redox-regulation of blood-brain barrier function has any bearing on an individual's susceptibility to high-altitude illness, notably acute mountain sickness (AMS) and high-altitude cerebral edema (HACE), will also be examined from a critical perspective. Finally, emerging evidence from our laboratory attests to the potential redox-initiated neuro-protective benefits of intermittent hypoxia as a means of "accelerating" cerebral hemodynamic adaptation to exercise. **Conclusion:** These findings confirm ROS-RNS as integral components of the signal transduction cascade that are physiologically essential in controlled amounts capable of initiating protective adaptation in the face of hypoxic-exercise stress for the maintenance of homeostasis. **Acknowledgments:** Prof Peter Bartsch, University of Heidelberg, Germany Profs Niels Secher, Bente Pedersen and Kirsten Moller, University of Copenhagen, Denmark.

8.

HIF-1α POLYMORPHISMS MODULATE HIGH ALTITUDE ACCLIMATIZATION PHENOTYPES IN CHINESE HANS.

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Introduction: Genetic variation is considered to be involved in the high altitude acclimatization. However, the role of genetic variation in the physiological process of acclimatization to altitude is poorly understood. **Methods:** In order to investigate the association between genetic susceptibility of hypoxia-inducible factor-1α(HIF-1α) and myoglobin (MB) genes and the acute and chronic high altitude acclimatization, we conducted a longitudinal cohort study which includes 711 newly recruited male soldiers. The soldiers were exposed from lowland areas to Lhasa or Shigatse areas, with an altitude of 3650 m and 3850 m, respectively. The oxygen utilization and a series of physiological phenotypes including systolic and diastolic blood pressure, SaO_2, FVC, FEV1, RBC, HGB, HCT, MCV, MCH, MCHC, WBC, LYM%, GRAN%, and PLT were tested. The genetic association study was conducted using a single nucleotide polymorphism (SNP)–tagging approach and data were analyzed using repeated measure general linear models (GLM) analysis. **Results:** The significant effect of HIF-1α polymorphisms rs1154967 on the FVC, FEV1, and SaO_2 and the HIF-1α polymorphism rs1154965 on the SaO_2 acclimatizing to acute and chronic high altitude exposure were found. In addition, the significant effect of HIF-1αpolymorphism rs2301112 on the LYM% and GRAN% acclimatizing to high altitude was observed. Moreover, a weak effect of MB polymorphism rs7293 on the MCH and MCHC acclimatizing to high altitude was also observed. **Conclusion:** Taken together, these results suggested that gene-environmental interaction effects of HIF-1α and MB polymorphisms on the physiological outcome (FVC,FEV1, SaO_2, LYM%, and GRAN %) acclimatizing to high altitude environment. **Acknowledgments:** This work supported by National Natural Science Foundation of China (30760274).

9.

MOUNTAIN CLIMATE AND PULMONARY SURFACTANT SYSTEM.

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Introduction. Aim: to investigate injury, reparation and adaptation mechanisms of the pulmonary surfactant system (PSS) in experimental animals and in man under exposure to mountain climate factors and possibilities for drug and physiotherapeutic treatment of related disorders. **Methods:** Physiological, biochemical (measurement of the phospholipid composition and peroxidation products in bronchoalveolar lavage and plasma), biophysical (surface activity of pulmonary extracts and lavage), computed morphometry (determination of cubic and area density of the respiratory part of the lungs), histochemical (copmputed fluorometry of lipids in Hackney's and Berg's stained sections), electronmicroscopic. Study materials: albino rats, rabbits and newborn rabbits, exhaled air condensate and bronchoalveolar lavage fluid from healthy volunteers and patients with bronchial asthma after a month's adaptation to high altitude

and permanent high-altitude residents, amniotic fluid from parturient women at high and low elevations. **Results:** Mountain climate factors (as isolated action in a model and combined action in natural conditions) caused structural and metabolic changes of PSS. In acute exposure to mountain climate factors negative changes leading to respiratory failure were observed. In the long stay of animals and humans in mountain climate conditions, the PSS adapted to the increased functional load. An increased metabolic level of the PSS occurred at the cost of reduced reserve capacities of PSS. Additional physical exercise at high altitude leads to adaptive disruption and development of pulmonary edema. Ambroxol, benzonal, intravascular laser irradiation of blood, extreme high frequency electromagnetic fields, ultrasonic inhalations of copper gumate and linseed was shown to be useful in preventing or correcting hypoxia-related injury of PSS. **Conclusion:** PSS shows itself to possess lability and compensatory potential. In high altitude climate conditions the synthesis and secretion of surfactant stimulated by Ambroxol and benzonal is able to prevent the development of mountain pulmonary edema.

10.

ESTIMATED AEROBIC FITNESS IN 9-10 YEAR OLD TIBETAN CHILDREN LIVING IN LHASA AND UNDER THE NORTH FACE OF MT. EVEREST.

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Objectives: To investigate the association between altitude/ethnicity and estimated aerobic fitness; the association between selected physiological factors (haemoglobin concentration, arterial oxygen saturation, forced vital capacity and heart rate) and estimated aerobic fitness; and finally, to investigate the impact on the association between altitude/ethnicity and estimated aerobic fitness by selected physiological factors as mediators. **Methods:** Two cross-sectional studies were carried out in Tibet, among 9-10 year old native Tibetan ($n = 406$) and Han Chinese ($n = 406$) children in Lhasa in 2005, and native Tibetan Children ($n = 430$) in Tingri district, under the North Face of Mt. Everest, in 2007. A random sample of nine to ten years old children from nine randomLy selected primary schools in Lhasa and 5 primary schools in Tingri were invited to the study. Only five refused to participate. The subjects were considered representative for 9-10 year olds living at altitudes of 3700 m (Lhasa) and 4300 m (Tingri) above sea level. Maximal power output, arterial oxygen saturation (Nellcor NPB-40, California, USA) and heart rate (Polar Electro OY, Kempele, Finland) were measured at rest and during a Maximal Watt Cycle Eegometer (MWCE) test and aerobic fitness was estimated. Forced vital capacity (FVC) was used as a measure of lung volume, and was measured using maximal expiratory flow-volume maneuvers with Spiro USB (Micro Medical Limited, Rochester, Kent, UK). Furthermore, hemoglobin concentration (HemoCue Hb 201 +, Ängelholm, Sweden) was measured and anthropometric measurements were recorded. Differences in mean values between groups were tested using a one-way ANOVA. Three models were constructed for determining the relationship between aerobic fitness and selected physiological factors using linear regression models. **Results:** Lhasa Tibetan children had higher estimated aerobic fitness than both Tingri Tibetan (boys: 1.38 ± 0.12 vs. 1.10 ± 0.17 L/min, $P < 0.001$; girls: 1.16 ± 0.15 vs. 0.95 ± 0.11 %, $P < 0.001$) and Lhasa Han Chinese children (boys: 1.38 ± 0.12 vs. 1.29 ± 0.14 %, $P < 0.001$; girls: 1.16 ± 0.15 vs. 1.11 ± 0.12 %, $P = 0.003$). Altitude/ethnicity showed direct association with aerobic fitness. All the selected physiological factors were associated with aerobic fitness. The association between altitude/ethnicity was working through the selected physiological factors; however other factors other than the selected physiological factors may also mediate the association. **Conclusions:** The higher aerobic fitness in the Tibetan children may indicate that they are better adapted than Han Chinese immigrant children at the same altitude (3658 m), as well as Tibetan children are better adapted to live at the lower altitude (3658 m) than higher altitude (4300 m). In addition to altitude and ethnicity, some physiological param contribute to explaining the variance in aerobic fitness. A follow-up study to record changes in the selected physiological param under study is warranted in order to understand the effect of prolonged high altitude exposure and therefore the mechanism of adaptation to high altitude. **Acknowledgments:** Appreciation is due the Network for University Cooperation Tibet-Norway for supporting this study.

11.

PHYSICAL GROWTH IN CHILDREN OF OF HALF HEIGHT OF AREQUIPA, PERU.

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Introduction: The investigations carried out in countries with geographical variations of high altitude, demonstrate that the hipoxia this associated to a small retard in the physical growth. Objective: The objective of the present study was to compare the characteristics of the physical growth of children of 6-12 years of both sexes of half altitude, in function to NCHS. **Methods:** They were selected in a probabilistic (stratified) way, being 119 men and 120 women of condition socio-economic stocking of public schools of the urban area of the City of Arequipa-Peru (2320 m). The corporal (kg) weight was evaluated using a mark scale Tanita with a precision of 200 g and a scale of 0 to 150 kg. Stature (cm) was evaluated through an aluminum estadiómetro graduated in millim, presenting a scale of 0-2.50 m. The pleat tricipital (mm) was measured using a compass of cutaneous pleats Harpenden that exercises a constant pressure of 10 gr/mm^2 and the circumference of the right relaxed (cm) arm using a metric tape of nylon milimetrada with a precision of (0.1cm). All the carried out measures present acceptable levels of ETM (0.8-2.1%). For the analysis of the results it was used the descriptive statistic of half arithmetic and standard deviation and to compare sexes between both the test it was used student t and the test of specificity of Tukey ($P < 0.001$) and for the comparison inter-class ANOVA was used for independent (one-way) samples with a probability of ($P < 0.001$). **Results:** The results show that the children of both sexes of half altitude of condition socioeconomic stocking of the urban area of Arequipa,Peru present curved of upward growth in all the evaluated variables. Likewise, they present corporal bigger weight that the reference (NCHS), not being this way in the stature where the children present lightly smaller stature and the girls similar values to the reference, except to the 6 and 7 years where the stature is

bigger. Finally, when the results were compared with other carried out studies of bigger height of the same Country, the results show that the children of both sexes of Arequipa have corporal bigger weight, stature and pleat tricipital. Considering that you leave of these opposing evidences he/she is due to the type feeding, socioeconomic factors, lifestyle, among other. **Conclusion:** The results suggest that the range of variation of the variables measures is typical of the populations of high altitudes.

12.

LONG-TERM EXPOSURE TO SIMULATED HIGH ALTITUDE IN RATS AFFECTS FEMUR CROSS-SECTIONAL GEOMETRY AND BONE TISSUE MATERIAL.

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Introduction: Hypoxia increases erythropoiesis that in turn induces hypertrophy of the erythropoietic marrow, which may induce bone resorption. This study investigates the effect of chronic exposure to hypobaric hypoxia (simulated high altitude, SHA) on biomechanics of rat femurs by mechanically testing the diaphyseal stiffness and strength and calculating some indicators of bone material properties. **Methods:** Adult female rats were exposed to SHA (5500 m, 23.5 h/d for 60d = HX rats; NX = normoxic rats). Treatment induced reticulocytosis and polycythemia. Bone mineral content (bone mass) did not differ between NX and HX rats at the end of the study. To assess cortical bone mechanical properties, the right femur was tested in 3-point bending test. **Results:** Endosteum and periosteum moved away from the central axis in HX rats as deduced by an increasing in the cross-sectional moment of inertia. The two indicators of bone material properties, the elastic modulus and the stress at the yield point, were significantly reduced. However, the strength of the femur as an intact organ ("load capacity" param) was not compromised by exposure to SHA. **Conclusion:** It is thus proposed that the negative effect of SHA on bone material quality was completely offset by the improvement in diaphyseal cross-sectional design, thus allowing a normal biomechanical response to bending of the femur as a whole. **Acknowledgments:** This work was supported by research grants from University of Buenos Aires (UBACYT O-005 and O-002)

13.

IMPACT OF ALTITUDE-INDUCED HYPOXEMIA ON MYOCARDIAL FUNCTION OF HEALTHY CLIMBERS.

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Introduction: Reduced exercise tolerance is commonly reported during high altitude accent and hypobaric chamber studies have demonstrated reduced left ventricular stroke volume despite normal cardiac functional reserve. Less is known, however, about diastolic function that might have an impact on exercise capacity. **Methods:** Twelve healthy climbers (8 men, 4 women, aged 35 ± 9 years) participated in a climbing expedition on Huayna Potosi in Bolivia. Echocardiography measurements of left ventricular ejection fraction (LVEF), stroke volume (LVSV), Early (E) and late (e1) diastolic flow, left ventricular tele diastolic dimension (LVTDD), pulmonary artery pressure (PAP), tissue Doppler imaging synchronism (time to peak systolic velocity) and myocardial performance index (MPI) were performed at baseline (353 m), 1st camp (4,000 m), 2nd camp (4750 m) and high camp (5,300 m) of Huayna Potosi using a General Electric model Logiq E portable echographic system. **Results:** Our results show that during the entire ascent, no differences in LVEF (%, $P = 0.4$), LVSV (mL, $P = 0.07$), E/e1 ($P = 0.1$) and LVTDD (mm, $P = 0.3$) were observed in climbers. However, as expected, PAP increased with the progressive exposition to altitude (13.17 ± 6.79 mmHg, 24.50 ± 12.9 mmHg, 25.33 ± 14.97, 31.00 ± 10.44 mmHg at 353 m; 4000 m; 4750 m and 5,300 m measurement respectively; $P < 0.01$). No intra- or interventricular dysynchrony was observed at all altitudes in climbers. In contrast with left MPI, right MPI was significantly increased at high camp (0.35 ± 0.11 at 4000 m, 0.28 ± 0.07 at 4,750 m; 0.42 ± 0.01 at 5,300 m; $P < 0.02$). **Conclusion:** In conclusion, using this mechanistic echocardiography approach, we show that altitude-induced hypoxemic conditions did not result in significant left ventricular abnormalities in our climbers. However, right diastolic dysfunction was observed which may explain the reduced exercise performance of climbers during progressive exposure to altitude. **Acknowledgments:** The study was partially funded by Midwestern University (TLB).

14.

WEIGHT LOSS AND ADIPOKINE CHANGES IN MOUNTAINEERS AT 5300 M.

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Introduction: Adipose tissue plays a central role in mediating weight loss and satiety yet its role in mediating high altitude anorexia has not been fully elucidated. Specifically, the adipose-tissue secreted hormone acylation stimulating protein (ASP), which plays an important role in fatty acid uptake into adipose tissue, has not been previously measured in high altitude mountaineering. The current study sought to evaluate the metabolic and inflammatory-hormone responses, in recreationally fit climbers. **Methods:** Over a period of 9 days, 10 healthy individuals (7 men, 3 women, age 26-49 years) participated in a climbing expedition to 5,300 m in Bolivia. Clinical and metabolic measurements were taken at sea level (SL: 353 m); 4000 m; 4750 m; and 5300 m. **Results:** Body mass index significantly decreased (SL 23.2 ± 1.5 kg/m^2; 4000 m 23.2 ± 1.4 kg/m^2; 4750 m 22.9 ± 1.3 kg/m^2; 5300 m 22.3 ± 1.2 kg/m^2; $P < 0.001$). There was no change in body fat percentage yet percentage fat free mass significantly decreased (SL $56.9 \pm 9.7\%$; 4000 m $55.3 \pm 9.3\%$; 4750 m $55.2 \pm 9.6\%$; 5300 m $54.9 \pm 8.4\%$; $P = 0.048$). Plasma non-esterified fatty acids and triglyceride increased, while high density lipoprotein cholesterol decreased ($P < 0.05$ to < 0.001). ASP (SL 42.2 ± 40.2 nM; 4000 m 117.0 ± 69.6 nM; 4750 m 107.9 ± 44.5 nM; 5300 m 82.2 ± 20.2 nM; $P = 0.019$) and adiponectin (SL 10.4 ± 6.5 ng/mL, 4000 m 13.9 ± 8.5 ng/mL, 4750 m 18.3 ± 8.3 ng/mL, 5300 m 14.7 ± 8.0 ng/mL $P = 0.015$) significantly increased, as did insulin and interleukin-6 (up to 71% and 168%, respectively, $P < 0.05$) with no change in leptin, complement C3, high sensitivity c-reactive protein or cortisol. **Conclusion:** In conclusion, the adipose tissue hormones ASP and adiponectin are increased during exposure to acute high altitude induced hypoxia and may be contributing to the preservation of adipose tissue despite weigh loss in healthy mountaineers. **Acknowledgments:** This study was partially supported by funding from the

Canadian Institute of Health Research to KC and by a Midwestern University Grant to TLB.

15.

EFFECT OF INTERMITTENT HYPOXIA ON ERYTHROPOIETIN, SOLUBLE ERYTHROPOIETIN RECEPTORS AND VENTILATION IN HEALTHY HUMANS.

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Introduction: It has recently been demonstrated that both Erythropoietin (Epo) and soluble Epo receptors (sEpoR) play a central role in the ventilatory acclimatization to hypoxia in mice. We hypothesized that i) sEpoR would be downregulated by exposure to intermittent hypoxia (IH), thereby allowing Epo concentration to rise; ii) these modifications would be correlated with the alteration in the acute hypoxic ventilatory response (AHVR). **Methods:** Nine healthy male subjects were exposed to 6 h of IH [2 min normoxia (peak end-tidal PO_2 ($PETO_2$) = 88.0 Torr) and 2 min hypoxia (nadir $PETO_2$ = 45.0 Torr)] for four consecutive days (Days 1-4), preceded by two normoxic control days (4 days apart; Baseline), and followed by one recovery day (4 days after IH; Day 8). Epo and sEpoR concentrations and AHVR were measured on Baseline, Days 1, 2, 4 and 8. **Results:** We observed a nadir in sEpoR on Day 2 (-70% vs. Baseline; $P < 0.01$), concomitant with the peak in Epo secretion (+50% vs. Baseline; $P < 0.01$). Following exposure to IH, ventilation (VE) as measured during the AHVR test rose because of the increase in tidal volume (VT). Similarly, AHVR increased progressively along with IH ($P = 0.008$). There was a negative correlation between Epo and sEpoR ($r = -0.261$, $P = 0.05$), and between sEpoR and VT ($r = -0.331$, $P = 0.02$). Epo was positively correlated with VE ($r = .458$, $P = 0.001$) and AHVR ($r = .475$, $P = 0.001$). **Conclusion:** We conclude that sEpoR is downregulated upon exposure to IH and thereby modulates the Epo response. Furthermore, the alterations in AHVR and breathing pattern following IH seem partially mediated by the increase in Epo. **Acknowledgments:** Funding: AHFMR, HSFC and Hotchkiss Brain Institute.

16.

A COMPARISON OF HEART RATES BETWEEN SIMULATED AND REAL ALTITUDE.

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Introduction: The aim of the present study is to make a comparison between heart rates measured at real altitude and at the simulated altitude, before and after the process of acclimatization. **Methods:** Sample of subjects: Our sample of subjects consisted of two female students (height 166 ± 9.8, mass 62.5 ± 2.1, age 25 ± 1.4) and four male students (height 179.5 ± 8.38, mass 76 ± 6.6, age 25.5 ± 3.6) of the Faculty of Sports, all participants in the Elbrus 2007 expedition. Description of the test. The subjects performed The Queen's College Step Test. They had undergone eighteen day-long acclimatization process on 2100 – 5642 m. Heart Rate (HR) was measured during the step test before and after the acclimatization, at two locations: high altitude simulation chamber in Ljubljana and real altitude in Elbrus both at 2100 m and 3800 m. Their HR was monitored by Suunto-t6. **Results:** At 2100 m average HR during the step test before the expedition was 146.65 beats/min (real altitude) and 139.60 beats/min (simulated altitude). After the expedition the results were 132.33 beats/min (real altitude) and 128.42 beats/min (simulated altitude). At 3800 m average HR was 149.88 beats/min (real altitude) and 144.94 (simulated altitude) before expedition. After the expedition the results were 139.24 beats/min (real altitude) and 140.54 beats/min (simulated altitude). The differences in average HR before and after the expedition were statistically significant except. There were no statistically significant differences found between simulated and real altitude at the corresponding height. **Conclusion:** We are getting closer to the establishment of HR as an indicator of acclimatization. For the people who stay at high altitudes this means easier and more adequate decision about the time of further ascent. It will lower the possibility of altitude sickness and even prevent death, which sometimes appear when the rules of acclimatization are neglected. An altitude room could serve as a form of standard pre-acclimatization for top mountaineers as well as other people who travel to high altitudes above 3000 m.

17.

HYPOXIA AND GLUCOCORTICOID ALONE AND CO-INDUCED ON THE EXPRESSIONS OF STOMATIN IN LUNG AND A549 CELLS.

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Introduction: Stomatin is an important membrane raft protein which can combine several membrane proteins, such as ion channel, skeleton protein, glucose transporter 1 (GLUT-1) and some signal transducers to regulate their function. In an attempt to elucidate the possible roles of stomatin in hypoxic stress, we investigated the effects of hypoxia exposure and treatment of dexamethasone(Dex), a synthesis of glucocorticoid alone or together on the stomatin expression. **Methods:** Methods: The expression of stomatin was determined by real time RT-PCR and Western blotting analysis. Lung index (LI) and the histological appearance of the lung of rats were also examined. **Results:** Results: We first found that hypoxia induced expression of stomatin not only occurred in A549 cells, an alveolar type II cell line, but also in lung of rats which was independent of hypothalamic–pituitary–adrenal axis activation. Dex also markedly induced stomatin expression in vivo and in vitro, and the effect is mediated by GR. Combination of hypoxia and Dex further increase the levels of stomatin mRNA and protein, indicating that stomatin is hypoxia and GC response gene. Furthermore, pulmonary edema induced by hypoxia showed self-limited characteristic as extending the hypoxia exposure, and Dex obviously alleviate pulmonary edema. **Conclusion:** Conclusion: Hypoxia and Dex not only significantly up-regulated the expression of stomatin alone, but also co-induced the expression of stomatin in lung of rats and in A549 cells. The increased expression of stomatin may play important protective role in enhancing the function of alveolar epithelial barrier and involved in hypoxia adaptation. **Acknowledgments:** This work was supported by the grant from The National Basic Research Program "973" No. 2006CB504100.

18.

SLEEP QUALITY OF ANDEAN INHABITANTS AT 3200 M ANCASH, PERÚ.

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Introduction: In relation to the hight altitude and quality of sleep, it has been observed that there are physiological changes in the migrants at sea level to high altitude, which are related to sleep disturbances. In Peru, sleep habits, in the high Andean areas have not been studied. For that reason we want to investigate the sleep quality of these residents. **Methods:** To describe the sleep quality in this population we used the Pittsburgh Sleep Quality index. We calculated a $n = 92$ by the method of proportions, and there was a systematic randomization of houses, surveying the residents present that time that met inclusion criteria. **Results:** 83 residents were surveyed, 46% were men, mean age was 40.59 ± 17.5 [18-65] and median PSQI score was 6 ± 4.5 (RIC) [2-18], found that 53 (63.8%) were poor sleepers. The most common sleep disorder was insomnia present in 47% of the population. The average number of hours of sleep was 7 ± 1.7 [2-11], 16 (19%) subjects slept between 6 and 7 hours. Fifty-six (47%) take less than 30 minutes to fall asleep. Thirty-nine (47%) participants were awakened at night 3 or more times per week. The subjective sleep quality was very poor; in 5 (6%) respondents and very good in 9 (12%), fifty-three (62%) had subjective sleep efficiency greater than 85%. **Conclusion:** The results show how frequent are the symptoms associated with various sleep disorders in a rural population living in high altitude documented by the Pittsburgh Sleep Quality Index, with modifications adapted to the socio-cultural environment. We believe this tool is useful and can be applied in rural-Andean. It is advisable to investigate further this issue, while confirming the findings of this pioneering study, which would implement educational interventions for the benefit of the inhabitants of these regions. **Acknowledgments:** IRIS

19.

OXYGEN SATURATION IN HEALTHY CHILDREN AGED 5 TO 16 YEARS RESIDING IN HUAYLLAY-PERU (4340 M).

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Introduction: Objective: Determine values of SaO_2 in a sample of healthy children 5 to 16 years residing in a village at 4340 m and whether there is variation with age and sex. Background: Hypoxemia is one of the deadly complications of pediatric pneumonia. The cutoff points for SaO_2 and hypoxemia vary with altitude. There is little evidence of such cutoff points above the 4000 m. **Methods:** We examined children aged 5 to 16 years as part of primary care visits of the health center of Huayllay (a rural community located about 4340 m). We included subjects considered clinically healthy. Physiological param were analyzed: SaO_2 (measured by pulse oximetry), heart rate and respiratory rate. Comparisons between age groups (5-6, 7-8, 9-10, 11-12, 13-14 and 15-16 years) and those param was performed using a multiple linear regression model. The correlation between SaO_2 and heart and respiratory rate was established with Pearson's r test **Results:** We evaluated 583 children, of whom 386 were included in the study. The average age was 10.3 years, 55.7% were women. The mean SaO_2, heart rate and respiratory rate was 85.7% (95% CI: 85.2-86.2), 80.4 per minute (95% CI: 79.0-81.9) and 19.9 per minute (95% CI: 19.6-20.2), respectively. SaO_2 increased with age (p value < 0.001) and presented a marked increase from age 11. The average minus two standard deviations of SaO_2 (cutoff point for hypoxemia) ranged from 73.8% to 81.8% by age group. **Conclusion:** We observed levels of SaO_2 and cutoff points for hipoxemia lower that those reported at < 4000 m in healthy children. Our results suggest the existence of adaptive mechanisms that lead to a rised in the levels of SaO_2 during adolescence in Andean population **Acknowledgments:** The authors wish to ackowledge Andres G. Lescano PHD for his commentaries an assistance in preparation of the manuscript.

20.

ACTIVITY OF ANTIOXIDANT ENZYMES IN GUINEA PIG BRAINS DURING ACUTE HIGH ALTITUDE EXPOSURE (4540 M).

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Introduction: In recent years, it has been shown the association between oxidative stress and hypoxia, and an increment in reactive oxygen derived substances has been found in models of hypoxia/reperfusion, during exhausting physical exercise and simulated hypoxia in hypobaric chambers, and during the ascent to high-altitude. Nevertheless, studies about the effect of acute exposition to high altitudes on cerebral oxidative metabolism are scarce; for this reason, we have considered of interest to assess the effect of acute hypoxia exposure on brain tissue antioxidant enzymes activity in sea- level raised guinea pigs, after being transferred to high altitude. **Methods:** Forty sea-level native guinea pigs were moved from Lima (150 m) to Morococha (4540 m, a 3 hr trip by road), and sacrificed on days 1,3,7 y 14 after arrival. A group of ten guinea pigs were sacrificed in Lima (control group). Superoxide dismutase (SOD) , catalase (CAT) and glutathione peroxidase (GPX) activity levels were determined. Likewise, Malondialdehide (MDA) and Lipid hydroperoxides (LOOH) levels were determined as markers of lipid oxidation; and phospholipase A2 (PLA2) activity was determined as a mediator of lipid peroxidation. **Results:** Lipid oxidation markers levels were found to be increased the first day; LOOH and MDA levels showed a decreasing tendency over time, but kept their high values. SOD activity increased up to the third day and finally diminished. GPX and CAT activities were significantly high since the first day whole study; PLA2 activity increased up to the 3rd day and then began to decrease. **Conclusion:** High altitude exposure has a direct influence on the brain lipid peroxidation process and antioxidant enzymes activities, especially in GPX, which plays an important role in LOOH detoxification. This could explain its tendency to decrease at level at the end of the study period.

21.

CHEWING COCA LEAVES AT HIGH ALTITUDE IS GOOD FOR PHYSICAL ACTIVITY.

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Introduction: The aim of this study was to investigate the effects of chewing coca leaves on biochemical and physiological param in physical activity. **Methods:** We subjected 10 healthy adult males (local residents) in Cajamarca (Peru, altitude 2700 m) to a standardised exercise routine on a stationary cycle ergometer. The blood pressure, oxygen saturation (digital), pulse, VO_{2m}ax and ECG (Holter monitor)

were recorded before the exercise. The VO_2 max was measured indirectly through the Test of Fox which measure heart rate while the subjected is subjected to a submaximal exercise by pedaling a bicycle ergometer under standard conditions, the values were calculated with the Fox equation for men and corrected by the factor for age Astrand and the results are expressed in mL x kg-1 x min-1. Cutaneous microdialysis catheters were introduced in the forearm to estimate systemic biochemical changes. The subjects were given to chew 8 g of coca leaves with a small amount of lime. They were then placed on the cycle ergometer for 20 minutes. Blood pressure, oxygen saturation, pulse, ECG and VO_2 max were recorded. Pyruvate, glucose, lactate, glycerol and glutamate levels were estimated. **Results:** Oxygen saturation, blood pressure, and pulse rate did not show any significant changes between the two groups. Glucose levels showed hyperglycaemic response. Glycerol, Lactate and Pyruvate increased. Glutamate remained unchanged. Similar changes were not seen in the controls. **Conclusions:** These results suggest that coca leaves have blocked the glycolytic pathway of glucose oxidation resulting in accumulation of glucose and pyruvate. The energy requirement for exercise is being met with beta-oxidation of fatty acids. The glycerol released was also getting accumulated since its pathway for oxidation was blocked. Testosterone and estradiol estimates did not show significant changes. These experimental findings suggest that chewing coca leaves is beneficial during exercise and that the effects are felt over a prolonged period of sustained physical activity. We feel that perhaps flavonoids in coca leaves influence the NO mechanism. We have done NO imaging and Griess assay to understand NO production from endothelial cells under epicatechin treatments. **Acknowledgments:** Cantley Medical Services (CMS) donated the Microdialysis catheters (Mfg. CMA, Microdialysis AB, Sweeten). The Nepean Hospital provided the reagents and the analyser. The National Institute of Andean Biology, Lima provided the space and the laboratory facilities to conduct the study and collect the samples. The citizens of Cajamarca subjected themselves to the study with very little persuasion. Prof. K. K. Srivastava, Professor Emeritus Delhi University agreed to comment on the biochemical changes. We are very grateful for his valuable input.

22.

INSULIN RESPONSE IN HEALTHY RESIDENTS IN HIGH ALTITUDE.

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Introduction. Aim: To know the insulin response in normal healthy residents in high altitude (HA) to acute hyperglycemia. **Methods:** We studied 17 normal men subjects. Group A : 11 residents at sea level (SL) (Lima, 150 m.a.s.l) and Group B : 6 from (HA) (Huancayo, 3200 m.a.s.l). Age $\pm$ 28.9 and $\pm$ 26 years, Body Mass Index (BMI) $\pm$ 23.7 and $\pm$ 25.4 kg/m 2 respectively. We used the hyperglycemic clamp at 125 m/dl for two hours. Insulinemia was measured at 0, 5, 10, 15, 20, 40, 60, 90 and 120 minutes. Glycemia at 0.6, 12, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, and 120 minutes. **Results:** We observed a significative elevation of insulin concentrations at 10(12.21 ± 1.55 uU/mL;7.38 ± 0.67 uU/mL,$P = 0.015$), 15(15.90 ± 2.25 uU/mL,7.72 ± 0.73 uU/mL,$P = 0.005$) and 20(16.66 ± 2.62 uU/mL,8.93 ± 0.80 uU/mL,$P = 0.016$) minutes in residents from SL. **Conclusion:** The early insulin response to acute hyperglycemia is lower in residents from high altitude. **Acknowledgments:** This work was supported by Alexander von Humboldt Foundation, Bonn, Germany and Universidad Nacional Mayor de San Marcos, Lima, Perú.

23.

GENETICS OF MITOCHONDRIAL ELECTRON TRANSPORT CHAIN IN REGULATING OXYGEN SENSING.

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Introduction: Physiological hypoxia results in a host of responses that include increased ventilation, constriction of the pulmonary artery, and a cellular transcriptional program that promotes glycolysis, angiogenesis, and erythropoiesis. The biology of hypoxia is also important for understanding diseases such as cancer. At the molecular level, hypoxia-inducible factors (HIF-1 and HIF-2) are the best characterized transcriptional regulators of hypoxic gene expression. In the past decade, my laboratory has elucidated that mitochondrial ROS generated at complex III are required for hypoxic activation of the HIF-1 [Brunelle et al. Cell Metabolism 1:409-414 and Bell et al. Journal of Cell Biology 177(6):1029-36]. Furthermore, we collaborated with Abbott Laboratories in finding small molecules that inhibit HIF transcriptional activity. The small molecules which displayed the greatest efficacy in diminishing HIF transcriptional activity were complex III inhibitors [Lin et al. PNAS 105(1):174-9]. We also demonstrated that a consequence of HIF-1 induction by complex III ROS in primary human cells is extension of replicative lifespan [Bell et al. Mol Cell Biol. 25:4853-62]. These results from my lab demonstrated that increases in ROS levels can be associated with an increase in replicative lifespan. To our knowledge, this is one of the first studies to link increases in ROS with increase in fitness of mammalian cells. The adaptation to hypoxia also involves the activation of AMPK. We genetically showed that mitochondrial complex III ROS are required for hypoxic activation of AMPK activity [Emerling et al. Free Radic Biol Med. 46(10):1386-91]. Recently, we have begun to test whether mitochondrial ROS regulates oxygen sensing in vivo. We have generated mice in which keratinocytes lack mitochondria. These mice do not have hair. We are currently exposing these mice to hypoxia and testing their EPO levels. Collectively our results indicate that mitochondrial complex III generated ROS are required for hypoxic responses [for review see Hamanaka and Chandel Curr. Opin. Cell Biol. 21(6):894-9]. **Acknowledgments:** This work was supported by a NIH Grant R01CA123067-04.

24.

EXPOSURE TO INDOOR BIOMASS FUEL AND TO HIGH ALTITUDE (4100 M) ON HEALTH STATUS AND CHRONIC MOUNTAIN SICKNESS: EFFECT OF CONSUMPTION OF MACA.

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Introduction: Exposure to indoor biomass fuel has important adverse effects on health. This may produce oxidative stress by hypoxia in populations living at high altitude. The present study was designed to determine the score of health status in persons using biomass fuel for cooking in the population of Carhuamayo in the Peruvian central Andes. This population is characterized to be a traditionally consumers of maca a plant growing over 4000 m in Peru. The effect of this consumption will be also assessed. **Methods:** The study has been performed in 557 persons aged 35-75 years and living in Carhuamayo (4100 m). From these, 352 uses gas ($n = 195$) or a combination with gas ($n = 78$) or they are not cooking ($n = 74$)and 205 persons use biomass for cooking. Health status was assessed using the modified SF-36 questionnaire with 20 questions about 7 health dimensions. The CMS score was assessed through a survey with 7 questions about signs and symptoms

of CMS. A questionnaire about maca consumption was also included. Data were analyzed with the SPSS. Data was expressed as mean ± standard error. $P < 0.05$ was considered as significant. **Results:** In this population located at 4100 m due to the lack of trees, the amount of houses that use wood for cooking was low, however mainly of them use a mixture of "ichu" or grass and dung, that they named "champa". Cooking with biomass reduced the score in the questionnaire of health from 66.62 ± 1.96 to 54.12 ± 2.75 ($P < 0.05$) and increased the score of signs and symptoms of CMS form 4.38 ± 0.31 to 5.48 ± 0.44 ($P < 0.001$). We also found that the consumption of maca could reduce the score of CMS from 5.34 ± 0.36 to 4.24 ± 0.16 ($P < 0.01$) and enhance the health status from 58.92 ± 2.27 to 64.01 ± 1.05 ($P < 0.05$). **Conclusion:** In conclusion, cooking with biomass at HA is negative for health and maca may constitute an alternative of treatment. **Acknowledgments:** This Study was supported by a Grant from the Fogarty Program of The National Institutes of Health of the United States (NIH Research Grant # 5-D43TW005746-04 funded by the Fogarty International Center, National Institutes on Environmental Health Services, National Institute for Occupational Safety and Health, and the Agency for Toxic Substances and Disease Registry).

25.

CHRONIC EXPOSURE TO HYPOBARIC HYPOXIA IN ALUMINUM INTOXICATED IMMATURE RATS IMPAIRS BONE TISSUE QUALITY.

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Introduction: Hypobaric hypoxia (HX) induces stress erythropoiesis leading to hypertrophy of the erythopoietic marrow and may affect bone resorption with decrease of cortical thickness. Chronic administration of aluminum (Al) induces a negative effect on bone tissue, affecting collagen synthesis and matrix mineralization with cumulative effects. The aim of this work is to evaluate the chronic effect of Al on the architectural properties and the biomechanical quality of femoral diaphysis under hypoxic conditions. **Methods:** Sprague Dawley rats, aged 21 days, received ip doses of 27 mg/Kg of elemental Al, 3 times a week, during 3 months. Control rats received vehicle. Half of each group ($n = 9$) were exposed to simulated high altitude (SHA, 506.5 mbar). General anthropometry was assessed using serial estimations of total weight and length. Morphometric femur studies were performed measuring the distance between stable anatomical points. Biomechanical performance was estimated by the three-point yielding method. **Results:** Al administration did not affect general or femoral anthropometries although significantly depressed stiffness, i.e. the resistance to elastic deformation as a possible consequence of alteration in the mineralization. On the histological analysis subcondral bone mass was significantly decreased in the SHA group and we observed additive effects in AlHx group. Both treatments decreased maximum capacity to withstand load, the load elastic limit and the capacity of absorbing energy in elastic conditions of bone (structural properties of bone). The indicators of bone material intrinsic properties, elastic modulus and stress at the yielding point, were significantly reduced and the moment of inertia was increased either by Al or by HX with no additive effect in the AlHX group. **Conclusion:** Results suggest that femur compensates the impairment of diaphyseal biomechanical properties with more peripheral distribution of cortical tissue. **Acknowledgments:** This investigation was supported by research grants from University of Buenos Aires (UBACyT O-407).

26.

EFFECT OF DAILY ROOM O_2-ENRICHMENT ON HYPOXIC VENTILATORY RESPONSE, VENTILATORY ACCLIMATIZATION AND HEMATOCRIT DURING CHRONIC HYPOBARIC HYPOXIA IN THE RAT MODEL.

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Introduction: Exposure to a high-altitude environment, especially above 2500 m, causes a syndrome known as acute mountain sickness (AMS). AMS includes several non-specific symptoms such as headaches, nausea, insomnia, and lack of appetite. In severe cases, AMS can lead to and potentially life-threatening conditions such as pulmonary and cerebral edema. Enrichment of rooms with O_2 for short periods has proved to decrease AMS signs and symptoms at high altitude, and thus prevent the severe effects of hypoxia and favor well-being of high-altitude visitors. The effects of room O_2-enrichment during a longer term exposure to high-altitude on physiological param such as hypoxic ventilatory response (HVR), ventilatory acclimatization to hypoxia (VAH) and hematocrit (hct) however are not known. **Methods:** Nineteen Sprague-Dawley male rats were weighed and a small tail-blood sample was taken for hct determination. Rats were grouped according to oxygenation treatment. Group HxOx ($n = 8$) was placed inside a hypobaric chamber set at 430 mmHg (equivalent to 4300 m or 12% O2) for 21 days and received 24% O2 while on hypobaria for 90 min daily. Group Hx ($n = 7$) was also placed hypobaria at 430 mmHg but received no additional O2. Group Nx ($n = 4$) was kept in normoxia during the course of the experiment. Resting ventilation (VE) and HVR were measured by whole-body unrestrained plethysmography at day 0, 7, 14 and 21. **Results:** VE, HVR, hct, and body weight (BW) had similar values in the three groups at the beginning of the study. As expected, hct in groups HxOx and Hx increased progressively during chronic hypoxic exposure. Group HxOx showed higher hct than group Hx at day 7 and afterwards at each time-point throughout the experimental period ($P < 0.05$). The progression of VE showed increases at each time point (VAH) in both HxOx and Hx groups but with no significant differences between them. **Conclusion:** The results suggest that O_2-enrichment of high-altitude rooms have no significant effect on VAH or HVR, but could result in higher hct values due to possible Epo pulses occurring daily in the cycle of addition and removal of O_2. This finding indicates that daily supplemental O_2 could contribute to the development of elevated hct values for the altitude of residence in the long-term.

27.

CIRCADIAN VARIATION OF ERYTHROPOIETIN AND ITS RELATIONSHIP WITH ARTERIAL OXYGEN SATURATION AT MODERATE ALTITUDE: EFFECT OF GENDER.

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Introduction: The aim of this study was to determine the existence of circadian rhythm in the secretion of erythropoietin (EPO) and its relationship with arterial oxygen saturation (SO_2) in subjects living at an altitude of 2600 m (Bogotá, Colombia). **Methods:** Plasma concentration of EPO was performed by ELISA method using the double antibody sandwich. Continuous measurements of SO_2 were obtained by pulse oximetry in 18 healthy young sedentary ($n = 11$ women, mean age 18.9 SD 0.2, mean hemoglobin concentration 14.8 SD 0.2 g/dL; men $n = 7$, mean age 19.4 SD 0.8, mean hemoglobin concentration 16.8 SD 0.4 g/dL) during 24

hours. Plasma concentration of EPO was measured every 4 hours for 24 hours. **Results:** Circadian rhythm was shown both EPO and SO_2 values. From morning until midnight SO_2 remained stable. From 00:00 to 04:00 hours, there was a decrease of 2.0% in SO_2. EPO plasma concentration increased from 4 to 5 U / L in response to reduced SO_2 at the same period. SO_2 levels and EPO concentrations were significantly different in men and women (ANOVA, $P < 0.01$). **Conclusion:** The circadian secretion of EPO was correlated with the SO_2 in a negative way both men and women. **Acknowledgments:** This study was supported by a grant from Banco de la República, Colombia (F. P. I. T.- 1201).

28.

CARDIOVASCULAR AND RESPIRATORY RESPONSES TO HIGH ALTITUDE EXPOSURE IN SEA LEVEL AND HIGH ALTITUDE RESIDENTS.

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Introduction: High altitude inhabitants have markedly different physiological responses to altitude exposure than sea level residents. Genetics have been reported to play an important role in these responses. This study evaluated the influence of altitude of residence on the cardiovascular and respiratory responses to acute exposure to very high altitude. **Methods:** Sixty-three subjects participated in the study after giving informed consent. Subjects were recruited and tested at the base refugio at Mount Chimborazo in Ecuador (15,900 ft). This is an ideal location because many Ecuadorians that reside at a variety of altitudes can easily and quickly drive to the refugio. Cardiovascular measurements included systolic and diastolic blood pressure, hemoglobin saturation, hemoglobin concentration and resting heart rate. Vital capacity, chest width and depth were also measured. All measurements were done upon arrival at the refugio. Subjects were then divided into three groups based on their altitude of residence: Low altitude residents - LOW (0-5,000 ft), moderate altitude residents - MOD (5,000- 10,000 ft) and high altitude residents - HIGH(>10,000 ft). **Results:** Resting heart rate was lower in HIGH (78.2 ± 14.1 bpm) than the MOD (88.3 ± 13.8 bpm) and LOW (95.4 ± 22.6) altitude groups. Hemoglobin saturation was highest in HIGH ($83.2 \pm 7.9\%$) as was hemoglobin concentration (16.4 ± 3.5 mg/dL). The highest altitude residents had greater chest widths (38.2 ± 3.6 cm) and depths (23.1 ± 3.7 cm). However, there were no differences in absolute vital capacities between groups. This is probably attributable to the fact that the HIGH residents were shorter ($1.64 \pm .08$ m) and lighter (64.1 ± 8.2 kg) than the MOD or LOW altitude groups. **Conclusion:** Height of altitude residence plays an important role in the cardiovascular and respiratory responses to acute high altitude exposure. These differences represent favorable adaptations to long-term high altitude residence.

29.

HEMIN TREATMENT PARTIALLY REVERTS PULMONARY ARTERIAL HYPERTENSION IN HIGH ALTITUDE NEWBORNS. A ROLE FOR BKCA CHANNELS AND PKG-1.

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Introduction: Pregnancy at high altitude yields neonates with pulmonary hypertension (1). Therapies available today to decrease pulmonary arterial pressure (PAP) are insufficient to treat an important number of human neonates. Hemin treatment in high altitude neonatal sheep showed a partial decrease in PAP (2) and a lesser smooth muscle thickness in small pulmonary arteries (3). Hypothesis: We hypothesize that the decrease in PAP after hemin-treated newborn lambs, was due partially to an increased protein expression and function of BKCa channels and an augmented protein expression and function of PKG-1. **Methods:** Ten lambs, whose gestation, birth and experimental procedures took place in high altitude (Putre, 3600 m), were divided in two groups. Five neonatal sheep were treated with hemin (Sigma-Aldrich Chemical, St Louis, MO, USA; 15 mg/Kg/day, subcutaneously) for 10 days and five neonatal lambs were used as controls. After treatment, they underwent euthanasia with an overdose of sodium thiopentone (100 mg•kg-1 IV) a) to study the vasoreactivity of small pulmonary artery, to a BKCa channel opener (NS 1619) and blocker (Paxilin), utilizing wire myography and b) to investigate protein expression of BKCa, PKG-1, and β-actin in total lung lysates by immunoblot with specific antibodies. **Results:** The vasoreactivity studies showed an increase maximal relaxation with the BKCa channel opener, between control and hemin-treated lambs ($84.12 + 4.70\%$ vs. $60.93 + 3.11\%$ respectively, $p < 0.05$). The contraction produced by the BKCa channel blocker, was increased in the hemin-treated lambs ($98.3 + 1.9\%$ vs. $123.9 + 9.9\%$; $p < 0.05$). The BKCa and PKG-1 protein expression was increased in the hemin-treated lambs ($1.32 + 0.34$ vs. $2.42 + 0.24$ and $1.76 + 0.23$ vs. $2.95 + 0.81$ respectively $p < 0.05$). **Conclusions:** The lower pulmonary arterial pressure in the hemin-treated newborns can be partially explained by the increased of PKG-1 and BKCa channel protein expression and an increased BKCa function. Studies are in progress to investigate further these possibilities. **Acknowledgments:** Supported by FONDECYT 1090355, 1080663-Chile. References: (1) Herrera EA. et al. Am. J. Physiol. 292(6):R2234-R2240.2007. (2) Ebensperger G. et al. Fetal and Neonatal Physiological Society Annual Meeting 2009. (3) Ebensperger G. et al. Society of Gynecological Investigations Annual Meeting 2010.

30.

IMMOBILIZATION AND SPLINTING IN MOUNTAIN RESCUE. OFFICIAL RECOMMENDATIONS OF THE INTERNATIONAL COMMISSION FOR MOUNTAIN EMERGENCY MEDICINE, ICAR MEDCOM.

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Introduction: Immobilization and splinting of fractures are essential to reduce morbidity and mortality in mountain rescue. **Methods:** Therefore, members of the International Commission for Mountain Emergency Medicine (ICAR MEDCOM) debated the results of a literature review carried out by the authors. **Results:** Focusing on common immobilization and splinting techniques relevant to mountain rescue, a consensus document was formulated. **Conclusion:** Pain relief of appropriate speed of onset and strength should be available on scene. Spinal immobilization is recommended for all casualties that have sustained head or spine injury. The preferred method is a vacuum mattress with an

appropriately sized rigid cervical collar. In such casualties, only those in an unsafe environment or with time-critical injuries should be evacuated before spinal immobilization is performed. In some casualties, the cervical spine may be cleared and a cervical collar may be omitted. In the presence of hemodynamic instability and where there is a suspicion of a fractured pelvis, an external compression splint should be applied. Splinting of a femoral shaft fracture is important to limit pain and life-threatening blood loss. If time allows, extremity fractures should be adequately splinted and, if the practitioner is skilled, a displaced fracture or joint dislocation should be reduced on scene with the use of appropriate analgesia.

31.
GENERAL CONSIDERATIONS, ORGANIZATION AND EQUIPMENT IN MOUNTAIN RESCUE.

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Introduction: This practical workshop will highlight the fundamental areas that need to be addressed when operating an organized mountain rescue service **Methods:** A short presentation will be followed by discussion and sharing of ideas between participants and members of the International Commission for Mountain Emergency Medicine. **Results:** Many service models can provide an effective mountain rescue service. Despite enormous differences, fundamental topics, such as scope of the service, command and control, communication and rescue equipment, and integration and co-operation with other emergency services require addressing. Safety must be considered at all stages. **Conclusion:** The quality of a mountain rescue service depends on many factors; as medical practitioners performing mountain emergency medicine, we need to appreciate the complete picture.

32.
ASSESSMENT OF CASUALTIES IN THE MOUNTAINS.

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Introduction: Trauma with cardio-respiratory arrest is the most common cause of death in the mountains. Accurate assessment of the victim is one of the most important skills for first responders, paramedics and emergency physicians. It is crucial to give correct instructions to the dispatch centre in order to activate emergency helicopters and other resources and in order to start effective treatment at the site of the accident. Especially in mountainous areas where there are additional hazards to the victim and the rescuers, an accurate initial diagnosis is critical to optimize treatment and transport. Airway management and diagnosis of hemorrhagic shock in blunt trauma or severe brain injury, with re-establishment of circulation are critical. Rapid, safe transportation depends on quick, but effective, initial assessment and stabilisation of vital functions in order to minimize core temperature drop and reduce prehospital time. **Methods:** The authors conducted a literature search using Medline, the Cochrane database and a hand search, using the terms: trauma, assessment, prehospital care, emergency medicine, and mountain rescue. There were no peer-reviewed studies concerning the specific topic of assessment of casualties in the mountains **Results:** Typical patterns of injury found in special situations such as avalanche, hypothermia, rock fall, canyoning and lightning injuries arepresented and the necessary steps of assessment are shown. **Conclusion:** Trauma in mountainous and remote areas often occurs under difficult environmental conditions and in dangerous terrain. Safety of the victim and the rescuers has the highest priority. In many cases, rapid evacuation is the first step to reduce further risks to the patient and rescuers. Assessment should follow established international algorithms, but this may not be possible in every situation. Assessment be as thorough as possible, but should not delay evacuation and initial treatment. **Acknowledgments:** This manuscript has been discussed at the annual ICAR MEDCOM meetings 2008 in Chamonix (France) and 2009 in Zermatt (Switzerland) and officially approved by the following members: Giancelso Agazzi (I), Jan Beaufort (CZ), Jeff Boyd (CA), Hermann Brugger (President) (I), Ramon Chiocconi (Argentina), Giovanni Cipolotti (I), Tore Dahlberg (N), Florian Demetz (I), Fidel Elsensohn (Vice President) (A), John Ellerton (GB), Gerhard Flora (A), Herbert Forster (D), Silvia Ferrandis (ES), Herbert Forster (D), Sylveriusz Kosinski (PL), Miroslav Kova (SK), Xavier Ledoux (F), Peter Mair (A), Herbert Mayer (D), Mario Milani (I), Arthur Morgan (SA), Maria-Antonia Nerin (E), Marie Nordgren (S), Peter Paal (I), Peter Rheinberger (FL), Erik Sandstrom (S), Marcel Sedlacko (SK), Günther Sumann (A), Dario Svajda (HR), Michael Swangard (CA), David Syme (GB), Oleg Tcholakov (BG), Iztok Tomazin (SLO), Karen Wanger (CA), Urs Wiget (Past President) (CH), Ken Zafren (Vice President) (USA), Gregoire Zen Ruffinen (CH), Igor Zuljan (HR).

33.
PULMONARY CIRCULATION AND NOT PULMONARY DIFFUSION MAY LIMIT EXERCISE CAPACITY IN SHERPAS AT HIGH ALTITUDE.

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Introduction: The aim of the study was to evaluate if Sherpas, Himalayan native highlanders, are better adapted to hypoxic conditions compared to acclimatized lowlanders at high altitudes. **Methods:** An incremental cycle ergometer cardiopulmonary exercise test, an echocardiographic study of the right ventricular function and the pulmonary circulation together with lung diffusion measurements (CO and NO transfers measured using the single breath method) were performed in 13 Sherpas aged 25 ± 1 years (mean $\pm$ SE) and in 13 acclimatized lowlanders aged 29 ± 2 years at the "Pyramid hut", at the altitude of 5050 m in Nepal. Both groups were matched for body size. **Results:** At high altitude, arterial oxygenation was similarly decreased in acclimatized lowlanders and Sherpas (83 ± 2 vs $86 \pm 1\%$). Lowlanders and highlanders reached the same maximal workload of 158 ± 8 vs 164 ± 10 W (PNS) and maximum O_2 uptake (VO_2 max) of 28 ± 1 vs 32 ± 3 mL/kg/min (PNS). Right cardiac function indexes were lower in highlanders than in lowlanders ($P < 0.05$); the tricuspid annular plane systolic displacement was decreased (29 ± 1 vs 25 ± 1 mm) and the Tei index was increased (0.31 ± 0.04 vs 0.55 ± 0.11) but resting estimated mean pulmonary artery pressure was lower in Sherpas (24 ± 2 vs 30 ± 2 mmHg, $P < 0.05$) and inversely correlated to VO_2 max in both ethnic groups. Mean TLCO corrected for haemoglobin concentration (TLCOcor), membrane diffusion capacity (Dm) and lung capillary blood volume corrected for haemoglobin

concentration (Vccor) expressed in % of sea level reference were respectively 173%, 134% and 194% in highlanders ($P < 0.001$). The ratios Vc/VA and Dm/VA were higher in Sherpas vs lowlanders ($P < 0.001$). Lung diffusion measures were correlated to $VO_{2m}ax$ in acclimatized lowlanders but not in highlanders. **Conclusion:** Despite an increased pulmonary diffusion capacity in Sherpas compared to acclimatized lowlanders, aerobic exercise capacity at high altitude is similarly decreased in both ethnic groups, and inversely correlated to pulmonary hypertension. This suggests that mild pulmonary hypertension might limit aerobic exercise capacity at high altitude, maybe through a limitation of right ventricular flow output as a cause of decreased convectional oxygen transport to the tissues. **Acknowledgments:** This study was carried out within the framework of the Ev-K2-CNR Project in collaboration with the Nepal Academy of Science and Technology, Nepal and Italy.

34.

EPIDEMIOLOGICAL INVESTIGATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN QINGHAI PROVINCE.

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Introduction: To evaluate the epidemiological characteristic and risk factors of chronic obstructive pulmonary disease (COPD) and to provide some scientific basis for making strategies of prevention and treatment of COPD in the Qinghai Plateau **Methods:** Using modified questionnaire of chronic obstructive pulmonary diseases and chronic cor pulmonale of America, the basic survey of the study was carried out on 23,725 over 15 years people by random disproportional cluster sampling in the Qinghai Plateau. The high-risk group was detected by pulmonary function. Those with FEV1/FVC < 70% in lung function were considered as having COPD. **Results:** The total prevalence of COPD was 0.66, and it was 1.52 in people over 40 years in the Qinghai Plateau. Each layer prevalence was compared with X2 test, the COPD prevalence increased along with age and it was significantly higher in male than that in female (0.83 vs 0.47, $X2 = 12.098$, $P = 0.001$). The COPD prevalence declined along with the altitude ascend, $X2 = 17.98$, $p < 0.01$. The COPD prevalence was highest in agriculture region, then in order were in the half-agriculture and Half-pasture region, city and the pasture region ($X2 = 32.78$, $p < 0.01$). Logistic regression model was conducted and statistical results showed that the independent risk factors for COPD mainly included age, altitude, chronic bronchitis and body mass index. **Conclusion:** The basic data demonstrate that the prevalence of COPD is low in the Qinghai Plateau and related with age, altitude, chronic bronchitis and body mass index.

35.

CHRONIC INTERMITTENT HYPOBARIC HYPOXIA LEADS TO LOWER GLYCEMIA VALUES IN RATS.

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Introduction: It has been suggested that chronic hypobaric hypoxia (CH) exerts a hypoglycemic effect. The aim was to determine the changes of glycemia in rats exposed to Chronic Intermittent Hypobaric Hypoxia (CIHH) compared to CH and Normoxic. Thirty adult male Wistar rats, were randomLy assigned to 3 groups and were studied for 30 days: CIHH (2 days hypoxia/2 days normoxia; $n = 10$), CH (permanent hypoxia;$n = 10$) and normoxic (NX;$n = 10$). **Methods:** The high altitude was simulated in a hypobaric chamber at 428 Torr (4600 m). All rats received the same amount of food (10 g daily) and were in separated cages. The following variables were assessed: Weight, BP, HR, hematocrit and hemoglobin, and glycemia every 4 days after 8 hrs fasting. After sacrifice at the end of the experiment, the right ventricular hypertrophy (RVH) was measured through RV/LV + S ratio. **Results:** The results showed that CH lost weight ($P < 0.05$), with no changes in CIHH and NX. The hematocrit and hemoglobin raised at day 15, remaining elevated until the end of the study in both exposed groups ($P < 0.001$). CH hematocrit was higher than CIHH ($P < 0.001$). RVH in both exposed group ($P < 0.001$), with no differences between them was also found. Glycemia decreased in both exposed group from the beginning and remained at lower values until the end of the study, although from day 14 the CH's glycemia values were lower than CIHH ($P < 0.001$). Also, an inverse correlation between glycemia-Day 30 and Hb-Day30 ($r = -0.61$; $r^2 = 0.37$; $P < 0.001$); and a correlation between glycaemia-Day 30 and RVH ($r = -0.47$; $r^2 = 0.22$; $P < 0.01$) were found. **Conclusion:** In conclusion, under hypobaric hypoxia, there would be lower values of glycemia with a milder decrease in CIHH. This alteration of glucose metabolism in CIHH despite a period at normoxia, deserves further studies to determine the possible role of an over expression of glut-4. **Acknowledgments:** Equipo de Instituto de Estudios de la Salud; Universidad Arturo Prat, Iquique, Chile.

36.

THE ASSOCIATION OF DEPRESSIONS WITH COMPREHENSIVE GERIATRIC FUNCTIONS OF ELDERLY HIGHLANDERS IN ETHIOPIA.

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Introduction: To examine the prevalence of screening-based depression and the association of depression with comprehensive geriatric functions of community-dwelling elderly highlanders in Ethiopia. **Methods:** The study population consisted of 161 community-dwelling elderly subjects 50 years or more living in Dordra in Ethiopia. Depressive symptoms were assessed using a 15-items geriatric depression scale (GDS-15). Subjects were interviewed on health status including activities of daily living (ADL) and quality of life (QOL). **Results:** Using a cut-point of 9/10 for the GDS-15, participants 26(16.1%) appears to have depression. Elderly subjects with depression had significantly lower scores in ADL and in QOL than those without depression. **Conclusion:** Depression is associated with comprehensive geriatric functions in elderly highlanders in Ethiopia. Although the results are same as ones in the elderly living in lowland such as Japan and Southeast Asian countries, further research on cut-off point of GDS with golden standard of major depression in local highland in the African cultural context of Africa must be needed. **Acknowledgments:** This study was

supported by Research Institute of Humanity and Nature: Human Life, Aging, and Disease in High-Altitude Environments: Physio-medical, Ecological and Cultural Adaptation in the Great "Highland Civilizations."

37.
MOUSE DIAPHRAGM ENDURANCE AND MITOCHONDRIAL FUNCTION AFTER 4 WEEKS OF NORMOBARIC HYPOXIA.

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Introduction: Skeletal muscle adaptation to chronic hypoxia includes loss of oxidative capacity. However, previous studies focused on limb muscles and animals are less active while they adapt to lower ambient PO_2. In contrast, the diaphragm increases its activity to cope with greater work of breathing. In other words, chronic hypoxia may force the diaphragm to retain its high endurance and oxidative capacity. Thus, we hypothesized that chronic hypoxia would not affect endurance and mitochondrial function in the mouse diaphragm. **Methods:** Adult male mice were kept in normoxia (Control) or normobaric hypoxia (Hypoxia, $FIO_2 = 10\%$) for 4 weeks. We measured endurance (resistance to fatigue) in vitro and functional and molecular characteristics of mitochondria from diaphragm and limb muscles. Mitochondrial oxygen consumption was measured in isolated mitochondria using a Clark type electrode. Western blot analysis was performed to evaluate the content of different mitochondrial proteins. **Results:** Hypoxia limb muscles fatigued faster (fatigue index was higher in Control, $21.5 \pm 2.6\%$ vs. $13.4 \pm 2.4\%$, $P < 0.05$), but there was no difference between Control and Hypoxia diaphragm muscles. Fiber cross sectional area was unchanged in the Hypoxia limb muscles, but it was 25% smaller in the diaphragm ($P < 0.001$). Mitochondrial respiration rates in Hypoxia limb muscles were lower: state 2 decreased 19%, state 3 31% and state 4 18% compared to Control, $P < 0.05$ for all comparisons. There were similar changes in the Hypoxia diaphragm: state 3 decreased 29% and state 4 17%, $P < 0.05$. However, 4 weeks of hypoxia altered mitochondrial composition differently in the two muscles: limb muscle mitochondria had less content of respiratory complex IV (cytochrome c oxidase), while diaphragm mitochondria had more content of respiratory complexes IV and V (F1/F0 ATP synthase) and less of uncoupling protein 3 (UCP-3). **Conclusion:** These data demonstrate that the diaphragm retains its endurance during chronic hypoxia, apparently due to a combination of shorter diffusion distances and the optimization of the mitochondrial energy production. **Acknowledgments:** This study was supported by an NIH/NIGMS fellowship to JLG (F31 gM846552).

38.
HIGH ALTITUDE PULMONARY EDEMA (HAPE) CLINICAL PRESENTATION.

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Introduction: Objectives: To highlight and recognize HAPE as an entity and pathology peculiar to the region of high mountain. **Methods:** Material and Method: A retrospective study was made of patients hospitalized with confirmed diagnosis of HAPE, in the past 5 years, in hospitals located more than 3500 m above sea level (North-Argentina). **Results:** 26 children were included in a period from 2004 to 2009. The mean age was 7.5 years; its relationship male- female was 1.4/1.0. The month of highest incidence was in March, coinciding with the holiday period for children. Its clinical presentation was characterized by: 99% were positive for epidemiology HAPE reentry, 100% had dyspnea and cyanosis, 10 patients were found in pulse oximetry below 70%, more than 90% had tachycardia and tachypnea, and in 32% was found fever over 38 degrees centigrade. Their complementary methods showed: signs of overload of right ventricle by ECG in 67%; the chest X-ray showed: 42% unilateral infiltrated and bilateral 26%. By Echocardiogram Color Doppler were observed pulmonary pressures exceeding 40 mmHg. In 100% of the patients began treatment with oxygen therapy and 80% required to be transferred (Using the decline as a therapy). In 37% diuretics were used, and steroids only in one case. In 5 patients of HAPE reentry, all of them had shown the same clinic characteristics in previous years. The average placement was 3.9 days with full recovery. **Conclusion:** Conclusions: Reentry epidemiology of HAPE is the basis of diagnosis. Its treatment is oxygen therapy and the descent.

39.
NEURAL CREST-DERIVED STEM CELLS ARE RESPONSIBLE FOR CAROTID BODY GROWTH IN CHRONIC HYPOXIA.

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Introduction: The carotid body (CB) is an arterial chemoreceptor organ responsible for the acute ventilatory response to hypoxemia. Unlike other neuronal crest-derived organs, the adult CB grows several-fold its normal size upon exposure to sustained hypoxia, an adaptive response that participates in ventilatory acclimatization to high altitude. The mechanisms underlying this fundamental homeostatic CB function are poorly known. The CB is formed during fetal life by migration of sympathoadrenal progenitors from the superior cervical ganglion. We hypothesized that a population of these progenitors might remain quiescent in the developed organ, thus they could be re-activated by hypoxia in adult life. **Methods:** Experiments were performed in rats and mice maintained in low O_2 tension. CB morphology was studied by standard histological techniques. Proliferation and differentiation of dispersed rat CB cells were analyzed by immunocytochemical methods. The functional properties of the cells were studied by patch clamp and amperometric techniques. **Results:** In animals exposed to hypoxia, CB growth was paralleled by increase in the number of neuron-like, tyrosine-hydroxylase positive (TH+), glomus cells. Although glomus cells retain some capacity for proliferation, most newly generated TH + cells appeared only after two-three days in hypoxia thus suggesting that they derived from precursors. Indeed, neurosphere assays performed with CB cells demonstrated the appearance of clonal colonies of nestin + progenitors that proliferate for a few days and subsequently differentiate into TH + glomus cells. These in vitro generated glomus cells had normal neurochemical, electrophysiological, and chemoreceptive properties. In vivo and in vitro cell fate mapping assays have suggested that the CB stem/progenitor cells are the glia-like, sustentacular, or type II cells. These are converted to nestin + , highly proliferative, intermediate progenitors, which, in turn, give rise to glomus cells. **Conclusion:** The data show that the CB is a neurogenic niche in the peripheral nervous system that resembles in many aspects the neurogenic centers in the mammalian brain.

40.
PERIPHERAL AND CEREBROVASCULAR RESPONSES IN HIGH ALTITUDE RESIDENTS.

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Methods: We have compared cardiovascular adaptations to high altitude living in three populations of long-term altitude

residents: Andeans (4338 m), Ethiopian highlanders (3622 m) and Ladakhis on the Tibetan plateau (4606 m). Peruvians and Ladakhis showed more erythrocytosis than Ethiopians and some showed evidence of chronic mountain sickness (CMS). All groups had high normalised blood volumes. In Peruvians and Ladakhis with CMS this was mainly due to the large packed cell volumes, whereas in Ethiopians both plasma and packed cell volumes were large. End-tidal carbon dioxide tension was higher in Ethiopians than in Peruvians or Ladakhis (37.1 ± 0.8 versus 27.3 ± 1.2 and 27.0 ± 0.6 mmHg) implying a smaller respiratory drive. Because the high end-tidal CO_2 levels of the Ethiopians was unexpected, in our latest study we determined arterial blood gas values in Ethiopians living in the highlands in both the Bale and the Simien mountains. These results supported the earlier end-tidal data. $PaCO_2$ values were 32.2 ± 0.82 and 33.0 ± 0.75 mmHg respectively. Cardiovascular control was assessed using an orthostatic stress test. This showed effective vasoconstriction in all groups although it was less in the Peruvians with CMS. **Results:** Despite this, orthostatic tolerance was greatest in the Peruvians ($P < 0.01$), most of whom (60%) did not develop presyncope despite a very high orthostatic stress. We determined cerebral blood flow velocity by transcranial Doppler and found it to be significantly less in Peruvians, especially those with CMS, than in Ethiopians. Ethiopians also showed better autoregulation of cerebral blood flow than the other groups and flow was insensitive to changes in oxygen tension but more sensitive to changes in CO_2, both during normoxia and hypoxia. **Conclusion:** We suggest that Ethiopians are best adapted to hypoxia. Their blood volumes were large but they were not excessively polycythaemic and none had CMS. CO_2 levels were little different from those of lowlanders. Cerebral autoregulation was good and the large vasodilatation to CO_2 would favor better cerebral perfusion and oxygenation.

41.

MECHANISMS AND LIMITS OF HYPOXEMIA TOLERANCE IN DIVING BIRDS AND MAMMALS.

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Introduction: Bio-logging instruments capable of continuously measuring PO_2 in the blood while diving have recently revealed exceptional hypoxemic tolerance and highly efficient O_2 utilization in the consummate avian and pinniped divers, the emperor penguin and elephant seal. **Methods:** Minimum PaO_2 values as low as 12-23 mmHg have been documented in diving elephant seals, corresponding to routine SaO_2 of 8-26%, the lowest values ever measured in a freely diving seal. This is well below limits of other animals, and is nearly equivalent to "critical PaO_2" (10 mmHg) of seals in forced submersions, defined by EEG marking the threshold of cerebral dysfunction. Characterization of the O_2-hemoglobin dissociation curves of these species revealed biochemical adaptations relevant to dive capacity. **Results:** Emperor penguin hemoglobin has significantly higher affinity for O_2 as compared to other birds, allowing more complete utilization of respiratory O_2 stores and increased blood O_2 content when PO_2 is low. Application of the dissociation curve to PO_2 profiles also indicates differing blood O2 store management strategies. In emperor penguins, arterial SO_2 remains near 100% for much of the dive, preserving high O_2 content in the arterial system for critical organs like the brain. Arterial SO_2 does not decrease significantly until final ascent, consistent with the decline in ambient pressure and decrease in air sac and arterial PO_2. These profiles demonstrate the significance of the respiratory O_2 store and high affinity hemoglobin of the emperor penguin. In contrast, although there is a transient rise and peak near 100% arterial SO_2 in the initial dive phase of elephant seals, these values decreased rapidly after this point. Venous SO_2 profiles demonstrate highly efficient and near complete utilization of the venous blood O_2 store during dives of both species. **Conclusion:** These findings reflect differences in the magnitude of the respiratory O_2 store and maintenance of gas exchange during diving between this bird and mammal, and depict attributes that undoubtedly contribute to their extraordinary dives. **Acknowledgments:** Paul J. Ponganis, M.D., Ph.D.
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42.

THE EFFECT OF LIVING IN THE HIGH PLATEAU ON CARDIOVASCULAR SYSTEM.

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Introduction: Place: "Dr. Pablo Soria" Hospital, San Salvador de Jujuy, Argentina. Town of La Quiaca, Province of Jujuy, Argentina. Purpose: To determine heart and lung hemodynamic changes seen in 12 years old children, in the town of La Quiaca, placed at 3500 m (about 10,000 feet) above sea level, as compared to normal standards. **Methods:** Method and Materials: A transversal descriptive study was performed. A school in La Quiaca was selected in which one hundred children, 12 years old, were chosen at random. The inclusion criteria were: Be a resident in that town for at least one year, be healthy at the moment of the research, to be 12 years old. The variables analyzed were: sex, weight, height, body mass index, pulse oximetry, systemic arterial tension, electrocardiogram, color Doppler echocardiogram. By means of the operationalization of variables it was attempted to determine some values to measure degrees of hypoxia and lung pressure. **Results:** Results: The study included 100 children of twelve years old; 53 boys and 47 girls. Their average weight was 30.34 kg. Their average height was 134 cm tall. Their average index of body mass was 18.9. Their average arterial tension was 96/63 mmHg. Among these values there were no important changes as compared to normal values. Pulse oximetry showed a saturation of 89,66%. The result of the electrocardiogram is the following: Only 5% was normal; 7% showed left pattern; and 87% showed an electric axis deviated to the right, being the mean of these children of+ 108°. By means of color Doppler echocardiography it was observed the following: 93% showed tricuspid insufficiency that helped to determine the pressure in the VD that was an average of 22 mmHg. The changes detected in the pulse oximetry, the electrocardiogram, and the VD pressure measured by color Doppler echocardiography, were statistically meaningful as compared to the normal standards. **Conclusion:** Children who live in the high plateau (3,500 m above sea level) developed hemodynamic changes in order to adapt to that geographic condition. This is influenced by low oxygen pressure at that level, causing an answer of adaptation that modifies the values of normal control. Therefore, they develop some degree of "lung hypertension". **Acknowledgments:** Hypothesis: At 3500 m above sea level there is a low pressure of oxygen (hypoxia). This is the case of the Puna high plateau, where the town of La Quiaca is located (Province of Jujuy, Argentina). This geographic condition generates important heart and lung hemodynamic changes as compared to children who live at sea level with normal standard measurements.

43.

INSULIN-STIMULATED GLUCOSE UPTAKE IN MOUSE SKELETAL MUSCLE IS ENHANCED BY CHRONIC HYPOXIA.

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Introduction: People living at high altitude appear to have lower blood glucose levels and decreased incidence of diabetes. Faster glucose uptake and increased insulin sensitivity are likely explanations for these findings: skeletal muscle is the largest glucose sink in the body and its adaptation to the hypoxia of altitude may influence glucose uptake and insulin sensitivity. This study tested the hypothesis that chronic normobaric hypoxia increases insulin-induced glucose uptake in skeletal muscle. **Methods:** Adult male C57BL/6J mice were kept in normoxia ($FIO_2 = 21\%$, Control) or normobaric hypoxia ($FIO_2 = 10\%$, Hypoxia) for 4 weeks. Then, we measured blood glucose and insulin levels. Glucose uptake was measured in vitro by incubating the muscles with and without insulin and determining the incorporation of 2D-3 hGlucose. Western blot analysis was used to evaluate indices of insulin signaling. **Results:** Blood glucose and insulin concentrations were lower in the Hypoxia group (glucose: Control, 14.3 ± 0.65 vs. Hypoxia, 9.9 ± 0.83 mM, $P < 0.001$; and insulin levels: 1.2 ± 0.2 vs. 0.7 ± 0.1 ng/mL, control and Hypoxia, $P < 0.05$). There was no significant difference in basal glucose uptake in vitro in soleus muscle (1.59 ± 0.24 vs. 1.71 ± 0.15 μmol/g/h; Control and Hypoxia respectively). However, insulin-stimulated glucose uptake was 30% higher in the soleus after 4 weeks of hypoxia (6.24 ± 0.23 μmol/g/h) compared to Control (4.87 ± 0.37 μmol/g/h $P < 0.02$). Muscle glycogen content was not significantly different between the two groups, although there was a tendency for lower levels in Hypoxia muscles. While the content of glucose transporters 4 and 1 (GLUT4 and GLUT1), phosphoinositide 3-kinase (PI3K), glycogen synthase kinase 3 (GSK3), and protein kinase B/AKT were not affected by chronic hypoxia, AKT phosphorylation following insulin stimulation in soleus muscle was significantly higher (27% greater in Hypoxia compared to Control, $P < 0.05$). GSK3 phosphorylation did not change after 4 weeks of hypoxia. **Conclusion:** These results demonstrate that the adaptation of skeletal muscles to chronic hypoxia includes increased insulin-stimulated glucose uptake. The molecular mechanisms mediating this environmental adaptation may be useful for the treatment of insulin resistant states. **Acknowledgments:** This study was supported by an NIH/NIGMS fellowship to JG (F31 gM846552).

44.

MATERNAL HEMOGLOBIN LEVEL AND FETAL OUTCOME AT LOW AND HIGH ALTITUDE.

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Introduction: Both, low (<7 g/dL) and high (>14.5 g/dL) maternal hemoglobin (Hb) levels have been related to poor fetal outcome (stillbirths, preterm deliveries and/or small for gestational age). At high altitude, the Hb cutoff to define anemia is increased as altitude increases. There is no evidence demonstrating that this correction is needed. The objective of the present study was to determine the association of maternal hemoglobin level and fetal outcome at low and at high altitudes. The study is based in a retrospective multicenter analysis of 293,158 pregnancies occurred in 33 Peruvian Public hospitals located in altitudes from sea level to 4340 m during the period between 2002 and 2010. In analyses of all women at both LA and HA, those with Hb < 9 g/dL had odds ratios (ORs) and 95% confidence intervals (CI) of 3.26 (CI:2.8-3.8), 1.87 (CI:1.71-2.03), and 1.16 (CI:1.06-1.27) for stillbirths, pre-term, and small for gestational age (SGA) births respectively, compared to women with 11-12.9 g/dL of Hb, after adjustment for confounders. From 0-1999 m optimal Hb values for low risk of stillbirths, pre-term deliveries and SGA were 9-12.9 g/dL, > 9 g/dL and 9-12.9 g/dL respectively. From 2000-2999 m, optimal Hb values were 11-14.4 g/dL fpr stillbirth and pre-terms and 9-12.9 g/dL for SGA. From altitudes between 3000 and 3999 m, 11-15.5 g/dL for stillbirths, > 11 g/dL for preterm and 9-12.9 g/dL for SGA respectively, whereas at 4000-4500 m, low risks for stillbirths were observed at Hb values > 9 g/dL; for preterm deliveries at > 9 g/dL and 9-14.4 g/dL for SGA. Data suggest that no correction of the definition of anemia is necessary for women at HA. Women living at altitude increases risks of stillbirths, pre-terms and SGA independent of the Hb effect. The risk for stillbirths increases significantly since 2000 m, for pre-terms since 3000 m and SGA from 3000 m. Conclusions: Both, high and low maternal hemoglobin levels were related to poor pregnancy outcome, with similar effect of low hemoglobin in both LA and HA. Our data suggest that maternal hemoglobin above 11 g/dL but below 13 g/dL is the area of minimal risk of poor adverse perinatal outcomes. Living at HA over 3000 m associated with Hb > 13 g/dL increases significantly the risk for SGA. The, it is important the monitoring of women with iron supplementation when they are living over 3000 m.

45.

ENERGY EXPENDITURE, SLEEP EFFICIENCY AND PHYSICAL ACTIVITY LEVEL DURING THE ASCENT TO MOUNT ACONCAGUA.

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Introduction: Accurate reports of the physical activity level (PAL) attained and calories burned by climbers that reached the summit of a 7000-meter mountain are sparse. PAL can now be accurately measured with activity monitors and is calculated as follows: Total energy expenditure (TEE) divided by the resting metabolic rate (RMR). Advanced monitors offer to measure sleep time and enable to calculate sleep efficiency, an important factor in altitude physiology. The purpose of this study was to assess the PAL and the total amount of calories spent by successful climbers of Mount Aconcagua. Secondarily, we assessed the progress of RMR adjusted to TEE and sleep efficiency (SE) during the ascent. **Methods:** TEE, RMR, PAL and SE were measured in 12 experienced male climbers (30.1 + /- 7.3 years) with a Sense wear Armband over the time from 2700 (base camp) to 5300 m (last camp before the summit). **Results:** The cumulative TEE during the 6 day-period of the expedition TEE was 315200 + /-11510 Kcal among the 12 subjects (and 58 130 adjusting for the summit day). Daily measures were as follows: (mean + /-SD) TEE was 4378 + /- 716 Kcal/day/subject (range 2900-7916), RMR was 1903 + /- 184 Kcal/day (range 1640-2289), PAL 2.3 + /- 0.3 (range 1.4-3.9) and SE 75.9 + /- 5.7% (range 40-94%). The median of steps during ascent days were 31573 compared to 11230 during acclimatization days. Mean RMR increased (1867 to 1932) and mean sleep efficiency did not change over the time. PAL of 3.9 was the maximum activity level detected in the ascent to Mt. Aconcagua (>2 indicates high daily physical activity). **Conclusion:** These results provide novel data on the energy cost, sleep efficiency and daily level of activity during an expedition to Mt. Aconcagua and could be valuable to understand the physiologic response to altitude, design physical training before the ascent and calculate food requirements of mountains expeditions.

46.

AROMATASE ACTIVITY IS REDUCED IN MEN AT HIGH ALTITUDES.

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Introduction: It has been suggested that high levels of testosterone may lead to excessive erythrocytosis (EE) (hemoglobin > 21 g/dL). High testosterone at high altitudes (HA) could be due to low aromatase activity. We assessed whether the inhibition of aromatization of testosterone using letrozole is higher in men at HA than at sea level (SL). **Methods:** We conducted a comparative study in Lima (150 m) and Cerro de Pasco (4340 m). There were 30 Sea Level native and resident adult men and 65 from HA between ages of 30 and 61 years. We suppressed aromatase activity using letrozole 5.0 mg once daily for 5 consecutive days and measured serum LH, FSH, prolactin, androstenedione, DHEAS, testosterone, and estradiol levels. Hemoglobin (g/dL) and erythropoietin levels were also measured. **Results:** Men with EE had lower basal aromatase activity than those without EE at HA ($P < 0.05$). At SL, letrozole reduced aromatase activity to 42.82% and, at HA to 34.45% ($P < 0.05$). T/LH ratio was reduced to 73.59% at SL and 49.2% at HA ($P < 0.05$). T/A ratio increased $136.35 \pm 9.81\%$ at HA, whereas at SL it was unchanged ($P < 0.05$). A negative relationship (coef -11.6; CI 95% $-20.6 - 2.67$) was observed between serum basal estradiol and increased serum testosterone post letrozole. **Conclusion:** Letrozole produced a remarkable increase of gonadotropin and serum testosterone levels as consequence of aromatase inhibition. This was associated to high 17 beta-HSD activity and low Leydig cell function. Lower aromatase activity was observed in men at HA than at SL. **Acknowledgments:** This Study was supported by a Grant from the Fogarty Program of The National Institutes of Health of the United States (NIH Research Grant # 5-D43TW005746-04 funded by the Fogarty International Center, National Institutes on Environmental Health Services, National Institute for Occupational Safety and Health, and the Agency for Toxic Substances and Disease Registry).

47.

CONSEQUENCES OF EPO-INDUCED EXCESSIVE ERYTHROCYTOSIS.

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Introduction: Application of erythropoietin (Epo) increases hematocrit (Htc) and, consequently, arterial O_2 content thereby increasing exercise performance. However, since elevated blood viscosity associated with increasing Htc levels may limit cardiac performance, it was suggested that the highest attainable Htc may not necessarily be associated with the highest attainable exercise capacity. To test the proposed hypothesis that an optimal Htc in acute and chronic Epo-treated mice exists, i.e. the Htc that facilitates the greatest O_2 flux during maximal exercise, Htc levels of wild type (wt) mice were acutely elevated by administering novel erythropoiesis stimulating protein (NESP; wtNESP). Furthermore, in the transgenic mouse line tg6 that reaches Htc levels of up to 0.9 due to constitutive overexpression of human Epo, the Htc was gradually reduced by application of the hemolysis-inducing compound phenylhydrazine (PHZ; tg6PHZ). Maximal cardiovascular performance was measured using telemetry in all exercising mice. Highest exercise intensities were reached at Htc values of 0.58 and 0.57 for wtNESP, and 0.68 and 0.66 for tg6PHZ, respectively. Blood viscosity correlated with O_2 max. Apart from enhancing erythropoiesis, non-erythroid functions of Epo enhancing performance such as improved ventilation or cognitive functions at hypoxia will be presented.

48.

DEVELOPMENTAL PROGRAMMING OF CARDIOVASCULAR DISEASE BY PRENATAL HYPOXIA: LESSONS FROM HIGH ALTITUDE.

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Introduction: In addition to traditional risks, such as smoking and obesity, the quality of our prenatal development plays a role in determining the risk of suffering disease in later life. In turn, the quality of the intrauterine environment is largely determined by the available nutrient and oxygen supply to the growing young. As such, the association between poor conditions in utero and increased risk of disease in adulthood has exploded a number of studies investigating the effects of changes in materno-fetal nutrition on programming of disease. In contrast to this international research effort, the contribution of fetal hypoxia, of the type that can occur during pre-eclampsia, placental insufficiency or pregnancy at high altitude, to developmental programming has been comparatively ignored. Further, the mechanisms underlying the early programming of disease in complicated pregnancy remain unknown, preventing the identification of potential therapeutic targets for clinical intervention. **Methods:** Here, we put forward the hypothesis that oxidative stress in the fetus underlies the molecular basis via which prenatal hypoxia alters fetal growth and contributes to the developmental programming of cardiovascular disease. **Results:** Observations in human pregnancy at high altitude and experiments in chick and rat embryos show that developmental hypoxia independent of changes in maternal nutrition not only alters the trajectory of fetal growth, but it also induces changes in the cardiovascular and metabolic systems, which are normally associated with disease states in later life. Treatment with antioxidants of animal pregnancies complicated with reduced oxygen delivery to the fetus prevents the alterations in fetal growth and the fetal cardiovascular and metabolic remodelling. **Conclusion:** Combined, the human and experimental data support the hypothesis tested and the work offers both insight into mechanisms and possible therapeutic targets for clinical intervention against the early origin of disease in hypoxic pregnancy. **Acknowledgments:** The Bristish Heart Foundation, The BBSRC, The Royal Society.

49.

CONFOCAL MICROSCOPY AS NEW TOOL FOR THE STUDY OF PULMONARY ARTERY REMODELLING AT A CELLULAR LEVEL IN RATS EXPOSED TO CHRONIC HYPOBARIC HYPOXIA.

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Introduction: We have previously described the application of confocal microscopy and image analysis to assess vascular remodelling in systemic resistance arteries in several pathological conditions. This methodology allows quantification of: Cellular density and distribution in the different layers of the vascular wall; infrequent events (i.e. apoptosis); and Biomolecules (i.e. NO, ROS) (Arribas et al., J. Physiol.58:5-9,

2007). Our aim was to introduce this technique as a new tool to study vascular remodelling in high altitude pulmonary hypertension. **Methods:** This previous methodology was adapted to study at a cellular level, possible changes in 3th order pulmonary arteries (PA) from rats exposed to chronic hypobaric hypoxia (CH; 4600 m; $n = 8$) compared to normoxic group (NX;$n = 8$). Pulmonary hypertension in CH rats was demonstrated by the elevated right ventricular hypertrophy. The arteries were carefully removed and stained with the nuclear dye DAPI (5ug/ul). Arterial rings and longitudinal sections were mounted on a slide with a small well to avoid arterial wall compression. Serial optical sections were obtained from the adventitial and medial layers with a confocal microscope (EX 405, EM 410-475) and the images quantified with Metamorph software. **Results:** Compared to NX, CH exhibited an increase in adventitial cell number ($P < 0.01$), without layer enlargement; 2) increased media thickness ($P < 0.05$) with no changes in cell number. No statistical differences were found in PA lumen size between groups. **Conclusion:** In conclusion, confocal microscopy enables to quantify cell number and thickness of the adventitia and media in pulmonary arteries, revealing adventitial hiper-cellularity and a medial thickening in CH. The possible implication of extracellular matrix synthesis, proliferation, migration or inflammatory responses induced by hypobaric hypoxia deserves further investigations to find the underlying mechanism involved in these structural changes. **Acknowledgments:** By grants from AECID A-023476-09, CEAL y UNAP.

50.

ERYTHROPOIETIN (EPO) IN HUMAN MILK: POTENTIAL ENTERAL FACTOR IN HIGH ALTITUDE HYPOXIA.

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Introduction: Erythropoietin (Epo) is a normal constituent of human milk. At sea level, it was found that mean milk-borne Epo concentrations are within the normal range for plasma Epo concentrations and rise with postpartum days. Moreover, it has been shown accelerated erythropoiesis or elevated Epo levels in neonatal (sucking) animals after maternal phlebotomy or maternal hypoxia exposure. **Methods:** In the present work we tested the hypothesis that mothers permanently exposed to high altitude hypoxia (3600 m at La Paz-Bolivia), have increased Epo concentration in milk than the observed at sea level. To address this question milk samples were collected daily from the delivery day until the postpartum day 20th. The aqueous fraction of the milk was used to analyze the total protein (by the bicinchoninic acid protein assay: BCA; Pierce, Rockford, IL), and the Epo (via double antibody radio immuno assay: RIA) concentrations. **Results:** Our preliminary results show that high altitude secreted milk contains significant higher concentration of Epo that the milk produced by mothers al sea level. **Conclusion:** Keeping in mind that milk compounds survive digestion in the neonatal gastrointestinal tract secondary to lower photolytic activity and increased protein permeability, these results suggest that maternal Epo strongly contributes to the development of physiological and pharmacologic roles of breast-feed neonates upon hypoxia. Furthermore, considering that Epo is a safe drug, our data might open new doors for the therapeutically use of Epo in paediatrics and neonatal disorders.

51.

ESTIMATED VALUES OF NOCTURNAL OXIMETRY AND SLEEP QUALITY IN A MINING TOWN THAT SLEEPS AT 2600 M (PRELIMINARY STUDY).

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Introduction: In Chile, the miners working at high alttitude are working under conditions of chronic and intermittent exposure to hypoxia, which mostly requires to stay overnight at camps. Sleeping at altitude produces arterial desaturation, which impact on pulmonary arterial pressure, sleep quality, daytime sleepiness, accidents and low performance. The aim of this study is to determine the oxigenation level and relate quality night's sleep and sleepiness in miners who sleep at 2,600 m. **Methods:** 38 men were evaluated BMI, neck circumference (CC), nocturnal oximetry (SaO_2 and HR) and sleep quality surveys and Epworth Sleepiness Spiegel. **Results:** Our results show BMI $= 27.7 \pm 3.2$, CC $= 40.8 \pm 2.1$, $SaO_2 = 91$ FC 61.9 ± 1.7 and ± 1.7. Regarding the perception of sleep Spiegel $= 12.6 \pm 3.5$ represents a good quality EPTWORTH regulate and 4.5 ± 3.4, indicates that represent normal values. **Conclusion:** In estimating the 95% for SaO_2 can recognize a lower limit value of 88%. Values above 88% could be considered normal for a mining town that sleeps at 2600 m. **Acknowledgments:** Supported by INNOVA CORFO 07CN13ISM-152.

52.

CLINICAL EVALUATION OF A NEW NON-INVASIVE SENSOR FOR CONTINUOUS CORE BODY TEMPERATURE MEASUREMENT IN HUMANS.

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Introduction: Accurate measurement of the core body temperature (cbt) is fundamental to the study of human temperature regulation. Recently, we developed a non-invasive cbt heat flux sensor (Double Sensor) (1,2). Two investigations are presented showing the applicability of this sensor under physical strain, extreme environmental conditions and in a clinical setting. **Methods:** The first study, evaluated the sensor in a laboratory study in 20 male subjects (39.5 ± 10.2 years, height 1.80 ± 0.06 m, 83.8 ± 11.0 kg). Thermal (rectal, nasopharyngeal, skin, Double Sensor temperatures) and cardiovascular data were collected continuously before, during and after different experimental set-ups (25-55% maximal intensity work load at 10, 25, and 40°C environmental temperatures). In the second study, we determined the cbt of 24 patients during cardiac operations and compared it to the vesical or rectal temperature. The patients were cooled to 14-16°C (deep hypothermia). After surgery the patients were heated up to normal body core temperature. Statistical methods: general linear model, paired t-Test (significant level: $P < 0.05$.), Bland-Altman diagrams (3), and Li and Chow(4), and Lin's(5) Concordance Correlation Coefficients (CCC). **Results:** The first study revealed that i) the device under test differed between –0.16 to 0.1°C from the average of the rectal temperature and the Double Sensor, ii) showed with increasing ambient temperatures increasing Li and Chow CCC (10°C: 0.49; 25°C: 0.69; 40°C: 0.75), and iii) exhibited a faster temperature decrease at all resting periods at all ambient conditions as compared to rectal temperature ($P < 0.01$). In the second study the sensor showed great accuracy to vesical and rectal temperature (Lin's CCC = 95%).

Conclusion: The device under test seems to be a reliable method of assessing cbt during clinical settings as well as in emergency care in the field, e.g. avalanche victims.

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53.

THE CORRELATION AMONG HIGH ALTITUDE POLYCYTHEMIA AND SEX HORMONES, IMMUNE, BLOOD CELLS OF ROAD MAINTENANCE WORKERS AT HIGH ALTITUDE.

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Introduction: Investigation prevalence of high altitude polycythemia (Hb $\geq$ 210 g/L) of road maintenance workers during chronic high altitude acclimatization. Revealing their characteristic changes and physiological and pathological association of sex hormones, immune, blood cells. **Methods:** 189 road maintenance workers at the elevation of 2800–2900 m, 3600–3740 m, m4250–4300 m were sampled. IgG, IgM, IgA with Immunization rate nephelometry, CD3, CD4, CD8 with Stream style cell instrument (Epics XL), 21 param in peripheral blood with the full-automatic blood cell analyses an instrument, sex hormone (FSH, LH, E2, P, PRL, T) with Bayer AG ACS180SE fully automated chemiluminescence instrument and supporting reagents were measured. **Results:** The prevalence of Hb $\geq$ 210 g/L group are 4.50%, 17.20% and 44.12% in three altitude level compared with Hb $<$ 210g/L group, they have characteristic changes, it is lower in LH and PLT, it is higher in E2 and Hct; also accompanied by a certain relation FSH, CD3, CD4, IgM, WBC, RBC raised and CD4 \ CD8 ratio decreased.Their results all were to adapt group and control, partial correlation, linear regression analysis. **Conclusion:** Conclusion In the high-altitude hypoxia environment, road maintenance workers who does labor intensity have higher prevalence of altitude polycythemia, over-proliferation of Hb has physiological and pathological association with these param.

54.

STATINS AFFECT THE FETAL CARDIOVASCULAR DEFENCE TO HYPOXIA BY INCREASING NITRIC OXIDE (NO) BIOAVAILABILITY.

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Introduction: Statins inhibit the enzyme HMG-CoA reductase, reducing cholesterol and LDLs, however their beneficial effects extend beyond alterations on lipid profile alone (McGown and Brookes, Br J Anaesth. 98:163, 2007). Further, few studies have determined the effects of statins on fetal cardiovascular function. Acute hypoxia in utero is a common challenge to the developing fetus, resulting in peripheral vasoconstriction to aid redistribution to essential central circulations (Cohn et al. AJOG 120:817, 1974). Here, we tested the hypothesis that fetal exposure to a statin alters the fetal cardiovascular defence response to acute hypoxia by increasing NO bioavailability in late gestation fetal sheep. **Methods:** Under general anaesthesia, 15 sheep at 0.8 gestation were instrumented with maternal and fetal catheters and a fetal femoral Transonic flowprobe. Ewes were subjected to 1 h normoxia, 05 h hypoxia (mat FiO_2 $\sim$0.06) and 1 h recovery 24 h before and after treatment with pravastatin (10 mg.kg-1 IV fetal, n = 8). In addition, a second group was subjected to the hypoxic challenge 24 h following pravastatin treatment in the presence of NO clamp (blockade of NO de novo synthesis, n = 7). **Results:** Pravastatin alone had no effect on basal fetal heart rate or blood pressure. During hypoxia, a similar fall in fetal PaO_2 occurred in all fetuses ($\sim$50%). Fetal treatment with pravastatin depressed the femoral vasoconstrictor response to acute hypoxia (5.1 + 1.2 mmHg.(mL/min)-1 pre statin vs 3.5 + 0.5 mmHg.(mL/min)-1 post statin, $P < 0.05$). This effect was reverted with the NO clamp treatment (7.1 + 1.3 mmHg.(mL/min)-1) and was independent of any changes in fetal arterial blood pressure or heart rate. **Conclusion:** Statins depress the fetal peripheral vasoconstrictor response to acute hypoxia by increasing NO bioavailability. **Acknowledgments:** Funded by The British Heart Foundation.

55.

SEXUAL FUNCTION IN HIGH-ALTITUDE RESIDENTS.

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Introduction: Chronic hypoxia is responsible for disorders of many physiologic functions and pathophysiologic changes, which is characterized by the decline in vigor, diminished physical capabilities and reducted quality of life. Sexual function is an important indicator of the quality of life. In the present study, the sexual function was surveyed and the serum levels of sex hormones were measured for evaluating the quality of life of Tibetans natives and Chinese Hans immigrants living in the high altitude. **Methods:** (1) Using questionnaire survey, the erectile function, coital frequency and duration of sexual intercourse for men and the coital frequency and the scores of the Brief Index of Sexual Function (BISF) for women were surveyed. The objects surveyed were 1,444 Chinese Hans (839 males and 605 females) and 1075 Tibetan natives (635 males and 440 females) of Dawu (3680 m), 1465 Chinese Hans (755 males and 710 females) of Xining (2260 m) and 1298 Chinese Hans (938 males and 360 females) of Xian (400 m). (2) The serum levels of testosterone and estradiol were determined by the chemiluminescence immunoassay in parts of objects surveyed **Results:** (1) The scores of BISF in Dawu group were significantly lower than those in the Xian group, but there was no difference between Xining group and Dawu group. The scores of BISF in the Tibetans were higher than that of the Han Chinese. (2) The coital frequency of males was lower in Dawu group than that in Xian group, and it was gradually fallen as the altitude increasing. The coital frequency of males was higher in Tibetans than that in Han Chinese. The coital frequency of females was lower in Dawu group than that in Xian and Xining groups, but no difference between the Xining and Xian groups. (3) The duration of sexual intercourse for men was no any difference among objects of

three altitudes or between Tibetans and Chinese Hans. (4) For male objects, the serum level of testosterone was higher in Xian group than those in Dawu group and was higher in Tibetans than that in Chinese Hans. (5) The serum levels of estradiol in female objects were higher in Xian and Xining groups than that in Dawu group and was higher in Tibetans than that in Chinese Hans. **Conclusion:** The sexual function is impaired for Chinese Hans immigrated to the high altitude, especially for those in 40-70 years old. The sexual function of Tibetans of 40-70 years old seems superior to Chinese Hans immigrants of same age bracket in high altitude, which may be profited from their well adaptability to high altitude.

56.

THALIDOMIDE REVERSED HYPOXIA-INDUCED APOPTOSIS OF RAT BONE MARROW CELLS.

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Introduction: High altitude polycythemia is characterized by an increase of the total erythrocytes in number and volume which is secondary to excessive erythrocytic proliferation in the bone marrow. However, little is known about cellular apoptosis during the pathogenesis of high altitude polycythemia. The present study is aimed to evaluate the bone marrow cells apoptosis of rat when its body is exposed to the hypoxia. **Methods:** Hypoxia-induced apoptosis in rat bone marrow was determined using terminal deoxynucleotidyl transferase-mediated dUTP nick end-labeling (TUNEL) method and assessed by apoptotic index. **Results:** The results showed that the apoptotic index was significantly decreased when the rats were exposed to hypoxia for 24 hours (hypoxia group 1.34 ± 0.65 vs. control 2.73 ± 0.51, $P < 0.001$). Interestingly, thalidomide, an angiogenesis inhibitor, increased the bone marrow cellular apoptosis in rats which were exposed to hypoxia for 21 days (hypoxia group 2.65 ± 0.98 vs. thalidomide group 5.63 ± 3.47, $P < 0.05$). **Conclusion:** In conclusion, our data suggest that erythrocytic proliferation is accompanied by cellular apoptosis in rat bone marrow in response to hypoxia during the pathogenesis of high altitude polycythemia. Thalidomide, an angiogenesis inhibitor, can reverse the reduced apoptosis in the bone marrow. We presume that thalidomide might become a candidate therapeutic agent for high altitude polycythemia in the future.

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THE DIFFERENT ADAPTATION TO HIGH ALTITUDES BETWEEN MEN AND WOMEN IN LADAKH.

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Introduction: Adaptation to high-altitude is known to differ according to area and race; however, gender differences in this adaptive ability among Asians have not yet been elucidated. To clarify the gender differences in the adaptation to high altitudes, we evaluated the cardiac and pulmonary function of men and women living in Ladakh, India (altitude; 3000–3700 m). **Methods:** We recruited 242 subjects (84 men, age $= 56.3 \pm 13.7$ years; 158 women, 53.9 ± 12.6 years) from Ladakh, India, in July 2009. We assessed the cardiac function by using the results of echocardiography, respiratory function tests, oxygen saturation in pulse oximetry (SpO_2), examination of pulse rate, results of laboratory tests, and chronic mountain sickness (CMS) score. **Results:** The ejection fraction (EF) in women was higher than that in men (women vs. men $= 66.2 \pm 9.2$ vs. $61.8 \pm 9.1\%$; $p < 0.01$). The hemoglobin (Hb) level in men was significantly higher than that in women (men vs. women $= 16.2 \pm 2.3$ vs. 13.7 ± 2.3 g/dL; $p < 0.01$). The EF was negatively correlated with Hb only in the case of women ($r^2 = 0.03$, $p < 0.01$). Respiratory function, including ratio of forced expiratory volume in 1 second to forced vital capacity (FEV1%) and percentage vital capacity (%VC), were not significantly different (82.2 ± 8.5 vs. $82.4 \pm 10.8\%$, 97.6 ± 20.5 vs. $95.1 \pm 19.0\%$, n.s.). There was no significant gender differences in the pulmonary artery pressure (men vs. women $= 16.5 \pm 15.1$ vs. 18.9 ± 13.7 mmHg; $p = 0.22$). There were no significant differences between SpO_2 ($90.7 \pm 4.7\%$ vs. $89.7 \pm 4.8\%$), the pulse rate (88 ± 17 beats/min vs. 90 ± 15 beats/min). Only 2 men showed severe polycythemia. None of the subjects satisfied the criteria for the diagnosis of CMS. **Conclusion:** The results of the study show that cardiac contraction in women was greater than that in men and had an inverse correlation with Hb in the case of women. These findings may represent differences between Indian men and women in their ability to adapt to high altitudes. **Acknowledgments:** This study was mainly supported by Grant-in-Aid of Research Institute for Humanity and Nature (3-4 FR): Human Life, Aging, and Disease in High-Altitude Environments: Physio-medical, Ecological and Cultural Adaptation in "Highland Civilizations." (Leader: Professor Kiyohito Okumiya).

58.

NUTRITIONAL AND SANITARY VALUATION OF SCHOOL CHILDREN IN THE HIGH-ANDEAN COMMUNITY OF OCUVIRI.

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Introduction: In the district of Ocuviri, county of Lampa (Puno, Peru), located to 4266 m, in the 2007 there was a faulty nutritional and sanitary profile, characterized by the infantile malnutrition, lacks of personnel of appropriate health, technology absence for the medical diagnosis and faulty environmental reparation. For all this, the ARASI mine (ARA) through the medical staff of the Clinical Bus was carried out an investigation to determine the initial nutritional and sanitarium state of the childhood of the I.E.C. N° 200 and P.E.I N° 70402 (capital of Ocuviri), among the months of July to September of the 2008. **Methods:** We examine for it to 192 scholars with ages among 4 to 14 years, as for weight, height, Body Mass Index (BMI) and school performance; 158 scholars regarding brachial perimeter (BP) and thoracic perimeter (TP); 129 students for the parasitological exam, 134 children for the hemoglobin analysis and 107 children for the exam thorax radiographic. It was also made the energy valuation and calculation of the necessity both macro and micronutrients for each one of the children in study. **Results:** The results show that it doesn't exist significant differences among the weight, the height, the BMI, the BP and the TP regarding the sex, situation that contrasts with the anthropometric indicators established by the World Health Organization.The weight and height of the children are in a critical situation below 50 % of normality. Comparing our measurements with those of other Andean high communities such as Marquiri (Cusco) and

Nuñoa (Puno), we observe certain superiority, being inferior to the measures of children of Tintaya (Cusco), who are also under the environment of another Mining one as it is Tintaya for 48 years (1960). Also, it has been in the children, an excellent one but it is that good correlation among the weight, the height, the BMI, the BP and TP, regarding the age and sex, allowing us to calculate the weight, height, BMI, BP and TP that will have a child of this area at this time with the predominant environmental and genetic conditions. We did not find a single undernourished children, with below weight (35%) and stature lowers (76%), but also children with an BMI of obesity (35%), besides 80% of scholars have parasites, being more prevalent in men than in women (83 vs 77%), especially between the 12 and 14 years, being Giardia lamblia, as the most frequent parasite, influencing somehow in that the evaluated scholars have a low stature (38%) and a low school performance (24%).There was also 88% of scholars with some type of iron deficiency anemia, being more frequent in men than in women, and it would be due to a iron deficiency contribution in their feeding, nevertheless that has also been that 83% of anemic presented parasitism. This condition bore to that 49% of them presents a low school performance. The exams thorax radiographics discarded the tuberculosis presence or lung hydatidosis, being only observed increase of the lung scheme (48%) due to acute respiratory affections. It is important to mention that the School Dining Room ARA, comes contributing with the 70% of the requirement daily energy. **Conclusion:** The children present a low weight (35%), a short height (76%), enteroparasitism (80%), anemia (88%) and predisposition to the breathing infections (48%). It is expected that the school dining room and the social work financed by the mining one revert this situation. The ARA Clinical Bus at the present time has begun the treatment of those scholars with diagnostic of parasitosis, with the competition of professors and family parents for the supervision of its execution. **Acknowledgments:** We are grateful the support to the present research to the Non-governmental organization Center of Communal Development "Andean High"; in the person of the Econ. Daigoro Chagua León and Ing. Guido Carrasco Quintana; and to ARASI S.A.C. Mining Company, represented by the Eng. Guido del Castillo, as well as to the Dr. José Marticorena Díaz of the Mining Medical Center for the offered advice.

59.

HEMOGLOBIN LEVELS IN HEMODIALYSIS PATIENTS IN TWO DIFFERENT ALTITUDES IN PERU.

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Introduction: Patients with end-stage renal disease (ESRD) require hemodialysis (HD) to live, due to their kidney don't produce erythropoietin (EPO), which produces anemia, which is also influenced by iron usage, EPO and HD doses. Objective: compare hemoglobin levels of patients (PTS) in HD in two cities a different altitude: Lima (L), 90 m (m), and Arequipa (A), 2328 m. **Methods:** Clinical and laboratory information was requested from PTS in HD, the information was compared with tests of central tendency and t-tests for a difference. **Results:** Information from 137 PTS (L: 52, A: 65) was gathered. Their age was similar (L: 59.4 ± 15.1 vs A: 54.4 ± 18.1, NS). ESRD causes varied (L: Hypertension: 16, Diabetes: 15, Unknow:10 Glomerulonephritis: 6, others: 6; A: Glomerulonephritis:15, Hypertension: 13, Diabetes: 13, others: 13, Unknow:11). Their time in HD was different (L: 2.9 ± 1.81 vs A: 4.7 ± 3.67, $p < 0.0023$). Their KTV was different (L: 1.66 ± 0.23 vs 1.41 ± 0.35, $p < 0.001$). The EPO dose per weeks was similar (L: 3750 ± 2113 vs A: $3446 \pm 1{,}950$, NS). The Hemoglobin levels were different (L: 9.64 ± 1.62 vs A 11.5 ± 2.34, $p < 0.0001$). **Conclusion:** Patients in HD who live in high altitude have higher levels of hemoglobin than those who live on sea level, despite receiving similar doses of EPO.

60.

ENDOTHELIAL FUNCTION ASSESSMENT IN HEALTHY SUBJECTS EXPOSED TO ACUTE HYPOBARIC HYPOXIA IN A DECOMPRESSION CHAMBER.

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Introduction: Knowledge of the physiopathology of altitude related illnesses are scarce. Some studies have put their interest in the endothelial dysfunction showed when the vascular wall was stressed by the exposition to hypobaric hypoxia (HH). Its well knows that acute exposure to HH raised pulmonary artery pressure and increased the release of cytokines related with vasoconstriction and inflammation. People susceptible to suffer acute high altitude pulmonary oedema also have shown endothelial dysfunction measured by acetylcholine vasodilatation test. To our best knowledge endothelial function measured by flow mediated vasodilatation test (FMVD) in the brachial artery by two dimensions Ultrasound wasn't studied. The objectives of this study were to assess the endothelial function by the FMVD test and biochemical variables in subjects who were exposes acutely to HH. **Methods:** We exposed 10 healthy subjects to an altitude of 4000 m above sea level in a hypobaric chamber for time of 4 hours. We performed a FMVD test and take blood samples pre a post exposure to HH. **Results:** Baseline characteristics were, means and SD: age: 31.11 ± 6.05 years, BMI: 23.64 ± 2.01 kg/m2, waist circumference: 77.6 ± 7.92 cm, glucose: 94.97 ± 7.32 mg/dL, Cholesterol: 170 ± 30.59 mg/dL, HDL-c: 44.95 ± 14.78 mg/dL, LDL-c: 96.85 ± 23.09 mg/dL, Triglycerides: 53.23 ± 23.38 mg/dL, PCRus: 0.33 ± 0.54 mg/L, Homocystein: 9.52 ± 1.48 mmol/ L and VO_2 max 51.7 ± 6.95 mL/kg/min. We use a one-tail T test for non-appeared datum to compare the differences between deltas of anterior posterior diameter and flow velocity pre and post hyperemic phase in the brachial artery. Δ pre exposition: 0.49 ± 0.28 mm, Δ post exposition: 0.64 ± 0.52 mm, difference between Δ was 0.19 ± 0.59 mm with a T value of 1.02 ($P < 0.05$; IC 95% -0.15 - $+0.53$. Respecting flow velocity: Δpre exposition: 14.1 ± 8.61 m/seg, Δpost exposition: 16.6 ± 10.07 m/seg, difference between Δ was 2.5 ± 11.07 with a T value of 0.71 ($P < 0.05$; IC 95% -3.9 - $+8.9$ m/seg). We also compared means of PCRus, el VCAM-1 and endothelin pre and post exposure (Wilcoxon test). PCRus: 1.7 ± 3.91 versus 2.76 ± 7.12 mg/L p: 0.004, VCAM-1: 32.25 ± 6.4 versus 33.42 ± 9.5 ng/mL p:ns y endothelin: 0.17 ± 0.12 versus 0.38 ± 0.14 pg/mL p:0.012. **Conclusion:** In healthy subjects acute HH exposure didn't worse endothelial capacity of vasodilatation base on FMVD. The contrary was shown in the biochemical data. These differences may be was related with a different times of activation of the two phenomenon. Note: Interleukin 6, Tumour Necrosis Factor α and Brain Natriuretic Peptide analysis are in progress. **Acknowledgments:** Vainstein Nora MD.

61.

DEPRESSION AMONG COMMUNITY-DWELLING ELDERLY PEOPLE IN THE HIGH-ALTITUDE REGIONS OF LADAKH AND QINGHAI.

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Introduction: Depression is one of the most common mental disorders seen in elderly people, but the prevalence of depression has varied widely. The frequency of depression is thought to increase at high altitudes, where the environment is severe, but there have been hardly any reports of evaluations of the prevalence of depression among high-altitude dwellers. The purpose of the present study was to conduct a survey of depression among the elderly residing in such regions and to compare prevalences and investigate differences in the symptoms of depression according to the culture. **Methods:** We recruited 114 Tibetan subjects from Ladakh, India (mean age, 69.2 years; female-male ratio, 58.8%) and 173 Tibetan subjects from Qinghai, China (mean age, 66.5 years; female-male ratio, 61.3%) in August 2009. The two-item Patient Health Questionnaire (PHQ-2) and the Geriatric Depression Scale (GDS) were administered to the subjects. A psychiatrist interviewed the residents with a single or double positive score in PHQ-2 and with a score of >4 points on the GDS. **Results:** The ratio of subjects with one or more positive score in PHQ-2 was 7.0% in Ladakh and 37.0% in Qinghai, and with a score of >4 points on the GDS was 75.4% and 56.1%. The prevalence of depression over 60 years old was 2.6% in Ladakh and 2.3% in Qinghai. A spouse's death was a major cause of depression in both regions; however, peer competition, financial problems, and children's education were also sources of depression in Qinghai. **Conclusion:** The prevalence of depression over 60 years old was 2.6% in Ladakh and 2.3% in Qinghai. There are differences in expression of the symptoms of depression according to the culture, and it is necessary to take cultural background into consideration when using screening tools and making the diagnosis. **Acknowledgments:** This study was mainly supported by Grant-in-Aid of Research Institute for Humanity and Nature (3-4 FR): Human Life, Aging, and Disease in High-Altitude Environments: Physio-medical, Ecological and Cultural Adaptation in "Highland Civilizations." (Leader: Professor Kiyohito Okumiya).

62.

CARDIOVENTILATORY ACCLIMATIZATION INDUCED BY INTERMITTENT HYPOXIA: THE ROLE OF OXIDATIVE STRESS.

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Introduction: It is well recognized that sustained hypoxia due to high altitude exposure enhances the hypoxic ventilatory response, a phenomenon known as ventilatory acclimatization. At the sea level, the most usual pattern of hypoxia in humans is the chronic intermittent hypoxia (CIH) resulting from the obstructive sleep apnea (OSA). The OSA syndrome, a growing health problem that affects 5% of the worldwide population, is recognized as an independent risk factor for hypertension. Sympathetic activation, oxidative stress and inflammation have been proposed as potential pathogenic mechanisms involved in the progression of hypertension. A major contributing mechanism to the sympathetic activation is the potentiation of the carotid body (CB) chemosensory response to hypoxia, which is responsible for the augmented ventilatory, and cardiovascular responses induced by hypoxia in OSA patients and animals exposed to CIH. Since hypoxic-reoxygenation cycles produce oxidative stress, we study if the treatment with an antioxidant may prevent the cardioventilatory acclimatization and the hypertension induced by CIH. **Methods:** We studied the effects of ascorbic acid supplemented in drink water (1.25 mg/mL) on the oxidative stress, CB chemosensory and cardioventilatory responses to acute hypoxia in male Sprague-Dawley rats exposed to CIH (5% O_2, 12 times/hr for 8 hrs) or sham condition during 21 days. **Results:** CIH increased plasma lipid peroxidation and nitrotyrosine formation in the CB, enhanced CB chemosensory and ventilatory hypoxic responses, modified the heart rate variability (HRV) power spectrum and produced hypertension. Ascorbic acid treatment prevented the increases in plasma lipid peroxidation and nitrotyrosine formation within the CB, the enhanced CB chemosensory and ventilatory responses to hypoxia, as well as HRV alterations and hypertension. **Conclusion:** Present results support a crucial role for oxidative stress in the potentiation of CB chemosensory and systemic cardiorespiratory acclimatization induced by CIH. **Acknowledgments:** Funding source: FONDECYT Grants 1070584 and 1100542.

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THROMBOEMBOLISM AT HIGH ALTITUDE.

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Introduction: Is hypoxia thrombogenic? This question is still controversial, but recurrent with anecdotal reports of thromboembolism during expeditions. First case of deep venous thrombosis (DVT) and pulmonary embolism (PE) was reported in 1953 during K2 expedition. Most biological studies on markers of coagulation at high altitude were made under acute exposure and below 5000 m, concluding to no or minimal changes. Several observations >5000 m are compatible with activation of blood coagulation with prolonged exposure but comprehensive studies are lacking. During expeditions, many factors can add their respective effects: increased viscosity due to polycythemia (often enhanced by dehydration and cold), immobilization in highest camps due to bad weather, combined with the well-known risk of long-haul flight for return (usually shortly after the summit attempt when polycythemia and dehydration are still present, and possible higher risk with alcohol and sleeping-pills consumption). **Methods:** However, these events are very rare and epidemiological controlled studies are quite impossible. Another approach is to collect and analyse case reports. We report 12 events in 9 patients (8 men, 1 woman): 9 DVT including 4 associated with PE, and 3 strokes. All occurred during high altitude trek or expedition, or just after return. Professional mountain guides are of highest concern and constitute most cases. Preceding risk factors were analysed and screening for thrombophilia was proposed. **Results:** Some patients are still under investigation, but all patients explored until now for thrombophilia show inherited or acquired anomaly, mostly factor V Leiden mutation. The woman combines oral contraception with this mutation. **Conclusion:** Our hypothesis is that thromboembolism at high

altitude probably concerns only subjects with thrombophilic predisposition. These subjects usually don't know this risk factor before their first hypoxic exposure and systematic screening is expensive and not advisable. Therefore general recommendations about hydration and against adverse medications must be enhanced. Screening could be proposed to subjects with family history before the first exposure.

64.
ANALYSIS OF PERINATAL BIRTH DEFECTS ON PLATEAU.
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Introduction: Birth defects are an important factor that seriously affects the quality of the population, the deformed children suffers pain, and bring burden to families and society. Birth defect is the result of certain factors leading to developmental disorders in embryos in the womb, including the structural deformity, dysfunction, metabolic disorder or behavioral abnormalities of fetus before birth. **Methods:** According to the Monitoring Program of Birth Defects, 14,531 cases of perinatal birth in 10 years were analyzed retrospectively in our hospital and compare to the sea level area. **Results:** there are 141 children with perinatal birth defects in 14,531 cases, the incidence of perinatal birth defects is 9.69 ‰. Incidence of congenital heart disease is the highest in all perinatal birth defects, it is closely related to environmental factors such as altitude-related hypoxia, while only 5.23‰ in sea level. **Conclusion:** In order to reduce perinatal birth defects at high altitude, especially birth of children with congenital heart disease, we should take healthcare educations for all married couples, including to the pre-marital medical check-ups, and pre-marital, pre-pregnancy healthcare, and raise the awareness of environmental protection, especial for living in the high altitude areas.

65.
THE RELATIONSHIP BETWEEN PERINATAL HYPOXIA AND SLEEP-DISORDERED BREATHING IN PRECLINICAL CHRONIC MOUNTAIN SICKNESS.
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Introduction: Chronic intermittent hypoxia due to sleep-disordered breathing is implicated as a potential etiological factor for chronic mountain sickness (CMS). Whether sleep-disordered breathing precedes or results from CMS is not known. Likewise, factors responsible for sleep-disordered breathing in CMS are not well understood. Based on our preliminary data that perinatal hypoxia increases susceptibility to excessive erythrocytosis (EE, Hb $\geq$ 18.3 g/dL), a preclinical phase of CMS, we sought to determine whether respiratory characteristics during wakefulness or sleep differ between EE subjects and controls and, if so, to determine the relationship of this variation with perinatal hypoxia. **Methods:** Respiratory characteristics during sleep and wakefulness, and the incidence of perinatal hypoxia were compared in 28 EE and 25 control subjects selected from a survey of 820 young men (18-25 yrs) residing in La Paz, Bolivia ($\geq$3600 m), and matched by age- and altitude of residence. Respiratory characteristics during wakefulness and sleep were assessed by standard spirometry and polysomnography, respectively. Perinatal conditions were assessed by medical record review and maternal interview. EE and control groups were compared using independent t-tests or appropriate. **Results:** FVCs, FEV1, FEV1/FVC and HVR were similar between EE and controls. EE subjects had lower FEF25-75 than controls ($<$0.05), suggesting alterations in the peripheral airways. EE subjects had more central apneas and hyponeas ($P < 0.05$), as well as lower nadir and average noctural SaO_2. Perinatal hypoxia [i.e., premature delivery, oxygen supplementation at delivery or preeclamptic mother] was more common in EE than controls, and was associated with altered respiratory function during wakefulness or sleep. Preeclampsia showed the strongest relationship to sleep-disordered breathing and EE, and was positively associated with hypopneas, central sleep apneas, and Hb. **Conclusion:** Perinatal hypoxia may contribute to impaired respiratory function during sleep at high altitude, and consequently EE and/or CMS. **Acknowledgments:** We would like to thank the generous participation of our research subjects, Dr. Rob Roach (ARC); Dra. Diva Bellido, Cristina Gonzales, Ana Maria Alarcón, Marta Aguillar, Catherine Romero, Yvonne Contreras (IBBA); Lic. Javier Fuentes (INSEF); Dra. Maritza Vargas and Lic. Walter Amezaga (Normal Superior Simon Bolivar); and financial support provided by NIH (R03TW007957-01A2).

66.
RELATIONSHIP BETWEEN TESTOSTERONE AND ZINC LEVELS IN EXCESSIVE ERYTHROCYTOSIS IN MEN LIVING AT HIGH ALTITUDE.
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Introduction: It is known that hypoxia induces an increase in zinc levels from low-diameter arteries endothelium. In addition, zinc increases erythropoietin expression, and the enzyme is also related to normal function of many enzymes like carbonic anhydrase which is important to maintain body pH and to regulate ventilatory function. The present study aimed to determine the relationship between zinc (Zn) or testosterone (T) and erythropoietin (EPO) and hemoglobin (Hb) levels in men living in Cerro de Pasco (4340 m) with or without excessive erythrocytosis (EE). **Methods:** 100 volunteers were allocated in the following three groups: one at low altitude ($n = 30$, 43.2 ± 1.3 years old) (Lima) and two at high altitude [37 volunteers with Hb $<$ 16-21 g/dL (43.5 ± 1.3 years old), and 33 volunteers with Hb^{3}21 g/dL (45.1 ± 1.7 years old) (EE)]. Hb, EPO, Zn and T, levels were determined. **Results:** Comparing men with EE and men without EE, no differences were found regarding to age ($P > 0.05$) and time of residence at high altitude (Hb $<$ 16-21 g/dL $= 29.3 \pm 2.4$ years vs Hb^{3}16-21 g/dL $= 30.5 \pm 2.9$ years, $P = 0.75$). Although Hb levels were different between all groups, EPO levels were higher in high altitude residents without differences between people with Hb $<$ 16-21 g/dL and those with Hb^{3}21 g/dL ($P = 0.293$). Zinc levels were higher in EE group than those at low altitude ($P = 0.027$) and those at with Hb $<$ 16-21 at high altitude ($P = 0.033$). Testosterone levels were higher in EE group than people without EE and than in those at low altitude ($P = 0.04$). Correlation analyses showed that Zn levels were related to Hb ($r = 0.324$, $P = 0.044$) but not with EPO ($r = -0.006$, $P = 0.961$) levels. Also, testosterone levels were correlated to Hb levels ($r = 0.317$, $P = 0.038$). No relation was observed between Zn and testosterone levels ($r = 0.003$, $P = 0.978$). **Conclusion:** The outcome of the present study suggest that testosterone may be related to the excessive erythrocytosis observed in men living at high altitude without any relationship with zinc levels.

67.
CHARACTERIZATION OF PRESENILIN FUNCTION IN THE OXYGEN-SENSING PATHWAY.
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Introduction: Presenilin 1 and 2 (PS1 and PS2) are the core components of the g-secretase complex which cleaves a variety of proteins such as the amyloid precursor protein (APP) and Notch. The proteolysis of APP leads to the formation of amyloid beta (Ab) that is crucially involved in the pathogenesis of Alzheimer's disease (AD). The cleavage of Notch leads to the generation of the Notch intracellular domain (NICD) which is involved in the control of cell fate and stem cells maintenance. Hypoxia plays an important role both in the progression of neurological disorders as well as in the maintenance of the undifferentiated cell state. The central activators of oxygen-dependent gene transcription are the heterodimeric hypoxia-inducible factors (HIFs). In normoxia, a family of prolyl-4-hydroxylase domain (PHD) proteins hydroxylate the HIF-a subunits which leads to their degradation via the ubiquitin-proteasome pathway. In hypoxia, prolyl hydroxylation is inhibited, HIF-a protein is stabilized and dimerizes with its constitutive counterpart HIF-b. **Results:** To study PS function in the oxygen sensing pathway, we analyzed PS1/PS2 wild-type (wt) and knock-out (ko) mouse embryonic fibroblasts (MEFs). HIF-1a transcript levels, hypoxic HIF-1a protein accumulation and HRE-dependent reporter gene activity were found to be decreased in PS1/2 ko MEFs. Hif1a promoter activity of both HIF-1a isoforms was lower in PS1/2 ko MEFs but not regulated by hypoxia as determined by reporter gene experiments. Reconstitution of either PS1 or PS2 (or both) partially rescued these effects, indicating a role of both PSs in the hypoxia pathway. Specific g-secretase inhibition led to a decrease of hypoxic HIF-1a protein levels, suggesting that the observed results are dependent on g-secretase function. Interestingly, PHD2 protein levels were also found to be decreased in PS1/2 ko MEFs. Given the fact that PHD2 itself is regulated by HIF, this finding might result from an absent PHD2 induction. **Conclusion:** Current research focuses on unravelling the mechanism by which presenilins regulate HIF-1a transcript levels and the hypoxic response. **Acknowledgments:** This work is supported by the Swiss National Foundation (SNF 3100A_129962/1).

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THE EFFECT OF 10-DAYS OF HYPOXIA ON MUSCLE AND CEREBRAL OXYGENATION DURING A SUB-MAXIMAL PERFORMANCE TEST.

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Introduction: We investigated the effects of chronic moderate hypoxia on cerebral, respiratory and leg muscle oxygenation during a submaximal constant-power test. **Methods:** Eight healthy trained males (age = 24 ± 4.4 yrs; $VO_{2m}ax = 60.6 \pm 9.5$ mL•kg-1•min-1) participated in a randomized cross-over designed study. They were assigned to two groups: one group (n = 4) was confined to a controlled hypoxic environment (HYPO; $FIO_2 = 0.15$) for 10-days, and the other (n = 4) to a normoxic environment (NOR; $FIO_2 = 0.21$) for the same period. After a 3-week washout period, the two groups switched living conditions; the group previously exposed to hypoxic confinement was now exposed to normoxic conditions, and vice versa. Before (Pre) and after (Post) each exposure period, all subjects performed a normoxic incremental-exercise test ($VO_{2m}ax$) to exhaustion, and a normoxic constant-power test (CPT) at 80% of Pre peak power output. During the CPT, regional concentration changes of oxyhemoglobin ($\Delta[O_{2h}b]$), deoxyhemoglobin (Δ[HHb]) and total hemoglobin (Δ[THb]) in the right vastus lateralis, the right serratus anterior and the left frontal cerebral cortex were monitored with near-infrared spectroscopy. **Results:** VO_2 max did not change in either group. Moreover, despite the unchanged CPT of both groups, minute ventilation increased significantly in the HYPO group (+17%; $P < 0.05$) after hypoxic exposure. Furthermore, the $\Delta[O_{2h}b]$ and the Δ[HHb] in the serratus anterior decreased in the HYPO group (Mean ± SE; Pre = $-22.12 \pm 1.15\ \mu$M, Post = $-16.23 \pm 0.95\ \mu$M; Pre = $20.76 \pm 1.23\ \mu$M; Post = $14.74 \pm 0.93\ \mu$M, respectively), but the Δ[THb] remained unchanged. Inspite of the aforementioned responses of the respiratory muscles, continuous hypoxic exposure did not influence cerebral nor vastus lateralis oxygenation during CPT. **Conclusion:** We conclude that 10-days of continuous moderate hypoxia may affect regional oxygenation of the respiratory muscles during a submaximal constant-power test without a concomitant change in performance. **Acknowledgments:** Supported by a grant from the Slovene Research Agency.

69.

FOOD DIVERSITY AND DIABETES IN TIBETAN HIGHLANDERS.

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Introduction: Value of taking various foods has been reported and it is especially important for health of the elderly people. Moreover, we have found that lack of food diversity was related with diabetes in the Japanese elderly. This study aims to examine the association between food diversity and diabetes in the Tibetan elderly living in highland settings where dietary diversity seems to be originally lower because of its harsh environment and culture. **Methods:** The study population consisted of 357 Tibetan elderly subjects aged 60 years or more living in Tibetan plateau (Haiyan and YuShu in Qinghai in China, Ladakh in India, about 3000-3500 m above sea level). Diabetes is determined by 2-hour Oral glucose tolerance test. Food diversity was assessed using an 11-item Food Diversity Score Kyoto (FDSK-11), ranging 0-11 and higher score shows higher food diversity. **Results:** Prevalence of diabetes in this study subjects was 12.3%. The mean score of FDSK-11 was 7.5. Tibetan elderly with diabetes had higher food diversity than those without (diabetes vs. non-diabetes: 8.1 vs. 7.3, $P = 0.048$). **Conclusion:** This study has revealed the very opposite results that higher food diversity was associated with diabetes in Tibetan elderly highlanders while previous studies in Japan or reports from any other countries has shown that less varied foods relates to diabetes. The higher food diversity suggest the recent quick change of modernized lifestyle in Tibetan people and they may be vulnerable to diabetes because their body had long-acquired adaptation to low nutrition in the harsh

high-altitude environment. **Acknowledgments:** This study was supported by Research Institute of Humanity and Nature: Human Life, Aging, and Disease in High-Altitude Environments: Physio-medical, Ecological and Cultural Adaptation in the Great "Highland Civilizations."

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FOOD DIVERSITY AND HEALTH OF HAN AND TIBETAN ELDERLY HIGHLANDERS IN QINGHAI, CHINA.

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Introduction: Taking varied food has long been recommended as a healthy diet and said to be especially important for the elderly. However, in highland, it seems to have been insufficient to get various foods because of the limitation of food resources. With this background, this study aims to examine the association between food diversity and health status of the Han and Tibetan elderly highlanders conducting the Comprehensive Geriatric Assessment in Qinghai plateau in China (about 3000 m high above sea level). Methods: The study population consisted of 240 community-dwelling elderly subjects aged 60 years or more (Han: 176, Tibetan: 64). Food diversity was determined using an 11-item Food Diversity Score Kyoto (FDSK-11). Health status including Activities of daily living (ADL)(independence of walking, climbing stairs and other objective activities), screening-based depression and subjective quality of life (QOL) were interviewed. Blood chemical investigation was carried out in association with food diversity. **Results:** ADL was significantly lower both in the Han and Tibetan elderly with lower food diversity than those with higher diversity. In Han elderly with lower food diversity, QOL were significantly lower in the items of subjective sense of health, relationship with family and subjective happiness, but not significant in Tibetan elderly. A close association was found between lower food diversity and lower financial satisfaction in both Han and Tibetan ones. Higher food diversity was associated with lower blood glucose level in Han elderly subjects, but opposite association was found in Tibetan ones. **Conclusion:** Food diversity was associated with ADL and subjective QOL even in highlanders. Food assessment is very important as a useful indicator to know the actual condition of diet and its relation to health status of the elderly as well as the change of economical background in Qinghai highland. **Acknowledgments:** This study was supported by Research Institute of Humanity and Nature: Human Life, Aging, and Disease in High-Altitude Environments: Physio-medical, Ecological and Cultural Adaptation in the Great "Highland Civilizations."

71.

RECOMBINANT ANGIOTENSIN CONVERTING ENZYME 2 IN ACUTE HYPOXIA: PULMONARY HEMODYNAMICS AND INERT GAS EXCHANGE.

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Introduction: Angiotensin-converting encyme 2 (ACE2) administration has been shown to alter heart and lung function. It is unknown if ACE2 administration alters pulmonary hemodynamics and pulmonary gas exchange in acute hypoxia. In this experiment we investigate how ACE2 administration affects pulmonary blood flow, gas exchange and cardiac performance in an animal model. **Methods:** Twelve anesthetized pigs instrumented with arterial and Swan-Ganz catheters were exposed to normobaric hypoxia ($FiO_2 = 0.125$) for 180 minutes. After taking baseline measurements in hypoxia, ACE2 400 μg · kg-1 was given. Ventilatory variables, arterial blood gases, systemic hemodynamics, and ventilation/perfusion relationships were assessed at 30, 60, 90, 120, 150 and 180 minutes after ACE2 administration. **Results:** We observed decreases in mean pulmonary arterial pressure at 90, 120, 150 and 180 minutes (maximum: 30 vs. 39 Torr at the 90 minute measurement) and pulmonary vascular resistance at 60, 90 and 120 minutes (maximum: 7 vs. 13 dyne · sec · cm^{-5} at the 120 minute measurement). Multiple inert gas elimination technique did not reveal pulmonary blood flow to lung units with subnormal VA/Q numbers or intrapulmonary shunt. Furthermore, heart rate and cardiac output in hypoxia remained unaffected by ACE2. Plasma Angiotensin II levels tended to be lower in ACE2 animals. **Conclusion:** In hypoxia - generated acute pulmonary hypertension, administration of ACE2 leads to relevant pulmonary vasodilation in anesthetized pigs. Since gas exchange remains unaffected, recombinant ACE2 could be used in those presentations of pulmonary hypertension, where hypoxia is part of the ethiology.

72.

COMBINED AUTOCPAP AND ACETAZOLAMIDE TREATMENT CONTROLS BREATHING DISTURBANCES IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME AT ALTITUDE.

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Introduction: Patients with the obstructive sleep apnea syndrome (OSA) have pronounced hypoxemia and frequent central and obstructive sleep apnea even at moderate altitude. The optimal treatment in this setting has not been established. Therefore, we evaluated whether computer-controlled autoCPAP therapy alone or combined with acetazolamide (AC) controls breathing disturbances in OSA patients at altitude. **Methods:** 35 OSA patients living at < 600 m on long-term CPAP therapy underwent 2 altitude sojourns of 3 days each at Davos, Switzerland, (2 days at 1630 m, 1 day at 2590 m), separated by a 2 week washout period at < 600 m. Patients remained on autoCPAP (pressure 5-15 cmH2O). In addition, they took either prophylactic AC (750 mg/d) or placebo according to a double-blind, randomized cross-over protocol. Nocturnal polysomnographies were performed in Zurich and at altitude. **Results:** Polysomnographies in patients on autoCPAP plus placebo revealed a reduced oxygen saturation at 1631 m and 2590 m (medians 91% and 88%, respectively, vs. 95% at 490 m) and an elevated apnea/hypopnea index (medians 10.1/h and 17.3/h vs. 6.9/h) due to central events ($P < 0.05$

1632 m & 2590 m, respectively, vs. 490 m). AC improved oxygen saturation (94% and 91% at 1631 m & 2590 m) and reduced the apnea/hypopnea index (4.9/h and 7.0/h at 1631 m & 2590 m) compared to placebo ($P < 0.05$ AC vs. placebo at corresponding altitude). **Conclusion:** In patients with OSA autoCPAP effectively eliminates obstructive apnea at low and at moderate altitude but AC is required for optimal oxygenation and control of breathing disturbances at altitude. **Acknowledgments:** Swiss National Science Foundation.

73.

DO OBSTRUCTIVE SLEEP APNEA PATIENTS DEVELOP SUBCLINICAL HIGH ALTITUDE PULMONARY EDEMA (HAPE) AT MODERATE ALTITUDE?

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Introduction: We evaluated whether lowlander patients suffering from obstructive sleep apnea syndrome (OSA) would develop subclinical HAPE after rapid ascent to 2590 m and whether they would benefit from acetazolamide prophylaxis at altitude. **Methods:** 50 OSA patients living at < 600 m (mean age ± SD 61 ± 8yrs, apnea/hypopnea index 53 ± 20/h) on long-term computer controlled autoCPAP underwent 2 altitude sojourns of 3 days each at Davos, Switzerland (2 days at 1630 m, 1 day at 2590 m), separated by a 2 week washout period at < 600 m. At altitude patients received either acetazolamide or placebo according to a double-blind, randomized cross-over trial. Symptoms, blood pressure, weight and pulmonary function were assessed at 490 m and 2590 m. **Results:** While on autoCPAP and placebo at 2590 m patients revealed mild acute mountain sickness (AMSc score 0.13 ± 0.27 vs. 0.10 ± 0.26 at 490 m), reduced daytime oxygen saturation (91 ± 2 vs. 95 ± 1%), elevated weight and mean arterial blood pressure (101.2 ± 18.6 vs. 100.8 ± 18.4 kg and 105 ± 10 vs. 99 ± 9 mmHg) ($P < 0.05$ all instances). FVC (106 ± 14 vs. 113 ± 15%pred), FEV1 (103 ± 16 vs. 107 ± 16% pred) and diffusing capacity (DLCO 82 ± 11 vs. 85 ± 13% pred.) were reduced (2590 m vs. 490 m, $P < 0.05$ all instances). Acetazolamide significantly improved AMSc scores, reduced weight and blood pressure and increased dynamic lung volumes compare to placebo but did not improve DLCO at 2590 m. **Conclusion:** The data suggest that OSA patients developed subclinical HAPE even at the moderate altitude of 2590 m. Alternatively, they might have had pulmonary congestion due to left ventricular heart failure. Acetazolamide prophylaxis prevented symptoms of acute mountain sickness, fluid retention and blood pressure elevation but did not improve pulmonary diffusion at altitude. **Acknowledgments:** Swiss National Science Foundation.

75.

AMS_CART ON ACONCAGUA.

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Introduction: Utilize CART analysis to derive a prediction rule to predict the outcome of severe AMS **Methods:** Secondary analysis of climbers at the end of an expedition to Aconcagua (6962 m) via the normal route who completed a questionnaire upon exiting the park. The questionnaire contained sections on demographic data, previous altitude experience, characteristics of the current expedition, development of AMS, and medical history. Severe AMS was defined as Lake Louise Score (LLS) ≥ 5 in the presence of a headache. CART 6.0 (Salford Systems, San Diego, CA) was applied to 38 categorical and 18 continuous variables contained within the questionnaire. V-fold validation was used to estimate model success and descriptive test characteristics with 95% CIs are reported **Results:** 919 climbers completed questionnaires. 97 (10.6%) were excluded for the following: summiting was not their objective (8.7%), incomplete LLS data (1.8%). Prevalence of AMS was 38.0%. During derivation, CART identified 3 variables that optimally predicted AMS: dyspnea on exertion, past history of high altitude headache, and use of analgesics during the expedition. Test statistics from the prediction tree resulted in area under ROC = 0.73, sensitivity = 75.6% (95% CI: 70.5-80.3), specificity = 59.8% (95% CI: 55.4-64.1), PPV = 53.5% (95% CI: 48.7-58.2), NPV = 80.1% (95% CI: 75.7-83.9) **Conclusion:** A CART-derived prediction tree identified dyspnea on exertion, past history of high altitude headache, and analgesic use as predictors of severe AMS on Aconcagua.

75.

CORRELATION BETWEEN HYPERTENSION AND DEVELOPMENT OF ACUTE MOUNTAIN SICKNESS ON ACONCAGUA (6962 M).

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Introduction: Determine if the hypertension is a predictor of altitude sickness in Aconcagua climbers. **Methods:** We enrolled 127 subjects at 4365 m while they were acclimating at base camp of Aconcagua. Subjects prospectively filled out a questionnaire with demographics, medical history, experience at altitude, and characteristics of their current expedition. We then recorded 1 set of vital signs on the subjects while at base camp and collected outcome data after their summit attempt. We currently have outcome data on 65 subjects. Our primary outcome is the presence of AMS, as measured by the Lake Louise Scoring System AMS self-report questionnaire (LLQS). Given the high incidence of AMS on Aconcagua and the low specificity of LLQS, we report those subjects with severe degree of AMS, as defined by a LLQS ≥ 5. **Results:** 12 of 65 subjects (19%) had a SBP of 160 mm Hg, of whom 6 (50%) had a severe degree of AMS. The 53 patients with SBP < 160 mm Hg, 27 (49%) had a severe degree of AMS. The difference in means between the non-hypertensive subjects and the hypertensive subjects was 1% ± 16% (95% CI of the difference: –33% to 31%). **Conclusion:** Among 65 climbers in whom a prospective measurement of blood pressure and LLQS scores were recorded, we found no correlation between hypertension and development of AMS. Our study was not designed or powered to test the relationship between AMS and hypertension. However, our preliminary data do not suggest that a single elevated

blood pressure measurement is predictive of AMS. Adequately powered prospective studies that investigate the relationship between hypertension at altitude and development of AMS are needed.

76.

PRIOR MOUNTAINEERING EXPERIENCE OF CLIMBERS ATTEMPTING TO SUMMIT ACONCAGUA.

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Introduction: Objectives. Quantify the prior mountaineering experience of climbers who attempt to summit Aconcagua. **Methods:** Post-hoc descriptive analysis of retrospective observational study. All climbers who exited the Aconcagua Park via the normal route and spoke English, Spanish, German, or French during the January 2001 were included. Climbers whose objective was not the summit or who had incomplete data were excluded. Subjects completed questionnaires containing baseline demographic information and information about their prior mountaineering experience. Standard descriptive statistics were generated using Stata 9.2. **Results:** There were 1403 eligible mountaineers during the study period, of whom 919 completed the survey (65.5% response rate). 108 subjects were excluded (80 because summiting was not their objective and 28 due to incomplete data), leaving 811 subjects available for complete data analysis. Mean age was 36.1 years and 86% were male. Mean altitude at place of residence was 442 m (95% CI: 404, 481). Mean previous maximum altitude reached was 6023 m (95% CI: 5943, 6104). Mean previous maximum sleeping altitude was 5208 m (95% CI: 5125, 5291). 53.9% of climbers had attempted one of the seven summits previously. 187 climbers (23.1%) had previously summited Aconcagua. 5.3% of climbers had never been above 4000 m. **Conclusions:** Although the majority of mountaineers who attempt Aconcagua have prior high altitude experience, a substantial number not have been above 4000 m.

77.

PROTECTIVE ROLE OF 5-HMF AGAINST HYPOXIA AND STABILIZING HIF-1α.

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Introduction: Hypoxia-induced diseases are involved in both high altitude and plain areas. Effective precaution to prevent against hypoxic injury will contribute to resist these diseases. Hypoxia Inducible Factor (HIF)-1 as a transcription factor can drive the adaptative process to severe hypoxia through acting its target genes (for example: EPO, VEGF, etc.). However, HIF-1α, an active unit of HIF-1, is unstable in normoxia. Just because of this property of HIF-1α, it becomes a potential target of anti-hypoxia drug design. **Methods:** A transgenic mice created in 2006 can be noninvasively imaged based on accumulation of the HIF-1α ODD-Luc reporter. ODD-Luc mice provide a rapid measurement of possible agonists of HIF-1 activity. Using these mice we screened several anti-oxidative compounds and found 5-HMF (5-Hydroxymethylfurfural) had the strongest role in stabilizing HIF-1α. 5-HMF is the final product of carbohydrate metabolism. It has been found its beneficial roles in anti-oxidation and amelioration of hemorheology. The role of 5-HMF in hypoxia, however, is not yet clear. In this study, we investigated the role of 5-HMF in hypobaric and normobaric hypoxia. **Results:** The result showed that after 4 h of 5-HMF intragastric administration, the survival time of the mice under both hypobaric and normobaric hypoxia was prolonged as compared to the control groups. We further observed the effect of 5-HMF on hypoxia using MTT and trypan blue exclusion assays in ECV304 cells. Cell viability was increased and cell mortality was prevented by 5-HMF after exposure to hypoxia for 24 h.Further study indicated that protective role of 5-HMF against hypoxia was not related to anti-apoptotic activity, but instead to anti-necrotic activity, and that HIF-1α activation by 5-HMF might be involved in this way. Next study we will focus on the role of HIF-1α activation by 5-HMF in its anti-hypoxia using the ODD-Luc transgenic mice and further investigate the correlated mechanism. **Conclusion:** It will be prospective that 5-HMF can be used as an anti-hypoxia drug to prevent against cerebral vascular or cardiovascular diseases in adaptation to various hypoxic environment. **Acknowledgments:** This work was supported by a grant from the National Basic Research Program of China (No. 2006CB504100).

78.

EVOLUTION OF HEIGHT AND NUTRITIONAL STATUS IN SCHOOL CHILDREN BETWEEN 1997 AND 2010 IN ANTOFAGASTA DE LA SIERRA, CATAMARCA, PUNA ARGENTINA.

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Introduction: The aim of this work was to analyze the evolution of height and nutritional status in schoolchildren from Antofagasta de la Sierra, Catamarca, Argentina, over a period of 14 years. The town of Antofagasta de la Sierra has 656 inhabitants; the eponymous department has an area of 28,260 km^2 and a population density of 0.045 inhabitants per km^2. It is one of the most depopulated places in the planet, with altitudes above 3000 m above the sea level, extreme desert climate, and a daily temperature reaching up to 30 ° C. It remained isolated for many years. In the '80s a road that linked it to the north of the province was opened. The new political system was applied and improved social programs and the development of tourism-related activities, public offices, as well as the income of money and economic movement. All this is demonstrated by the drastic decline of households with unsatisfied basic needs (NBI). **Methods:** In 2010, the weight (W), height (H) and body mass index (BMI) calculated for all school children between 6 and 14 years old were obtained. Nutritional indicators W / age, H / age, BMI / age were determined through the 2007 WHO standards. Height and nutritional indicators were compared with those from prior assessment in 1997. **Results:** In all age groups an increase in height is revealed. In turn the prevalence of underweight and stunting decreased, overweight was doubled and obesity was quadrupled between 1997 and 2010. **Conclusion:** In conclusion, this population has shown a secular change in height, which can be interpreted as a result of lifestyles changes in a relatively short period. On the other hand, the influence of globalization together with the participation of private companies and government agencies impacted the decline in the prevalence of low weight and low height and the increase in overweight and obesity for each age. **Acknowledgments:** This work was funded by the ANPCYT under the project PICTO 32 451 of FONCYT and UNCA.

79.
HYPOXIA AND MERCURY (HG) AFFECT AUTONOMIC NERVOUS SYSTEM (ANS) FUNCTION; 400 YEARS OF AMBIENT EXPOSURE TO BOTH.

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Introduction: The largest Hg processing in the Western Hemisphere was in Huancavelica (H) in the Peruvian Andes, at ~4000 m. These deposits have been mined since pre-Hispanic times. The mine was officially closed 30 years ago. High morbidity and mortality amongst miners from extreme temperatures, Hg poisoning, intense physical labor, and ambient hypoxia earned the mine the designation the "mine of death". Hg is a known neurotoxin which affects the ANS and ambient hypoxia affects both the ANS and the entire nervous system. The generational impacts of combined Hg exposure and ambient hypoxia have not, hitherto, been explored. The ANS influences biologic rhythms as seen in heart rate variability and the fast and slow periodicities of hair growth. We assessed biologic rhythms by examining the periodicities in hair growth in present day H residents. **Methods:** We determined hydrogen isotope ratios (HIR) by the continuous flow-high-temperature-reduction technique and Hg levels in the hair of 5 H and 4 (C) from other continents. The series of isotope ratios derived from consecutive fragments of hair along its length were analyzed with spectral methods that give insights into biologic rhythms. **Results:** The Hg content in hair ranged from 0 to 90.9 ug/L. The annual growth rate of hair in H was 5.7 ± 2.0 (SD) versus 15.3 ± 2.9 cms./year in C ($P < 0.001$). The standard deviation of the variation in the HIR along the length of the hair was less in H ($P = 0.001$). The fast frequency of pooled HIR spectra in H was faster than in each of the C. **Conclusion:** We show that ambient Hg and altitude exposure, over generations, affect ANS function and biologic rhythms in clinically normal contemporaneous H residents. **Acknowledgments:** Funded by NMHEMC Research Foundation, Albuquerque, NM, USA.

80.
PATIENTS WITH CHRONIC CARDIAC DISEASES AT HIGH ALTITUDE.

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Introduction: With the growing interest in adventure travel, increasing numbers of individuals are venturing to high altitude. As medical care for many common conditions improves, it is likely that many of these travelers will have underlying medical problems that may be adversely affected by acute high altitude exposure. Given that many of the primary physiologic responses to acute hypoxia, including hypoxic pulmonary vasoconstriction, and increased sympathetic nervous system activity involve the cardiorespiratory system, patients with chronic cardiac diseases are one group that deserves particular attention prior to any planned high altitude travel. In this talk, we review the effects of acute high altitude exposure on patients with coronary artery disease, chronic heart failure, congenital heart disease and pulmonary hypertension. Although the literature on such patients at high altitude are limited at this time, it is possible to draw on an understanding of the main physiologic responses to high altitude and how those responses will interact with the underlying pathophysiology in each of these disease states and draw tentative conclusions about how these patients will do in acute hypoxia. Theoretical concerns with each patient group will be explored, the available data reviewed and recommendations made about how to evaluate the safety of planned high altitude travel in these groups.

81.
EFFECT OF EXOGENOUSTESTOSTERONE IN THE RIGHT VENTRICULAR HYPERTROPHY IN RATS INDUCED TO HYPOBARIC HYPOXIA.

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Introduction: Chronic hypoxia induces right ventricular hypertrophy (RVH) and pulmonary hypertension. RVH induced by chronic hypoxia is due to different mechanical stress upon the ventricular wall and the pulmonary arterial hypertension. It is known that testosterone is erythropoietic, inhibits ventilation, and activates ACE gene in heart. Then, it is possible that this hormone may have an effect on RVH. **Methods:** Two groups were divided according to the exposure (normoxia or hypoxia). Then, each group was subdivided in two groups according the treatment (vehicle (0.2 mL) and TE (50 mg)), each subgroup was further divided in three groups according to the time of exposure (7, 14, and 21 days). We assessed the left (LV) and right (RV) ventricles weights. In addition, we measured the initial and final hematocrit. The RVH was determined using the Fulton ratio. **Results:** Two-way ANOVA revealed an effect of the exposure to hypoxia ($F1,76 = 51.41$; $P < 0.001$) and TE administration ($F1,76 = 13.88$; $P < 0.001$) ($r^2 = 0.60$) on Fulton ratio. In normoxia, no differences in Fulton ratio were observed between rats with or without TE ($P > 0.05$). In rats without TE, RVH was noted after 21 days of exposure to hypoxia showing a 20% of increase in Fulton ratio ($P < 0.05$). In TE-treated rats, RVH increases after 14 (61%) and 21 (63%) days of exposure to hypoxia compared to rats in normoxia ($P < 0.05$) showing an additive effect. At sea level, rats treated with TE showed higher hematocrit values after 14 and 21 days than rats without TE at the same time (14 days: 56.08 ± 1.48 vs. 42.17 ± 2.56; and 21 days: 52.10 ± 0.62 vs. 49.00 ± 0.86, $P < 0.05$). In hypoxia, hematocrit levels were increased at all times of exposure compared to rats in normoxia ($P < 0.05$); but no differences were observed in hematocrit values between rats with or without TE in hypoxia ($P > 0.05$). In addition, it was observed an effect of the interaction of the exposure to hypoxia, time of exposure and TE treatment ($F2,74 = 21.06$; $P < 0.001$) ($r^2 = 0.70$) on hematocrit level. A positive correlation was observed between Fulton ratio and hematocrit ($r = 0.40$, $P < 0.001$) and between TE treatment and Fulton ration ($r = 0.31$, $P < 0.01$). **Conclusion:** The present study shows that exogenous testosterone administration accelerates the occurrence of right ventricular hypertrophy and increases erythropoiesis in rats exposed to hypoxia.

82.
GLUCOSE LEVELS AND LIPID PROFILE IN A HIGH ALTITUDE PERUVIAN POPULATION.

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Introduction: Objective: To describe the lipid profile and glucose levels in the population over 18 years old in the

village of Lari, Caylloma province in Arequipa department. **Methods:** This is a descriptive, random sampling, cross-sectional study at high altitude (3600 m). We collected information from 75 individuals over 18 years old as part of the Project IRIS: "Intervención Rural de Investigación y Saneamiento", through a questionnaire that included socio-demographic information and blood tests for lipid profile and fasting blood glucose. We worked together professionals and students of the of medicine faculty and medical technology school. **Results:** A random sample of 75 individuals (37.3% were males) mean age was 51.7 + /- 18 years, was included in the study. We observed a high prevalence of hypertriglyceridemia (49.3%), 25.3% had levels higher than 200 gm/dL. We also found a high prevalence of hypercholesterolemia (41.3%), where 1/3 had levels between 200 and 239 mg/dL and 9.3% with levels higher than 240 mg/dL. A very high prevalence of low high density lipoprotein (HDL) was seen women compared to men (93.5% vs. 50%, respectively; $P < 0.001$). The prevalence of high low density lipoprotein (LDL) cholesterol was 70.7% (36% between 100 and 129 mg/dL and 14.7% with levels higher than 160 mg/dL). Impaired fasting glucose was found in 27% of the study population. The mean LDL cholesterol levels (121.0 mg/dL + /- 35.7) and HDL cholesterol (39.4 mg/dL + /- 5.1) were abnormal, while mean triglyceride levels (151.1 mg/dL + /- 73.9), total cholesterol (189.5 mg/dL + /- 40.5), and glucose (90.4 mg/dL + /- 13.5) were normal. **Conclusion:** We found a high prevalence of hypercholesterolemia, hypertriglyceridemia and low HDL, all of which are important risk factors for cardiovascular disease (CVD) in high altitude natives. Future longitudinal study to assess the impact of this on actual CVD is warranteed. **Acknowledgments:** Thank you to the "Facultad de Medicina Alberto Hurtado" and "Escuela de Tecnologia Médica" and Universidad Peruana Cayetano Heredia for the financial support.

83.

HEMATOCRIT AND HEMOGLOBIN LEVELS AT ADULTHOOD ARE DETERMINED BY NEONATAL HYPOXIC EXPOSURE IN RATS LIVING AT HIGH ALTITUDE.

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Introduction: In previous work performed at sea level we reported that exposure to neonatal hypoxia impairs ventilatory and hematological responses to chronic hypoxia later in life. These findings supported the hypothesis that neonatal hypoxia might be a critical factor in the development of chronic mountain sickness, which mainly occurs in men at high altitude, and is characterized by hypoventilation and excessive erythocytosis. In the present work we tested the hypothesis that hypoxia during early life has long-lasting impacts on the hematological acclimation in adult rats permanently living at high altitude. **Methods:** All rats were born and raised at high altitude (3600 m, IBBA, La Paz, Bolivia, mean barometric pressure: 495 mmHg). Between gestational day 20 and postnatal day 15, newborn rats were raised in room air (termed HAn rats), or in a chamber flushed with 35% O_2, simulating sea level PiO_2 (SLn rats). Body weight, hematocrit (Ht) and hemoglobin (Hb) values were measured in male and female rats at postnatal days 15 (P15) and 90 (adults). **Results:** At P15, body weight was similar between SLn and HAn rats, for both males and females. In adults, body weight was slightly higher in SLn vs. HAn male rats (291 ± 8 g vs. 261 ± 5 g, $P = 0.008$), this effect was not observed in females (188 ± 2 g vs. 186 ± 3 g). Both Ht and Hb values were reduced in SLn males and females at P15, and this effect persisted in adults. In adult SLn males Hb was 18.7 ± 0.6 g/dL, vs. 20.7 ± 0.4 g/dL in HAn ($P = 0.002$), while Ht was $50.4 \pm 1.7\%$ in SLn vs. $57.6 \pm 0.6\%$ in HAn ($P = 0.0002$). Differences of similar magnitude were observed in females. **Conclusion:** These results show that neonatal hypoxia in high altitude rats contributes to set hematocrit and hemoglobin levels reached at adulthood. This further supports the hypothesis of a neonatal origin of chronic mountain sickness. Ongoing studies aim at defining the associated ventilatory responses. **Acknowledgments:** Founded by NSERC.

84.

PREVALENCE OF EXCESSIVE ERYTHROCYTOSIS (EE) AND HIGHER CHRONIC MOUNTAIN SICKNESS IN THE POPULATION OF CARHUAMAYO (4100 M) IN THE PERUVIAN CENTRAL ANDES: RISK FACTORS FOR THE DEVELOPMENT OF EE.

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Introduction: CMS is a disease that occurs in populations living at high altitude. It develops after a long time of exposure to high altitude. It is associated to hypoxemia and excessive erythrocytosis. The present study was designed to determine in a population living over 4000 m the risk factors associated to high CMS score (>7points in the questionnaire) and to excessive erythrocytosis. **Methods:** The study has been performed in 557 persons aged 35-75 years and living in Carhuamayo (4100 m). CMS score was assessed through a survey with 7 questions about signs and symptoms. Blood samples were taken to assess cholesterol, acid uric, hemoglobin, hematocrit, glucose, creatinine, vldl, ldl. Also, heart rate, and systolic and diastolic pressure were determined. The intake of maca in the population was measured using a questionnaire. The associations between the biologic param, health and MMC score with maca were analyzed with lineal regression controlled confounding variables. Data were analyzed with STATA V.10. **Results:** Prevalence of excessive erythrocytosis was 22.9% in men and 8.9% in women ($P < 0.01$). The prevalence of higher CMS score was 4.9% in women and 10.4% in men. Age was associated with high scores of signs and symptoms of CMS (OR = 1.05; CI95%: 1.0 - 1.1). Different to other populations, hemoglobin was not increased with age. Premenopausal women have a protective effect in relation to postmenopausal women and men in relation to hemoglobin values. Post menopausal women were characterized by low pulse oxygen saturation and high hemoglobin values. High bilirrubin levels and high uric acid levels were associated to high Hb values ($P < 0.05$). High HDL was associated, low cholesterol levels and high Body Mass Index was associated with low Hb values. Maca consumption was associated with a protective effect to have higher CMS score [OR = .08, CI 95% 0.01 - 0.64]. In women, no difference in Hb levels was found between those consuming and no consuming maca. Using a

regression model we found that in men, maca was associated with low Hb values than in those who do not consume maca. (Coef. − 2.95; CI 95% − 5.63 − 0.262). **Conclusion:** In conclusion, Hb does not increase with age in the population of Carhuamayo. It is possible that this effect in other populations may be due to the presence of maca in the diet. Finally regression models showed that Hb levels may be associated to food intake of maca. **Acknowledgments:** This Study was supported by a Grant from the Fogarty Program of The National Institutes of Health of the United States (NIH Research Grant # 5-D43TW005746-04 funded by the Fogarty International Center, National Institutes on Environmental Health Services, National Institute for Occupational Safety and Health, and the Agency for Toxic Substances and Disease Registry).

85.

PREVIOUS EXPOSURE TO HYPOBARIC HYPOXIA ENHANCES STIMULATED ERYTHROPOIETIN SECRETION IN POLYCYTHEMIC MICE.

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Introduction: Erythropoietin (EPO) is a hormone that is part of a feedback system that adjust the volume of the red cell mass (RCM) to tissue oxygen demands. Increased plasma EPO concentration (pcEPO) accompanies reduced oxygen supply or increased demands, whereas low levels of pcEPO are observed with increased oxygen supply or reduced demands. Therefore, the increment of RCM induced by transfusion (HT mouse) will enhance oxygen supply to tissues and depress EPO secretion when they are subjected to hypobaric hypoxia (HH, a potent stimulus for EPO secretion). When mice made polycythemic by sustained exposure to HH (PH mouse) are re-exposed to the stimulus after a brief period at sea level conditions, they react synthesizing EPO as do normocythemic mice. This study was designed to compare HH-stimulated EPO production in mice in which polycythemia was induced by different maneuvers. **Methods:** Polycythemia was induced by exposure to HH (6350 m) for 2 wks, transfusion of homologuous erythrocytes (0.8 mL of packed erythrocytes ip), sustained exposure to air containing 0.06% CO, sustained administration of rHu-EPO (5.5 IU day/2wk) and repeated injections of phenylhidrazine (60 mg/kg/3 wk) followed by transfusion. After treatments were completed, all animals were exposed to 337 mmHg for 6 h. Blood collected by cardiac puncture and pcEPO measured by immunoassay (R&D systems). **Results:** pcEPO was significantly elevated in normocythemic and PH mice in relation to non-exposed controls, whereas pcEPO was not increased in response to HH in the remaining groups. In another experiment, mice were exposed for 2 wk a different simulated altitudes (0, 2500, 3600, 4600, 5500 and 7300 m). They were re-exposed to HH for 6 hr. Linear regression analysis between the variable X (simulated high altitude) and the variable Y (pcEPO) showed a slope of 563.4 ± 116.1 pg/1000 m and an $r^2 = 0.887$. **Conclusion:** Data indicate that the enhancement of EPO secretion in response to the hypoxic challenge in polycythemic mice only occurs in mice that have been previously exposed to hypoxia. However, the operating mechanism of hypoxia in this state of EPO hypersecretion remains as an open question. **Acknowledgments:** This investigation was supported by a research grant from University of Buenos Aires (UBACYT O-005).

86.

HYPOXIC ADAPTATION AND ADL, QOL AND METABOLIC SYNDROME OF ELDERLY IN QINGHAI PLATEAU IN CHINA.

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Introduction: To reveal the comparison of comprehensive geriatric functions of elderly highlanders in Qinghai plateau in China among 3 different ethnics. **Methods:** Activities of daily living (ADL), screening-based depression, quality of life (QOL) and checking-up of metabolic syndrome including community-based oral glucose tolerance test were assessed in 393 community-dwelling elderly subjects aged 60 years or more (247 Han elderly subjects, 49 Mongolian ones and 97 Tibetan ones) living in Haiyuan and 219 Tibetans in Yushu in Qinghai in China. **Results:** Tibetan elderly highlanders were more disabled in ADL, but had higher QOL than Han elderly ones in Haiyuan. Blood pressure measurements, rate of hypertension and hemoglobin concentrations in Tibetan elderly highlanders were lower than Han ones. Rates of diabetes in elderly highlanders were higher in Tibetan elderly in Yushu than ones in Haiyuan. **Conclusion:** Prevalence of metabolic syndrome in elderly highlanders in Yushu was increasing with urbanization. Further investigation on physiological adaptability to hypoxic environment and human ageing phenomena in global context may open new research frontier for ageing science. **Acknowledgments:** All the budget was supported by RIHN.

87.

HEMOGLOBIN POLYMORPHISM IN ANDEAN DUCKS.

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Introduction: Theory predicts that parallel evolution should be common when the number of beneficial mutations is limited by selective constraints on protein structure. However, confirmation is scarce in natural populations. **Methods:** We studied the major hemoglobin genes of eight Andean duck lineages and compared them to 115 other waterfowl species, including the bar-headed goose (Anser indicus) and Abyssinian blue-winged goose (Cyanochen cyanopterus), two additional species living at high altitude. **Results:** One to five amino acid replacements were significantly overrepresented or derived in each highland population, and parallel substitutions were more common than in simulated sequences evolved under a neutral model. Two substitutions evolved in parallel in the α A subunit of two (Ala-α 8) and five (Thr-α 77) taxa, and five identical βA subunit substitutions were observed in two (Ser-β4, Glu-β94, Met-β133) or three (Ser-β13, Ser-β116) taxa. Substitutions at adjacent sites within the same functional protein region were also observed. Five such replacements were in exterior,

solvent-accessible positions on the A helix and AB corner of the α A subunit. Five others were in close proximity to inositolpentaphosphate binding sites, and two pairs of independent replacements occurred at two different α β intersubunit contacts. More than half of the substitutions in highland lineages resulted in the acquisition of serine or threonine (18 gains vs. 2 losses), both of which possess a hydroxyl group that can hydrogen bond to a variety of polar substrates. **Conclusion:** The patterns of parallel evolution observed in these waterfowl suggest that adaptation to high-altitude hypoxia has resulted from selection on unique but overlapping sets of one to five amino acid substitutions in each lineage. **Acknowledgments:** Funding was provided by the National Science Foundation (DEB-0444748).

88.

MEDSOTEDHF INCREASES ACETYLCHOLINE-INDUCED VASODILATATION IN PULMONARY ARTERIAL RINGS IN BROILERS WITH PAH.

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Introduction: The morphophysiological alterations in pulmonary vessels, the lung and heart have been well described in both mammals and poultry, including broiler chickens, developing pulmonary hypertension. It is accepted that endothelial disfunction triggers the abovementioned conditioned by an excess of endothelin 1 and nitric oxide deficiency. Some endothelial molecules which might intervene in the mechanism of constriction or vasodilatation in PH, have not been studied as yet. **Methods:** The present investigation was carried out as to determine a posible role of the molecule known as hyperpolarizing endothelial derived factor (EDHF) in pulmonary vasodilatation in both, hypertensive (PHB) and non-pulmonary hypertensive broilers (NPHB), using isolated vascular rings. **Results:** Phenylephrine, a α 1-adrenergic agonist, induced similar contractile responses, in vascular rings of PHB and NPHB. Acetylcholine (Ach) induced a greater vasodilatation in vascular rings of PHB as compared to rings taken in NPHB. This response was dependent on the endothelium. Such a response was thought to be independent of nitric oxide action, and given that prostacyclin does not play a direct role in pulmonary vasodilatation in broilers, the effect of endothelial derived hyperpolarizing factor (EDHF) on vascular rings dilatation was studied. To do that, the physiological and pharmacological actions of EDHF were abolished, using a) anti polarizing $K+$ concentrations and b) Charybdotoxin and apamin which are inhibitors of Ca activated $K+$ channels. These two treatments abolished the Ach vascular response in PHB. **Conclusion:** These findings suggest that EDHF could compensate pulmonary vasoconstriction in PHB. Also, that EDHF could be used as to reduce PH and counteract the effect of vasoconstrictors, such as ET-1. **Acknowledgments:** This work was possible by funds given to C.O. by the Dirección de Investigación, Sede Bogotá. Universidad Nacional de Colombia.

89.

EVALUATION OF HYPOXIC TRAINING PROTOCOLS.

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Introduction: Acute exposure to high altitude impairs performance, both aerobic and psychomotor. Consequently preparation of personnel to be deployed to high attitude regions should incorporate a programme of altitude acclimatisation. The aim of the present study was to evaluate the effect of several training programmes on sea level and altitude performance: Live low-Train High (LL-TH), Intermittent Hypoxic Training (IHT), Respiratory Muscle Training (RMT), and Sleep High-Train Low (SH-TL). **Methods:** A total of 50 healthy male subjects were assigned to either a control group, or to one of the four hypoxic training groups. Each group comprised 10 subjects. Subjects conducted daily 1 hr training sessions on a cycle ergometer at a work rate equivalent to 50% of their previously determined peak power output (PPO). During the one month training programme, they maintained their exercise heart rate at a level corresponding to 50% PPO. Before, during and after the training programme, subjects conducted a VO_{2m}ax and Endurance test under hypoxic and normoxic conditions. Endurance was defined as time to exhaustion when exercising on a cycle ergometer at 80% PPO. Complete haemograms were obtained before, during and after the training programmes. **Results:** Compared to the Control group, the LL-TH, IHT and SH-T groups exhibited an improvement ($P < 0.05$) in hypoxic VO_2 max. Only the SH-TL group also demonstrated improvement ($P < 0.05$) in the endurance test. Normoxic performance (VO_2 max, Endurance) improved ($P < 0.05$) only in the SH-TL group. Improvements in pulmonary function (maximum voluntary ventilation, MVV) were observed in the SH-TL and RMT groups. **Conclusion:** Of the methods evaluated, the optimal method for improving sea level and altitude aerobic performance is SH-TL. It initiated the largest improvements in VO_{2m}ax and endurance. **Acknowledgments:** The study was supported, in part, by grants from the Slovene Research Agency, the Ministry of Defence of the Republic of Slovenia, the Sport Foundation (Slovenia) and the Slovene Olympic Committee.

90.

BLUNTED HYPERCAPNIC VENTILATORY RESPONSE IN TRANSGENIC MICE OVEREXPRESSING ERYTHROPOIETIN.

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Introduction: Apart from enhancing red blood cell production, we discovered that erythropoietin (Epo) increases the ventilatory response when oxygen supply is lowered. Upon this condition however, the CO_2 partial pressure is altered in arterial blood. Considering that CO_2 is a potent ventilatory stimulant, we aimed in this work to define the impact of Epo and the resulting excessive erythrocytosis in the control of hypercapnic ventilatory response (HCVR). **Methods:** To this end we used our transgenic mouse line that shows high levels of human Epo in brain and plasma (Tg6), the later

leading to a hematocrit of 80%. **Results:** We found that the HCVR evaluated by plethysmography and electrophysiology (in vivo) techniques was dramatically decreased in Tg6 mice than corresponding WT siblings. Knowing that arterial change of CO_2 is buffered in red blood cells, we reduced the hematocrit of Tg6 mice to normal values by using phenylhydrazine (hemolytic compound). Since phenylhydrazine significantly increased the HCVR of treated Tg6 mice, HCVR was not fully reconstituted. As such, keeping in mind that Epo in brain interacts with respiratory centers, we evaluated the HCVR in a second mouse line overexpressing Epo only in brain, but holding normal levels of hematocrit (Tg21). Interestingly, we found that Epo in brain blunts the HCVR, probably by desensitizing the impact of CO_2 in central chemoreceptors. **Conclusion:** In summary our results suggest that erythrocytosis and high Epo level in brain decrease the ventilatory response induced by the augmentation of arterial CO_2. These findings are relevant for understanding better the respiratory disorders, including those occurring at high altitude.

91.

ELEVATED SERUM ZINC LEVELS AND EXCESSIVE ERYTHROCYTOSIS.

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Introduction: Excessive erythrocytosis and severe hypoxemia are main characteristics of Chronic mountain sickness (CMS), a disorder affecting an important part of the Andean population living at high-altitude. Although the pathophysiology of CMS is in part already known, some factors such as divalent metals could play a significant role on triggering or aggravating this condition. Much of the mining activity in the Andes takes place within or nearby cities, and contamination by metals is considered an important health and environmental problem. Thus, in the present study we examined the relationship between blood Zn_2^+, Cu_2^+, and Pb_2^+ concentration and hematocrit, arterial O_2 saturation (SaO_2), and its impact on the CMS score, in residents of the mining town of Cerro de Pasco, Perú (4340 m). **Methods:** Forty five men, residents of Cerro de Pasco, Peru (altitude 4340 m), were recruited on the basis of the no history of occupational exposure to metals. Exclusion criteria were the presence of pulmonary, cardiovascular or renal disease, recent phlebotomy (less than 1 year) and smoking. CMS was diagnosed based on a scoring system approved by international concensus. Two groups were formed according to their CMS scores. The CMS group was composed by 23 subjects with moderate to severe CMS and hematocrit values greater than 63% (hemoglobin (Hb) concentration > 21 g/dL). On the other hand, the control group was composed by 22 healthy subjects with hematocrit values lower than 59% (Hb concentration < 19.6 g/dL; mean of the population). In both groups, SaO_2 was measured by digital oximetry and a 10 mL blood sample was taken by venopuncture in heparinized Vacutainer tubes. Samples were kept at room temperature (4°C–7°C) and a micro blood sample (10μL) was used to measure hematocrit. Serum Cu_2^+ and Zn_2^+ concentrations were measured by atomic absortion spectrophotometry. Pb_2^+ concentration was measured in 50μL whole blood samples using a Lead Care II blood Lead testing system. **Results:** Serum [Zn_2^+] was significantly higher in the CMS group compared to controls (1.03 vs 0.53 mg/L; $P < 0.001$). Serum [Zn_2^+] and hematocrit correlated positively ($r = .77$, $P < 0.001$). [Zn_2^+] and CMS score had a weaker but significant positive association ($r = .32$, $P < 0.05$) and [Zn_2^+] and SaO_2 correlated negatively ($r = -0.31$. $P < 0.05$). Mean blood [Pb_2^+] values were similar in the control and the study group and no correlation was found between [Pb_2^+] and hematocrit or SaO2. In both groups, serum [Cu_2^+] was within the normal range (0.4-1.4 mg/l) and had similar mean values with no correlation with hematocrit or SaO_2. **Conclusion:** The present study shows that serum [Zn_2^+] is directly associated to increased hematocrit values and high CMS scores in high-altitude residents. Thus, it is possible that besides its pathophysiological mechanisms, increased concentration or certain metals, such as Zn_2^+ and CO_2^+, in residents of high-altitude mining communities in the Andes and worldwide represents an important factor that aggravates excessive erythrocytosis and contributes to CMS. **Acknowledgments:** Programa Internacional de Entrenamiento en Investigación en Salud Ambiental y Ocupacional con Emory University Fondo Concursable para la Investigacion-UPCH.

92.

ADAPTATION TO HIGH-ALTITUDE: AN INSIGHT INTO HYPOXIC SIGNALING PATHWAY.

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Introduction: High-altitude pulmonary edema (HAPE), a non-cardiogenic pulmonary edema characterized by pulmonary hypertension, vasoconstriction and endothelial dysfunction, develops in rapidly ascending sojourners. Acute hypoxic stimulus triggers an adaptive response mediated mainly by hypoxia-inducible transcription factor and associated signaling pathways which actually act as oxygen sensors in the cells. The Tibeto-Burman Ladakhi population residing for several thousand years at high-altitude (>3500 m) is well adapted compared to the sojourners. **Method:** We attempted to understand the integrated response of humans to hypobaric hypoxia condition by using hypoxia signaling pathway PCR array kit having 84 genes of 12 different pathways (SABiosciences corporation, USA) in Healthy highland native (HLs), High-altitude pulmonary edema-resistant controls (HAPE-r), High-altitude pulmonary edema-patient (HAPE-p) and healthy lowland controls (LLCs). Two mL blood was drawn from 12 individuals (3 each of HLs, HAPE-r, HAPE-c and LLCs) for RNA isolation by TRIzol method and cDNA was synthesized to study expression of the genes in the kit. Expression of 38 genes involving 6 pathways was similar in HAPE-r and HLs, differing substantially from HAPE-p which suggested the involvement of these genes in the pathophysiology of HAPE. The expression of stress pathway, signal transduction pathway and Oxidoreductase pathway genes was down-regulated approx. 4-fold, 3.5-fold and 3-fold, respectively, in HAPE-p. Other pathways like Metabolism, ECM related molecules and cardiac excitation-contraction coupling were also down-regulated. Hence, same behavioral pattern of the expression of genes in HAPE-r and HLs is suggestive of the involvement of these pathways in adaptation to low O_2 tension at HA and any deviation from this pattern suggested homeostatic imbalance that results in the occurrence of mountain disorders via HAPE in sojourners. **Acknowledgments:** CSIR, India under SIP0006 provided the financial support.

93.

ADMINISTRATION OF HIGH DOSES OF ZINC LEADS TO HIGHER HEMATOCRIT AND RIGHT VENTRICLE HYPERTROPHY IN RATS EXPOSED TO CHRONIC INTERMITTENT HYPOBARIC HYPOXIA.

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Introduction: It has been reported that high level of zinc could be associated to higher hematocrit and right ventricle hypertrophy (RVH) under chronic hypoxia (CH) in humans. The aim was to evaluate the changes in hematocrit and RVH in rats exposed to Chronic Intermittent Hypobaric Hypoxia (CIHH) (2 days hypoxia/2 days normoxia; $n = 16$), compared to CH ($n = 16$) and a normoxic group (NX; $n = 16$). **Methods:** Hypobaric conditions were simulated in a hypobaric chamber at 428 Torr (4600 m) during 30 days, assessing Htc-Hb and weight. At the end of the study, RVH was measured through RV/LV + S ratio. Plasma zinc level was measured at day 0 and day 30. All rats received a fixed daily amount of food (10 g). Eight rats of each group (treatment groups; randomLy chosen) were administered an intraperitoneally solution of zinc sulfate 1% (5 mg/kg body weight) every 4 days, whereas other 8 of each non-treatment groups received the same amount of saline solution **Results:** Normoxic rat supplemented with zinc showed a weight increase, while in all the others groups decreased. Plasma zinc level decreased in all non-zinc hypoxia exposed groups ($P < 0.001$), and no differences in zinc hypoxia groups was found. All groups under hypoxia showed RVH ($P < 0.05$), where the zinc HC depicted the more severe grade of RVH ($P < 0.05$). Hematocrit and hemoglobin increased in all hypoxia groups. A greater Htc-Hb increase in Zinc-CIHH compared to non zinc CIHH was seen ($P < 0.05$), but not reaching CH levels. Interestingly, an inverse correlation between plasma zinc level at day 30 and Hb day 30 ($r = -0.68$; $r^2 = 0.46$; $P < 0.001$) and a correlation between RVH and Hb day 30 ($r = 0.76$; $r^2 = 0.58$; $P < 0.001$), were found. **Conclusion:** In conclusion, under hypobaric hypoxia, administration of high doses of Zinc would lead to higher hematocrit, especially in CIHH; and higher rates of RVH and lower plasmatic zinc levels. Therefore, these results, suggest a zinc influence under hypoxia whose mechanisms could be a counter regulatory effect in vasodilatation via protein C-quinase, and/or an alteration in Metallothionein level and zinc binding. **Acknowledgments:** By grants from GORE-TARAPACA and UNAP.

94.

A FIRST CHARACTERIZATION OF WIND CHILL AND FROSTBITE ON MOUNT EVEREST.

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Introduction: There are increasing numbers of adventurers, armed forces personnel and indigenous populations that are being exposed to high altitude environments. These environments are characterized by low barometric pressure, cold temperatures and high windspeeds; and as a result, there is an elevated risk of both hypoxia and hypothermia. With regard to hypothermia, little is known about the high altitude environmental conditions that predispose people to the risk of cold injury. Here we characterize for the first time this risk near the summit of Mount Everest. **Methods:** We utilize a validated meteorological dataset that accurately represents the weather dynamics at the South Col of Mount Everest. We previously used the same data to document the extreme conditions during the 1996 'Into Thin Air' storm, which had the highest mortality of any event in Everest's history. We also employ wind tunnel studies of heat loss from human subjects that has lead to new expressions for two widely used cold injury risk param; the wind chill temperature and the frostbite time. The wind chill temperature is the temperature in still air that would result in the same steady state facial heat loss as occurs at a given temperature and windspeed; while the frostbite time is the time it takes facial flesh to freeze. These expressions were derived for sea-level conditions and there are a number of high altitude environmental and physiological factors that are not incorporated. We are nevertheless confident that net effect of these additional factors is such that the existing expressions provide valid estimates as to the risk of high altitude cold injury. **Results:** Throughout the year, the mean summit wind chill temperature is always lower than $-25^{\circ}C$ and the mean frostbite time is always less than 20 minutes. During the winter months, the mean summit wind chill temperature can be as low as $-65^{\circ}C$ with frostbite times typically being less than 2 minutes. Most summit attempts occur during the month of May and during this period, climbers near the summit of Mount Everest would typically experience wind chill temperatures of $-50^{\circ}C$ and frostbite times of 5 minutes. The 'Into Thin Air' storm was responsible for the deaths of 8 climbers during a 2-day period in May 1996. During the storm, the wind chill temperature was as low as $-58^{\circ}C$ and the frostbite time was less than one minute. **Conclusions:** Our results provide additional confirmation as to the extreme environmental conditions experienced by those attempting to summit Mount Everest. Average wind chill temperature and frostbite times are low throughout the year confirming that hypothermia and frostbite are important risk factors near the summit of Mount Everest. Mean conditions are often not characteristic of what occurs during high impact storm events. Using the 'Into Thin Air' storm as an example, we found values during this event approach the mean values typically observed during the depth of winter. This suggests that the risk of exposure is significantly increased during high impact storm events. Finally, our results offer a warning that cold injury is a significant risk even in less extreme high altitude environments. **Acknowledgments:** Funding for this research was provided by the Natural Sciences and Engineering Research Council of Canada.

95.

ACCLIMATISATION TO HIGH ALTITUDE HYPOXIA IN HUMAN SKELETAL MUSCLE IS DRIVEN BY CO-ORDINATED CHANGES IN MITOCHONDRIAL ENERGETICS AND FATTY ACID METABOLISM.

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Introduction: Elite mountaineers returning from high altitude have decreased skeletal muscle mitochondrial densities. Similarly, mitochondrial autophagy in hypoxic cultured mammalian cells has been suggested to decrease production of harmful reactive oxygen species (ROS) whilst a switch to anaerobic glycolysis maintains ATP levels. The in vivo mechanism by which human skeletal muscle mitochondria respond to chronic hypoxia, however, remains poorly understood. **Methods:** Here we measured levels of mitochondrial electron transport chain (ETC) proteins, and metabolic

regulators in skeletal muscle biopsies from 12 healthy individuals before and after an ascent > 6400 m on Mt. Everest. Biopsies were sampled at sea level, prior to departure, and at Everest Base Camp (5300 m) after ~3 months acclimatisation. **Results:** Complexes II, III and V remained unchanged. Levels of PGC-1α, a regulator of mitochondrial biogenesis, were decreased by 22% in the same individuals ($P < 0.05$), and levels of the transcription factor peroxisome-proliferator activated receptor α (PPARα), which promotes fatty acid oxidation, increased by 52% ($P < 0.05$). There was no difference in levels of hypoxia-inducible factor 1α (HIF1α), perhaps because the post-ascent biopsies were taken when the subjects had returned to a lower altitude than that to which they had acclimatised. **Conclusion:** We therefore suggest that acclimatisation to high altitude is associated with specific, co-ordinated changes in skeletal muscle mitochondrial metabolism aimed at decreasing oxygen consumption and ROS production, but maintaining fatty acid oxidation, perhaps to spare limited glucose reserves for other organs. **Acknowledgments:** We wish to thank our colleagues and collaborators in the Caudwell Xtreme Everest Research Group, in particular the Project Manager Kay Mitchell.

96.

PLASMATIC LEVELS OF BRAIN NATRIURETIC PEPTIDE (BNP) AT THE SEA LEVEL AND AT THE HIGH ALTITUDE EXPOSURE.

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Introduction: The Brain natriuretic peptide (BNP) is a protein released by the heart tissue in response to stretching of heart muscle cells and cardiac output. If we considered the hypoxemia produces cardiovascular homodynamic changes, it could change the plasma levels of BNP. **Methods:** We evaluated the effect of acute hypoxemia on BNP blood levels in 14 healthy subjects (8 females and 6 males), the plasmatic BNP was measured first at the sea level and after they were exposed to high altitude 3280 m to the 24 and 72 hours. We proceeded to quantify the BNP in the AXSYM immune analyzer by the method enzymatic immune of micro particles (MEIA). **Results:** At the sea level, the mean of BNP was in females $33.39\,pg/mL \pm 10.05$ and $20.63 \pm 10.19\,pg/mL$ in males. After 24 hours in high altitude, the mean was in females $40.48 \pm 11.05\,pg/mL$ ($p = 0.15$) and $53.80 \pm 14.89\,pg/mL$ in males ($P = 0.01$). After 72 hours the mean was in females $42.70 \pm 11.46\,pg/mL$ ($P = 0.01$) and $21.93 \pm 8.74\,pg/mL$ in males ($P = 0.83$). **Conclusion:** Acute exposure to altitude increases BNP plasma values in both the male and the female; we observed a faster response in males (24 hours) than in females (72 hours). **Acknowledgments:** To Research Unit, Faculty of Medicine, UNMSM for his contribution to the funding of this study. To Dr. Guillermo Ríos Ríos, Chief Laboratory of the Clinic "San Pablo" for the facilities extended for the completion of this work.

97.

TIME-COURSE EXPRESSION OF ENDOTHELIAL, INDUCIBLE NITRIC OXIDE SYNTHASE, AND NYTROTIROSINES IN THE CAROTID BODY OF RATS EXPOSED TO INTERMITTENT HYPOXIA.

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Introduction: Nitric oxide (NO) has been involved in the potentiaton of carotid body (CB) chemosensory responses induced by acute hypoxia in rats exposed to chronic sustained hypoxia. Indeed, rats exposed to chronic hypoxia showed an increased expression of inducible nitric oxide synthase (iNOS) in the CB. Since chronic intermittent hypoxia (CIH) also enhances CB chemosensory responses to hypoxia, we hypothesized that an increased level of NO due to changes in the expression of nitric oxide synthases isoforms may contribute to the potentiated chemosensory responses. **Methods:** We recorded CB chemosensory responses to hypoxia in rats exposed to 7, 14 and 21 days of CIH (5% O_2 for 20 s, applied 12 times/hr, 8 hrs/day). The CBs from CIH and sham rats were harvested, fixed in paraformaldehyde 4%, included in paraffin and cut in 5 μm sections for immunohistochemical detection of endothelial nitric oxide synthase (eNOS) and iNOS. 3-nitrotyrosine formation was measured as index of oxidative stress due to peroxinitrite formation induced by high NO levels. **Results:** Exposures to 7, 14 and 21 days of CIH potentiated the CB chemosensory responses to hypoxia. We found a decrease in the eNOS expression at the 7th day of CIH-exposure, which tended to recover after 21 days of CIH. By contrast, the iNOS expression increased at the day 21 of CIH exposure. In addition, we found that the immunoreactive expression of 3-nitrotyrosine residues in the CB was higher in rats exposed to 7, 14 and 21 days of CIH. **Conclusion:** Present results showing a marked increase of 3-nitrotyrosine in the CB suggest that NO react with the superoxide radical to form peroxynitrite. Thus, NO may contribute to the chemosensory potentiation through nitration of tyrosine residues. This interpretation agrees with our previous finding that treatment of CIH-rats with an antioxidant prevented both chemosensory potentiation and the increased 3-nitrotyrosine formation in the CB. **Acknowledgments:** FONDECYT 1100542 and Interdisciplinary Grant 04-2009 VRAID, PUC.

98.

CONTRASTING EFFECTS OF SUSTAINED AND INTERMITTENT HYPOXIA ON HERG K^+ CHANNEL TRAFFICKING: ROLE OF CALCIUM ACTIVATED CALPAINS.

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Introduction: Hypoxia i.e., decreased availability of oxygen, occurs under a variety of patho-physiological conditions. People experience sustained hypoxia (SH) during sojourns at high altitude whereas people living at sea level often experience intermittent hypoxia (IH) as a consequence breathing disorders manifested as recurrent apneas. K^+ channels control a wide variety of cellular responses to hypoxia. Acute hypoxia affects the gating properties of K^+ channel currents and prolonged hypoxia profoundly influences the synthesis, processing and trafficking of K^+ channel protein to the cell surface. Human ether-go-go-related gene (hERG) channel is one such K^+ channel which has been implicated in a wide variety of cellular functions including regulation of cell excitability. In the present study, we studied the effects of SH and IH on hERG protein trafficking and assessed the underlying mechanisms. **Methods:** Experiments were performed on neuroblastoma cells (SH-SY5Y) exposed to SH (1% O_2 for 2 and 4 days) or IH (1% O_2 for 30 sec followed by 21% O2 for 5 min, 6 hrs/day/2 days). hERG channel protein expression and localizations were determined by western blots and immunocytochemistry, respectively. hERG currents were monitored by patch clamp. **Results:** IH decreased the expression of both the surface and the endoplasmic reticulum

(ER) forms of hERG in a stimulus-dependent and irreversible manner. In contrast, SH down- regulated surface expression of hERG protein with accumulation of the ER form which was stimulus dependent and reversible. hERG tail currents monitored by patch clamp technique showed that both IH and SH decreased currents by 40-50%. Calcium chelator (BAPTA) and calpain protease inhibitors (ALLM, PD90185) prevented IH-evoked but not SH-evoked degradation of hERG. IH exposed cells exhibited increased basal calcium levels and calpain activity. **Conclusion:** These studies demonstrate that SH and IH regulate hERG expression and function by different mechanisms. **Acknowledgments:** Supported by grants from NIH-HL-90554.

99.

EFFECT OF EXERCISE AT MODERATE ALTITUDE ON SECRETORY IGA AND SALIVARY CORTISOL.

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Introduction: Intense exercise can cause a suppression of secretory IgA (sIgA) levels, increasing the risk of infection and this could be due to the immunosuppressive effects of cortisol. Our objective was to asses if the circadian rhythm of cortisol and sIgA levels were altered by intense exercise at moderate altitude. **Methods:** To test this hypothesis 4 male climbers, who had performed a preliminary super-aerobic training, were evaluated. The climb lasted 5 days reaching a maximum height of 4270 m. Blood samples were taken before and after the voyage. During the ascent, saliva samples were collected every morning and every nigth in sterile tubes and were kept at a temperature below to 10 °C. Cortisol and salivary cortisol were measured using Cobas ® autoanalyzer with reagents from Roche® brand and the determinations of IgA and sIgA were made by Immunonephelometry in Array360® automatized equipment from Beckman Coulter ®. Acute Mountain Sickness (AMS) was assessed by the Lake Louise Score. Results are presented as means and SD. **Results:** Participants showed no prior deficit in cortisol: 14.7 (3.45) mg/dL and all kept the circadian rhythm: morning: 0.87 (0.37) mg/dL vs. night: 0.32 (0.22) mg/dL ($P < 0.01$) regardless the fact that 2 of them presented moderate AMS of 4 and 5 points that were normalized with acclimatization. The morning salivary cortisol showed higher values at higher altitudes (r: 0.27). None of the participants had previous deficit of IgA or sIgA: 162 mg% (SD: 52.3) and 17.9 mg% (SD. 8.64) respectively. sIgA morning values were higher than at night: 21.03 mg% (SD. 18.9) vs. 9.88 mg% (SD 7.50) $p = 0.03$. The correlation coefficient between IgAs and salivary cortisol was positive with $r = 0.35$. **Conclusion:** The statistical power is low due to the number of climbers. This fact does not allow us to make firm conclusions, but the circadian rhythm of cortisol was altered neither by intense exercise at moderate altitude nor by moderate AMS (that two of the climbers suffered). Increased levels of salivary cortisol did not affect the production of secretory IgA.

100.

SLEEP IN HYPOXIA: IMPACT ON HIGH ALTITUDE SICKNESS.

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Introduction: The aim of this study was to investigate sleep in simulated altitude in patients with recurrent life-threatening altitude intolerance (AI i.e. severe acute mountain sickness and/or pulmonary or cerebral oedema), in comparison with paired controls with a good tolerance to altitude (similar age, gender, physical fitness, altitude experience). **Methods:** 12 AI subjects recruited for the study and 12 paired controls underwent two full night polysomnography (i) in hypoxia ($FiO_2 = 14.5\%$) versus (ii) normoxia in a similar normoxic tent. Poïkilocapnic and isocapnic ventilatory response to hypoxia (pHVR and iHVR) were determined as well as the hypercapnic ventilatory response (HCVR). **Results:** There was no difference of sleep in normoxia. None of the subjects displayed any sleep disorders. In hypoxia significant differences were observed: (i) mean and minimal oxygen saturation (SpO_2) were lower in AI ($81.6 \pm 2.2\%$ vs. $86.3 \pm 2.06\%$, $P = 0.003$; $73.8 \pm 3.12\%$ vs. $78.4 \pm 2.59\%$, $P = 0.008$, in AI and controls respectively). Conversely, Apnea/Hypopnea Index (AHI) was higher in controls (39.4 ± 20 vs. 19.9 ± 18.4/h, $P = 0.04$). Sleep structure was also modified: stage I was reduced in AI (9.8 ± 4.6 % vs. 16.1 ± 7.9 % of Total Sleep Time (TST) in AI and controls respectively, $P = 0.03$) with a greater sleep stage III/IV (19.7 ± 7.2 vs. 14.0 ± 6.6 % TST, $P = 0.02$). AI subjects had a lower iHVR (iHVR5: 0.40 ± 0.51 vs. 0.90 ± 0.49 vs. l/min/$\%SpO_2$, $P = 0.01$). There was no difference in pHVR. HCVR showed a higher central chemosensitivity in control vs AI (slope: 4.30 ± 1.86 vs 2.60 ± 1.49 l/min/mmHg, $P < 001$; ventilatory threshold 45.1 ± 3.5 mmHg vs. 49.9 ± 2.8 mmHg, $P = 0.01$). Spontaneous eucapnic $PETCO_2$ was lower in control than in AI subjects (35.9 ± 2.5 mmHg vs. 40.2 ± 2.5 mmHg, $P < 0.001$). **Conclusion:** These findings indicate that in spite a higher AHI, tolerance to altitude is associated with a better preserved mean SpO_2. Peripheral response to hypoxia, as well as central chemosensitivity to CO_2 are higher in well adapted subjects. Collectively, our findings provide new insights into physiological mechanisms of high altitude sickness. **Acknowledgments:** This research was supported by the Grenoble University Hospital Research Clinic Administration. Thanks to all who made this study possible.

101.

NON-HEMATOPOIETIC ACTIVITY OF ENDOGENOUS ERYTHROPOIETIN.

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Introduction: Erythropoietin (EPO), the principle regulator of erythropoiesis, is upregulated in response to hypoxic stress resulting in increased red blood cell production to increase oxygen delivery. However, EPO receptor (EpoR) is also expressed in other tissue including high level in embryonic brain of wild type (WT) mice. **Methods:** Deletion of endogenous EpoR in mice is used to determine EPO activity beyond hematopoietic tissue. **Results:** Mice that lack EpoR die in utero of severe anemia and also exhibit increased brain apoptosis. Selective rescue of EpoR to restore expression in erythroid tissue but not in brain results in viable mice with decreased neurogenesis and increased susceptibility to insult, suggesting neural activity of endogenous Epo. Unexpectedly, mice expressing EpoR only in erythroid cells (Tg mice) also exhibit glucose intolerance and increased fat mass accumulation. At 6 months Tg mice had 25%-30% more body mass and were insulin resistant. No differences in food intake were observed, but Tg mice exhibited increased energy efficiency and decreased energy expenditure. EPO treatment in WT mice stimulated erythropoiesis and also decreased fat mass accumulation and blood glucose. EPO treatment in Tg mice increased hematocrit, but the change in fat mass accumulation compared with saline treatment observed in WT mice was not evident. In contrast to other non-hematopoietic tissue, we

observed high EpoR expression in white adipose tissue (WAT). To study this further, we examined an in vitro model of adipogenesis using primary mouse embryonic fibroblasts (MEF). In cultures of differentiating MEF cells, EPO inhibited adipogenesis, activated signal transduction pathways and increased PPARgamma phosphorylation, a transcription factor required for adipogenesis. **Conclusion:** These data indicate that in addition to erythroid tissue, EPO signaling is functional in select non-hematopoietic tissue such as brain and WAT, and contributes to development, maintenance or stress response. **Acknowledgments:** Support for this work was provided by the National Institute of Diabetes and Digestive and Kidney Diseases Intramural Research Program.

102.

STRONG ASSOCIATION BETWEEN POLYCYTHEMIA AND GLUCOSE INTOLERANCE IN ELDERLY HIGH-ALTITUDE DWELLERS IN ASIA.

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Introduction. Objective: To reveal the association between glucose intolerance and polycythemia in elderly people living in two highland areas in Asia. **Methods:** Participants underwent a 75-g OGTT to screen for diabetes or impaired glucose tolerance based on World Health Organization criteria. Polycythemia was defined as Hb $\geq$ 18 g/dL for males and $\geq$ 16 g/dL for females. The subjects were 209 Tibetans (mean age, 66.1 years) living in Jiegu Town in Yushu, Qinghai, China (3700 m), and 117 Ladakhi (69.3 years) living in Domkhar Village, Ladakh, India (2900–3800 m). **Results:** We found a strong association between polycythemia and glucose intolerance in elderly highlanders living in two distinct regions of Asia, despite differences in the prevalence of obesity and hypertension with the different influence of socioeconomic globalization. **Conclusion:** There appear to be two reasons for the association between polycythemia and glucose intolerance. First, glucose intolerance may cause deterioration of blood vessels, metabolic dysfunctions and subsequent insufficient supply of oxygen to the human body; polycythemia might develop as a compensatory response. Second, people with polycythemia seem to be particularly vulnerable to glucose intolerance, suggesting poorer adaptation to hypoxia than in people without polycythemia, because Tibetan people are known to have acquired adaptive way to hypoxia without polycythemia. **Acknowledgement:** All the budget was supported by RIHN.

103.

GENETIC LANDSCAPE OF HIGH-ALTITUDE ADAPTATION/MALADAPTATION IN INDIAN POPULATION.

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Introduction: Genetic and environmental factors contribute interactively to High-altitude (HA) adaptation/maladaptation, a multifactor trait. The candidate gene and high-throughput approaches have achieved considerable success in elucidating individual's predisposition and provided insight into the dynamics of genome-evolution. Confluencing both the traditional and contemporary approaches, we investigated polymorphisms of several candidate genes viz: ACE, AGT, NOS3, CYP11B2, EDN1 and ADRB2 in healthy native Himalayan-highlanders (HLs) and sojourners i.e. High-altitude pulmonary edema-resistant control (HAPE-r) and HAPE-patient (HAPE-p). **Methods:** Individual allele/genotype, haplotypes, genotypes/gene-gene interactions and relevant biomarkers were analyzed. Further in a genome-wide study, we compared > 4000 SNPs distributed across the entire genome of two ethnically similar populations contrasting altitude residence. **Results:** The allele/genotype distribution at the same locus varied significantly among these groups. The alleles ACE I, NOS3 894 g and 4b, EDN-1 2288 g and CYP11B2 –344T were higher in HLs than HAPE-r ($P < 0.05$). Whereas, over-representation of D, 894T and 4a, and 2288T alleles was obtained in HAPE-p (p between 0.03 and 0.002) when compared against HAPE-r. Genotype-interactions revealed over-representation of GGbb of NOS3, II/GG of ACE/END1 in HAPE-r than HAPE-p ($P < 0.05$). The higher ACE activity, endothelin and aldosterone levels and lower nitric oxide level correlated with respective variants in HAPE-p ($P < 0.0001$). The MDR model depicted ADRB2 polymorphisms 46A/G, 79C/G and 523C/A as the best disease predicting combination; whereas, greater power was demonstrated by ADRB2 haplotypes to predict HAPE. The genome-wide comparison corroborates difference in SNPs of genes or regions close to the above candidate genes. **Conclusion:** The participation of vascular homeostasis genes in adaptation to HA environment is perceptible. The high throughput genetic tools have laid a platform to diagnose genetic markers of predisposition to HA adaptation/mal-adaptation. **Acknowledgments:** CSIR, India under SIP0006 provided the financial support.

104.

HIGH ALTITUDE EXPEDITION: MARKERS OF INFLAMMATION DURING HYPOBARIC HYPOXIA.

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Introduction: The role of inflammation during high altitude exposure has always been of interest. So far, studies were limited to very small cohorts or experimental settings that did not reflect authentic conditions. A Swiss research expedition to mount Muztagh Ata (7549 m) in Western China now allowed for a comprehensive approach to inflammation in hypobaric hypoxia. **Methods:** Serum samples from 34 healthy mountaineers were taken at a pre-expedition examination in Zurich (409 m) and at four camps ranging from 4497 m to 6865 m of altitude, frozen immediately after centrifugation and stored until final analysis. Specific serum param of inflammation were quantified by flow-cytometry using Luminex beads (cytokines such as IL-6, TNF-α, and INF- Γ or immunoassays (CRP). Furthermore, a mass spectrometry-based targeted metabolomics platform was used to analyze a set of endogenous

inflammation-related metabolites comprising (lyso-)phospholipids, free fatty acids, eicosanoids and other oxidation products of polyunsaturated fatty acids (PUFAs). After statistical analysis, data were mapped onto biochemical pathways for further interpretation. **Results:** Differential analysis of pro-inflammatory cytokines and metabolites revealed a specific pattern of altitude-related changes. Levels of prostaglandins and leukotrienes significantly increased in an early phase during high altitude exposure. This corresponded well with changes in serum levels of CRP, TNF-α, and IL-6. Furthermore, the metabolic cascade leading from the release of PUFAs from phospholipids by phospholipases to the synthesis of inflammation mediators by cyclooxygenases, lipoxygenases or reactive oxygen species could be described in detail. Due to optimal sample quality, even peroxidic intermediates of arachidonic acid oxidation could be quantified. **Conclusion:** Targeted metabolomics facilitated a high-resolution analysis of the inflammatory cascades during prolonged hypobaric hypoxia. The findings correlated well with standard inflammation param and cytokines but allowed for a more differentiated view on the differential regulation of the involved pathways.

105.

METABOLOMICS OF HYPOBARIC HYPOXIA: OXIDATIVE STRESS AND ITS METABOLIC SIGNATURE.

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Introduction: There is increasing evidence that hypoxia itself causes oxidative stress. Experimental settings such as ischemia in animal models or observations in hypobaric chambers cannot reflect the actual effects of prolonged hypoxic conditions. To study physiological alterations under more authentic circumstances we collected samples from 34 healthy mountaineers during a Swiss research expedition to mount Muztagh Ata (7549 m) in Western China. **Methods:** Serum samples were taken at a pre-expedition medical examination in Zurich (409 m), at the base camp (4497 m), at camp 1 (5533 m), at camp 2 (6265 m), and at camp 3 (6865 m), frozen immediately after centrifugation and stored until final analysis. A mass spectrometry-based targeted metabolomics platform comprising FIA-MS/MS, HPLC-MS/MS, and GC-MS was used to quantify several hundred endogenous metabolites, e.g. amino acids, acylcarnitines, biogenic amines, fatty acids, phospho- and sphingolipids, eicosanoids and other oxidized polyunsaturated fatty acids. After statistical analysis, data were mapped onto biochemical pathways for further interpretation. **Results:** Comprehensive metabolomics analysis revealed dramatic hypoxia-associated effects on various pathways. In particular, we observed a set of highly significant changes related to oxidative stress such as increased sulfoxidation of methionine residues, increased omega-oxidation of fatty acids, increased lipid peroxidation, and a shift in the sphingolipid pattern towards hydroxylated species. Moreover, functional impairment of enzymes that require oxidation-sensitive co-factors could be demonstrated; specifically, tetrahydrobiopterin-dependent enzymes such as phenylalanine hydroxylase or nitric oxide synthase (NOS) showed significantly lower activities. **Conclusion:** Quantitative analysis of intermediary metabolism proved that prolonged hypobaric hypoxia indeed causes pronounced systemic oxidative stress. This novel approach extends the mechanistic understanding of hypoxia-related oxidative damage and may identify diagnostic biomarkers and new targets for therapeutic intervention.

106.

VENTILATORY AND CARDIAC ADJUSTMENTS IN PLATEAU PIKA (OCHOTONA CURZONIAE).

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Introduction: We assessed long term cardiac and ventilatory adjustment in small lagomorphs living in high altitude and intermittently exposed to hypoxic burrows: the Plateau Pikas (ochotona curzoniae). **Methods:** We measured maximal heart rate in rats and Pikas, and we evaluated the parasympathetic and sympathetic control of the heart in these animals by studying dose response curves to atropine and isoproterenol and mRNA expression of beta-adrenoceptors (beta-AR) and muscarinic receptors (M1 and M2). VEGF mRNA expression and morphological adaptations of the heart to long term exposure to hypoxia were also measured. Then, we evaluated the effects of hypoxia on ventilation by using plethysmography in conscious Pikas and control low altitude and high altitude acclimatized rats. Hypoxic ventilatory response (HVR) and ventilatory acclimatization to hypoxia were measured after nNOS inhibitor and dopamine antagonist injections in Pikas at their living altitude and during a hypoxic challenge. **Results:** Pikas showed a blunted parasympathetic and sympathetic modulation response of the heart. These functional findings were reinforced by the lower mRNA expression of both beta1-AR and M2 receptors observed in Pika hearts as compared to rats. Pikas also exhibited a left ventricular hypertrophy as compared with rats when adjusted for body weight. They also displayed a higher VEGF mRNA expression suggesting a greater vascularisation of the heart. We observed an improvement in ventilation in Pikas as compared to non- or acclimatized rats which is the consequence of an increase in tidal volume, without change in HVR. Dopamine does not seem to have any effect on long term ventilatory adaptation in this animal. Conversely to our initial hypothesis, the sensitivity to acute hypoxia in Pikas seems to be limited via a nNOS dependant mechanism. **Conclusion:** All these results suppose a better cardiorespiratory efficiency in Pikas, limiting ventilation and improving cardiac outflow during severe acute hypoxia occurring in burrows on high altitude Tibetan plateaus. **Acknowledgments:** Supports: National Basic Research Program of China, No.2006CB504100, National Natural Science Foundation of China, No. 30393133 (to Pr Ge Ri-Li), Agence Nationale de la Recherche No. 08-GENOPAT-029, and Bureau des Relations Internationales of the Paris 13 University. We thank the Officials of the Kekexili Reserve.

107.

CHANGES IN ENERGY METABOLISM DURING HIGH ALTITUDE EXPOSURE: A METABOLOMICS APPROACH.

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Introduction: High altitude represents a challenging environment. Prolonged hypoxia, huge demand for energy, and accelerated dehydration are counter-acted by various physiological alterations. Details of the metabolic adaptation to these conditions have not been studied because observations in hypobaric chambers could not reflect the prolonged exposure to hypoxia and the increased physical activity at the same time. **Methods:** A Swiss research expedition to mount Muztagh Ata (7549 m) in Western China now allowed for a comprehensive study of alterations of energy metabolism in hypobaric hypoxia. Serum samples from 34 healthy mountaineers were taken at a previous examination in Zurich (409 m) and at camps ranging from 4497 m to 6865 m of altitude, frozen immediately after centrifugation and stored until final analysis. A targeted metabolomics platform comprising FIA-MS/MS, HPLC-MS/MS, and GC-MS was used to quantify several hundred endogenous metabolites. After statistical analysis, data were mapped onto biochemical pathways for further interpretation. **Results:** Metabolomics demonstrated that the metabolic situation during the ascent was generally catabolic and characterized by moderate proteolysis. Several other adaptations to the increased energy demand took place. Glycolytic activity was hardly upregulated but hypoxia-induced activation of lactate dehydrogenase led to a drastic depletion of pyruvate and a transient increase in lactate production. The most significant alteration was a continuously increased uptake of fatty acids into the mitochondria as shown by elevated levels of long-chain acylcarnitines. This was perfectly matched by acetylcarnitine mirroring increased throughput of beta-oxidation for energy generation. **Conclusion:** The findings of this first detailed analysis of energy metabolism at high altitudes demonstrated that, despite optimal nutrition, the increased energy demand was not primarily compensated by glycolytic activity. Even under hypoxic conditions, beta-oxidation of fatty acids was strongly activated which might explain the demand for food rich in fats that most mountaineers experienced.

108.

PHYSIOLOGICAL RESPONSES TO INTERMITTENT HYPOXIA IN HEALTHY HUMANS: IMPLICATIONS FOR OBSTRUCTIVE SLEEP APNEA AND PERIODIC BREATHING.

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Introduction: We have recently shown in a small group of patients with obstructive sleep apnea (OSA) a negative association between the severity of OSA and associated hypoxemia, and the cerebral blood flow response to hypoxia (Foster, G.E. et al., Am. J Resp. Crit. Care Med. 175:720-25, 2007). Our data indicated that cerebrovascular sensitivity to hypoxia, which determines the capacity of the cerebral vessels to respond and compensate for reduced oxygen supply, is reduced in patients with OSA but increases to normal levels after treatment of OSA with continuous positive airway pressure. **Methods:** More recently, we have developed a novel experimental human model of intermittent hypoxia to investigate the mechanisms underlying this association. Our human model represents a substantial improvement relative to previous animal and human models that have been used to evaluate potential mechanisms for the association between OSA and cardiovascular disease. The objective of this presentation is to review the physiological responses that are elicited by our model of intermittent hypoxia. **Results:** Data obtained from our model reveal adaptive cerebrovascular, cardiovascular, and respiratory responses to intermittent hypoxia that resemble those observed in OSA, and are reversible within days after termination of exposure to intermittent hypoxia. Moreover, new data emerging from our group and others will be presented to describe some of the molecular changes that take place in response to intermittent hypoxia (i.e., erythropoiesis, angiogenesis, oxidative stress, endothelial dysfunction), and the mechanisms that may underlie these adaptive processes in healthy humans will be examined. **Conclusion:** Finally, the implications for patients with OSA and periodic breathing will be discussed. **Acknowledgments:** Funding Sources: This project was funded by the Alberta Heritage Foundation for Medical Research (AHFMR), the Canadian Institutes of Health Research (CIHR) and the R. Samuel McLaughlin Travelling Medical Education Fund (University of Calgary).

109.

EXAGGERATED EXERCISE-INDUCED PULMONARY HYPERTENSION CAUSES LUNG WATER ACCUMULATION AND RIGHT VENTRICULAR DYSFUNCTION IN PATIENTS WITH CHRONIC MOUNTAIN SICKNESS.

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Introduction: Chronic mountain sickness (CMS) is characterized by exaggerated exercise-induced pulmonary hypertension. Evidences suggest that exercise may cause lung fluid accumulation at high altitude. We hypothesized that, in patients with CMS, exercise causes lung fluid accumulation. **Methods:** In 21 male CMS patients and 20 matched healthy controls born and permanently living in La Paz (Bolivia, 3600 m) we assessed with echocardiogram, pulmonary artery pressure (PASP), right and left ventricular function and ultrasound lung comets (ULCs, a marker of lung fluid accumulation) at rest and during mild bicycle exercise (10 min at 50W). **Results:** CMS patients presented a more than 2-fold greater exercise-induced increase in pulmonary artery pressure than controls (17.1 ± 8.3 vs 7.2 ± 7.9 mmHg, $P = 0.003$). This exaggerated PASP response to exercise was associated with a roughly 3-fold greater increase in UCLs in patients with CMS than in controls (6.3 ± 5.1 vs. 2.1 ± 5.3, $P < 0.05$), and there existed a significant relationship between PASP and UCLs ($r = .44$, $P < 0.001$). Finally, TDI on lateral tricuspid annulus decreased during exercise in patients with CMS (from 13.2 ± 3.2 to 11.5 ± 2.1 cm s -1, $P = 0.03$), but increased in controls (from 13.1 ± 2.9 to 14.9 ± 2.6 cm s -1, $P = 0.04$). Left ventricular function remained unaltered in the 2 groups. **Conclusions:** in CMS, mild exercise is associated to abnormal rise in PASP, lung water accumulation and right-ventricular dysfunction, which all may contribute to exercise intolerance in these subjects.

110.

COMPARISON OF METABOLIC RISK FACTORS BETWEEN TIBETAN AND HAN AT AN ALTITUDE OF 3000 M.

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Introduction: To understand the metabolic risk factors' distribution for different ethnic groups of the elderly in the plateau region, an investigation and analysis was done for Tibetan and Han Chinese in Haiyan County, Haibei Tibetan Autonomous Prefecture, Qinghai Province. **Methods:** Two hundred and seventy-eight of Tibetan and Han residents with over the age of 60 were analyzed for metabolic risk factors as a random sampling method in Haiyan County, Qinghai Province (average elevation ≥ 3000 m). Among them, 157 are Han Chinese aged 66.94 ± 8.70 years, male 65 and female 92 while Tibetan are 121 cases aged 67.75 ± 7.71 years old, male 71 and female 50. The average plateau life was 66.17 ± 4.51 years. **Results:** The Tibetan old fasting insulin (FINS) levels (6.66 ± 5.16) umol/L, body mass index (BMI) (24.9 ± 4.60) kg/cm^2, and cholesterol (TC) levels (5.85 ± 1.30 mmol/L) which were higher than those Han Chinese (5.14 ± 3.67) umol/L, (23.50 ± 3.95) kg/ cm^2, (5.11 ± 1.16) mmol/L, $P < 0.05$; triglyceride (TG) levels (1.35 ± 0.67) mmol/L was lower than the Han Chinese (1.71 ± 0.92) mmol/L, $P < 0.05$; The Tibetan older women TC levels (6.11 ± 1.52) mmol/L which was higher than the Han Chinese (5.30 ± 1.20) mmol/L; TG levels (1.27 ± 0.46) mmol/L was lower than the Han Chinese (1.70 ± 0.68) mmol/L, $P < 0.05$; the Tibetan older men FINS, BMI, and TC levels (6.73 ± 5.96) umol/L, (24.89 ± 4.63) kg/cm^2, (5.53 ± 0.96) mmol/L which were higher than the Han Chinese (3.95 ± 2.44) umol/L, (23.25 ± 2.96) kg/cm^2, (4.85 ± 1.06) mmol/L, $P < 0.05$; the Tibetans' systolic blood pressure (SBP) (131.02 ± 22.69) mmHg and diastolic blood pressure (DBP) (79.45 ± 15.03) mmHg which were lower than the Han (141.41 ± 27.86) mmHg and (87.02 ± 15.79) mmHg, $P < 0.05$; fasting blood glucose (FBG), postprandial 2 h plasma glucose (2 hBG), postprandial 2 h plasma insulin and homocysteine (Hcy) levels for elderly Tibetan and Han Chinese in Tibetan plateau region have no obvious abnormalities in the distribution, $P > 0.05$. **Conclusion:** Part of the metabolic of risk factors differences in the distribution among the elderly Tibetan and Han Chinese as well as different sex at high altitude, which may be related to high-altitude environment, eating habits and genetic background which prompt us the focus of interventions for different populations different, but this difference would affect the different peoples in highland areas the incidence of cardio-cerebral vascular diseases needed to be further explored.

111.
VASOACTIVE BIOMARKERS IN PATIENTS WITH CHRONIC MOUNTAIN SICKNESS.

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Introduction: Background: Individuals living at high altitude may develop pulmonary hypertension and in more chronic altitude exposure may develop chronic mountain sickness (CMS). The aim of this study was to investigate associations between CMS and levels of B-type natriuretic peptide (BNP), vascular endothelial growth factor (VEGF), endothelial nitric oxide synthase (eNOS), and endothelin-1 (ET-1). **Methods:** Design: A total of 24 CMS patients (16 Hans, 8 Tibetans) and 50 control subjects (12 Hans, 38 Tibetans) residing at 4380 m on the Qinghai Plateau participated in this study. Measurements: Demographics, vital signs, and basic laboratories were measured in all subjects. Cardiac structure and mean pulmonary arterial pressure (mPAP) were measured by echocardiography. Serum concentration of BNP, VEGF, eNOS and ET-1 were measured by the ELISA technique. **Results:** Results: Patients with CMS had significantly greater mPAP compared with controls (27.4 ± 6.4 mmHg vs 20.1 ± 7.5 mmHg; $P < .001$), and had lower oxygen saturations (SaO_2, $85.3 \pm 2.8\%$ vs $88.8 \pm 3.2\%$; $P < .001$). Serum BNP and VEGF levels were correlated positively with both mPAP and Hb, and negatively with SaO_2, while NOS/ET-1 was positively correlated with SaO_2; negatively with both mPAP and Hb. Mean concentrations of BNP were significantly greater in the CMS patients compared with those without CMS (367.64 ± 65.65 pg/mL vs 237.61 ± 73.39 pg/mL; $P < .001$). Similarly, concentrations of VEGF (486.31 ± 109.30 pg/mL vs 252.95 ± 99.31 pg/mL, $P < .001$), and ET-1 (14.97 ± 3.18 pg/mL vs 11.75 ± 3.28 pg/mL; $P < .001$) were higher in those with CMS compared to those without, while eNOS was lower in CMS group than the non-CMS group (9.08 ± 2.08pg/mLvs 11.4 ± 3.07pg/mL, $P < 0.01$). **Conclusion:** Conclusions: Severe chronic hypoxemia and consequent pulmonary hypertension in patients with CMS may stimulate release of natriuretic peptides and angiogenic cytokines. These vasoactive peptides may play an important role in the pathogenesis and clinical expression of CMS, and may indicate the potential prognostic factors in CMS. **Acknowledgments:** This work supported by National Basic Research Program of China (No.2006CB504100) and National Natural Science Foundation of China (No. 30393133).

112.
DETERMINE THE EFFECT OF GGA ON THE SURVIVAL OF MICE AND BRAIN DAMAGE UNDER ACUTE HYPOBARIC HYPOXIA.

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Introduction: It has been shown that induction of HSP70 by administration of geranylgeranylacetone (GGA) leads to protection against ischemia/reperfusion injury. **Methods:** The present study was performed to determine the effect of GGA on the survival of mice and brain damage under acute hypobaric hypoxia. **Results:** The data showed that the mice injected with GGA survived significantly longer than control animals (survival time of 9.55 ± 3.12 min, $n = 16$ vs. controls at 4.28 ± 4.29 min, $n = 15$, $P < 0.005$). Accordingly, the cellular necrosis or degeneration of hippocampus and cortex induced by sublethal hypoxia for 6 h could be attenuated by pre-injection with GGA, especially in the CA2 and CA3 regions of hippocampus. In addition, the activity of NOS of hippocampus and cortex was increased after exposure of sublethal hypoxia for 6 h, but could be inhibited by the pre-injection of GGA. Furthermore, the expression of HSP 70 was significantly increased at 1 h after GGA injection. **Conclusion:** These results suggest that administration of GGA improved survival rate and prevents brain from acute hypoxia damage, the underlying mechanism was involved in inducing HSP70 expression and inhibiting the NOS activity. **Acknowledgments:** This work was supported by a grant

from the National Basic Research Program of China (No. 2006CB504100).

113.

CHRONIC INTERMITTENT HYPOXIA INCREASES PRO-INFLAMMATORY CYTOKINES IN THE ADULT RAT CAROTID BODY: IMPLICATIONS FOR CHEMOSENSORY POTENTIATION.

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Introduction: Exposure to chronic sustained hypoxia (i.e. high altitude) induces physiological changes in the carotid body (CB) chemoreceptor, characterized by a potentiation of the chemosensory response to acute hypoxia. This effect has been related to an increased expression of pro-inflammatory cytokines within the CB due to immune cell invasion. Chronic intermittent hypoxia (CIH), a main feature of obstructive sleep apnea syndrome which affects 5-7% of the worldwide population, produces sympathovagal dysfunction and hypertension attributed in part to a potentiation of CB chemosensory responses to hypoxia. The mechanisms underlying the enhanced CB chemosensory responses to hypoxia induced by exposure to CIH are not fully understood. Since sustained hypoxia enhances CB chemosensory responses to hypoxia, we hypothesized that CIH may modify the expression of pro-inflammatory cytokines in the rat CB. **Methods:** In male Sprague-Dawley rats exposed to CIH (5% O_2, 12 times/hr for 8 hr for 21 days) that develop hypertension, we studied the expression in the CB of tumour necrosis factor alpha (TNF-α), interleukin 1 beta (IL-1β) and interleukin 6 (IL-6) by immunohistochemistry. Rats were fixed with paraformaldehyde 4% by perfusion and the CBs from Sham and CIH-exposed rats were harvested, post-fixed, included in paraffin wax and cut in 5 μm sections. The immunoreactive staning was measured with a deconvolution algorithm using the IMAGE J software. **Results:** We found that exposure to 21 days of CIH produced a significant increase in the relative immunoreactive levels of TNF-α and IL-1β in the glomus cells of the CB, which strongly correlates with the enhanced CB chemosensory responses to hypoxia in the CIH group, but not in the Sham group. In contrast, we did not find any changes in the expression of IL-6 between both groups. **Conclusion:** Our results suggest that TNF-α and IL-1β may be involved in the CB chemosensory potentiation induced by CIH. **Acknowledgments:** Funding source: FONDECYT 1100542 and Interdisciplinary Grant 04-2009 VRAID, PUC.

114.

VISUAL ANALOG SCALES FOR ASSESSMENT OF SEVERE AMS ON ACONCAGUA (6962 M).

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Introduction: Compare Visual analog scales (VAS) for each of the five symptoms used to calculate LLS with the individual symptom scores used to calculate LLS. Additionally, a sixth VAS for overall altitude sickness was compared directly to the overall LLS **Methods:** The study group consisted of volunteers from among climbers on the normal route of Mt. Aconcagua, Argentina. Each VAS consisted of a 100 mm line with the words "none" and "severe" at either end. For each VAS subjects were instructed to "Please put a single slash mark on the line at the place that best represents the magnitude of each of the following symptoms (headache, gastrointestinal symptoms, fatigue, lightheadedness, difficulty sleeping, and overall altitude sickness) on the day you were feeling worst." Spearman's rank correlation coefficients were calculated for each of the combination of the five graded Lake Louise (LL) symptoms and the corresponding VAS, as well as, for overall LLS score and its corresponding VAS **Results:** All of the VAS were highly correlated with their respective LL symptoms (headache $r = 0.8549$, $P = 0.000$; gastrointestinal symptoms $r = 0.5738$, $P = 0.0000$; fatigue $r = 0.7948$, $P = 0.0000$; lightheadedness $r = 0.7208$, $P = 0.0000$; difficulty sleeping $r = 0.7469$, $P = 0.0000$; and overall altitude sickness $r = 0.7133$, $P = 0.0000$). The mean difference in the VAS score between raters was < 0.5 mm **Conclusion:** The correlation between VAS for both the individual LL symptom components and overall LLS was high. VAS appears to be a good corollary for evaluating AMS. This may allow a simplified scoring system for AMS based on LLS but using VAS to be developed. This would be especially helpful on expeditions where multiple languages are encountered.

115.

OXIDATIVE STRESS IN TIBETAN AND HAN ELDERLY HIGHLANDERS.

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Introduction: Oxidative stress is hypothesized to be one of the main causes of senescence. Although there are several environmental factors which may contribute to the oxidative stress at high altitude, little is known about the association between oxidative stress and senescence in the community-dwelling elderly at high altitude. **Methods:** We examined reactive oxygen species (ROS) and comprehensive geriatric functions (CGA) among community-dwelling elderly subjects aged 60 years or more in Tibetan plateau. ROS and CGA were examined among 235 community-dwelling elderly subjects (146 Hans and 89 Tibetans). As a marker of ROS, the levels of reactive oxygen metabolites (ROM) were measured using the d-ROM test (Diacron, Parma, Italy). **Results:** The rate of independence of basic activities of daily living among Tibetan elderly highlanders was significantly higher than that among Han elderly highlanders. The d-ROM level was higher among the Tibetan elderly than those among the Han elderly (Tibetan 465.6 ± 97.9 Carr U, Han 415.3 ± 72.0 Carr U, $p = 0.003$). The ROM level was higher among females than those among males. Stepwise multiple regression analysis showed that the Tibetan, female, hemoglobin and oxygen saturation were independent associated factors of increasing d-ROM level. The high levels of ROM were significantly associated with dependence of basic ADL after adjustment for age, sex and ethnicity. The high levels of ROM (d-ROM > 500 Carr U) were significantly associated with independence of basic activities of daily living after adjustment

for age, sex and ethnicity (Odds ratio 2.51, $p = 0.028$). **Conclusion:** The generation of oxidative stress is necessary thing in human activity. If produced in excess, however, the stress may contribute to the acceleration of senescence. Further studies are needed to show the association among adaptation pattern to high altitude, oxidative stress and senescence. **Acknowledgments:** We appreciate all of the elderly highlanders who participated into the community-based geriatric examination in Haiyuan prefecture in Qinghai province. And we would like to express our cordial gratitude to young staff of Medical Institute of Qinghai University,all staff of Haiyuan Hospital, and all staff of Research Institute for Humanity and Nature who kindly helped us. This study was mainly supported by Grant-in-Aid of Research Institute of Humanity and Nature (3-4 FR): Human Life, Aging, and Disease in High-Altitude Environments: Physio-medical, Ecological and Cultural Adaptation in "Highland Civilizations." (Leader: Okumiya Kihohito) and also partly supported by the Grant-in-Aid of the JSPS Global COE Program (E-04): In Search of Sustainable Humanosphere in Asia and Africa.

116.

OXYGEN ADMINISTRATION FOR WORK IN HIGH ALTITUDE. A PILOT STUDY.

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Introduction: Working at high-altitude involves the exposition to hypobaric hypoxia which is harmful to the exposed individuals' health and productivity. The purpose of this study is the implementation of personalized oxygen administration during work at a mining site. **Methods:** The study was carried out in Chile, at a mine site located at approximately 4000 m. Twelve symptomatic workers were selected, using the Lake Louis questionnaire. They received oxygen 12 hours a day during two weeks, while they worked, by means of a CAIRE's SPIRIT portable device. Oxygen was delivered through a nasal cannula, at a flow enough to obtain transcutaneous saturation over 93 %. Symptoms and satisfaction with its use were assessed and pulse oximetry was carried out during the administration period. **Results:** Six workers used the oxygen over 50% of the programmed time. Several workers discontinued their use for logistical and cultural issues; those who continued using the oxygen, appeared particularly satisfied. There were problems of nasal irritation and epistaxis. **Conclusion:** The personalized administration of oxygen presents logistic and technical improvable problems and cultural problems that require further evaluation to correct them. A group of workers clearly seems to benefit from its use, in spite of the problems met. Further studies concerning this aspect are required.

117.

FATIGUE, PRESENTEEISM AND ACUTE MOUNTAIN SICKNESS SYMPTOMS.

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Introduction: Working in altitude involves exposition to hypobaric hypoxia, which may affect productivity of exposed individuals. The concept of presenteeism implies working at non optimum conditions and it is a high impact phenomenon. The purpose of this study was to determine the relation among fatigue, presenteeism and Acute Mountain Sickness (AMS) symptoms. **Methods:** The study was carried out in Chile, at a mine located at approximately 1800 m. Demographic variations, anthropometrics and pulse oximetry were recorded. Lake Louis questionnaire was used to quantify AMS; for fatigue "Check List Individual Strength" self report was used and in order to quantify presenteeism, inquiries by self reporting on performance were carried out. The statistical analysis was done using the Spearman rank correlations and logistics regression. **Results.** A sample of 417 workers was obtained, of average 30.3 years old and 93.0% men. 16.1% of AMS and 20.6% presenteeism was found in the last year. The analysis through Spearman correlation showed a significant association between presenteeism and AMS ($r = 0.17$; $p < 0.001$), depression ($r = 0.29$; $p < 0.001$), anxiety ($r = 0.26$; $p < 0.001$) and body mass index ($r = 0.11$; $p = 0.0023$). In the multivariate analysis the only significant predictor were the depression symptoms ($p = 0.013$). **Conclusion.** There is a notable rate of presenteeism in the sample analyzed. There were associations to depression and anxiety symptoms, which can be expected, but also AMS and obesity symptoms. Other studies are required as well as the development of actions to verify the associations found.

118.

FEASIBILITY OF PERFORMING THE SIX-MINUTE WALK TEST (6 MWT) IN HEALTHY ADULTS AT HIGH ALTITUDE ON ACONCAGUA.

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Introduction: Determine if six-minute walk distance (6 mWD) or post-exercise vital sign (VS) measurements predict successful summiting or development of acute mountain sickness (AMS) on Aconcagua **Methods:** Prospective observational cohort at Plaza de Mulas base camp (4365 m), Aconcagua Provincial Park, Argentina. Climbers who hiked the normal route by foot, checked in with base camp physicians, were > 17 years old, and spoke English, Spanish, French, or German were included. There were no exclusion criteria. VS were measured before (resting) and after (post-exercise) completion of a 6 mWT (post-exercise) while subjects acclimated. Subjects proceeded towards the summit at their own pace and upon descent returned a questionnaire with maximum altitude reached and Lake Louise Score (LLS) for assessment of AMS **Results:** 64 subjects completed the 6 mWT. Mean 6 mWD was 458 m. 64 subjects (51.6%) completed questionnaires; 55% summited. Median LLS was 4 (IQR: 3.0 to 6.5). There was no association between any resting or post-exercise VS measurements and AMS. However, mean post-exercise SpO_2 was 80.8% in summiters and 76.4% in non-summiters, a difference of −4.4% (95% CI for difference: −6.7 to −2.0, $P = 0.0005$). Post-exercise SpO_2 was 97.2% sensitive in predicting the outcome of successful summiting: only one climber with $SpO_2 < 75\%$ successfully summited **Conclusion:** This study provides the first published data on 6 mWD recorded in the field at high altitude. Post-exercise $SpO_2 < 75\%$ may be a useful screening test for predicting the outcome of successful summit attempts on Aconcagua.

119.

DEVELOPMENTAL ORIGIN OF VASCULAR DYSFUNCTION AT HIGH ALTITUDE.

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Introduction: Epidemiological studies have shown an association between pathologic events occurring during early life and the development of cardiovascular and metabolic disease in adulthood. These observations have led to the so-called "fetal programming of adult disease hypothesis". In line with this hypothesis, short-term exposure to hypoxia after birth predisposes to exaggerated hypoxic pulmonary vasoconstriction later in life in rats, and transient perinatal hypoxia predisposes to exaggerated pulmonary hypertension during short-term exposure to high altitude in humans. Along the same lines, in recent studies in Bolivian high-altitude dwellers, we found that preeclampsia predisposes the offspring to pulmonary and systemic endothelial dysfunction possibly related to impaired NO bioavailability and augmented oxidative stress. Very recent data from our lab suggest that assisted reproductive technologies may represent another important example consistent with this hypothesis. The mechanisms underpinning the developmental origin of this vascular dysfunction are poorly understood. Increasing evidence suggests that epigenetic alterations, such as DNA methylation or histone acetylation. may play a role.

120.
EXAGGERATED HYPOXIA-INDUCED PULMONARY HYPERTENSION: NOVEL MECHANISMS, UNSUSPECTED PREDISPOSING FACTORS.
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Introduction: High altitude constitutes an exciting natural laboratory for medical research. While initially, the aim of high-altitude research was to understand the adaption of the organism to hypoxia and find treatments for altitude-related diseases, over the past decade or so, the scope of this research has broadened considerably. Two important observations led the foundation for the broadening of the scientific scope of high-altitude research. First, high-altitude pulmonary edema (HAPE) represents a unique model that allows studying fundamental mechanisms of pulmonary hypertension and lung edema in humans. Second, the ambient hypoxia associated with high-altitude exposure facilitates the detection of pulmonary and systemic vascular dysfunction at an early stage. Here, we will review studies that, by capitalizing on these observations, have led to the description of novel mechanisms underpinning lung edema and pulmonary hypertension and to the first direct demonstration of fetal programming of vascular dysfunction in humans. **Acknowledgments:** Swiss National Science Foundation, Placide Nicod Foundation.

121.
FLYING ACROSS THE HIMALAYAS: THE UNIQUE PHYSIOLOGY OF BAR-HEADED GEESE.
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Introduction: Bar-headed geese reach altitudes of up to 9000 m during their biannual migration over the Himalayas. The ability of this species to maintain O_2 supply in the severe hypoxia at these elevations is impressive when considering the high metabolic costs of flight in birds. **Methods:** We examined how the O_2 transport pathway has evolved in this species to help determine the physiological basis for this feat. **Results:** Bar-headed geese can breathe much more than low-altitude birds during hypoxia, largely due to alterations in the pattern and chemosensitivity of breathing. This species also has larger lungs and a higher haemoglobin-O_2 affinity. As a result of these characteristics, pulmonary O_2 uptake during hypoxia is markedly improved. Evolutionary changes in the heart, such as a higher capillarity, also improve circulatory O_2 delivery. Oxygen diffusion capacity in the flight muscle is improved by an enhanced capillarity and a redistribution of mitochondria towards the cell membrane. These unique characteristics exist without prior exercise or hypoxia exposure. However, mitochondria isolated from bar-headed goose muscle are equally sensitive to reductions in O_2 tension to those from other geese. **Conclusion:** High-altitude adaptations that enhance O_2 supply, and sustain O_2 tensions at the mitochondria, therefore appear to be essential for the exceptional ability of bar-headed geese to fly high. **Acknowledements:** Supported by NSERC of Canada.

122.
CLIMATE CHANGE IN THE HIGH HIMALAYA: IMPLICATIONS FOR MOUNTAINEERS AND INDIGENOUS COMMUNITIES.
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Introduction: The impact that climate change has on remote populations is of increasing importance. The Himalaya have warmed by $\sim 0.6^{\circ}$C since the middle of the 19th century and this warming is predicted to continue. In addition, pollution from the adjoining Indian subcontinent is expected to worsen as this region continues its rapid industrialization. Here we report on some of the implications that these changes will have on populations who live in and visit the Himalaya **Methods:** We make use of a 60 year-long meteorological dataset that has been validated against observations made at the South Col of Mount Everest. We also make use of direct measurements of surface ozone, a tracer for pollution as well as the presence of stratospheric air, that we have collected along the Khumbu Valley since 2005. **Results:** The warming has resulted in a thickening of the atmosphere in the Mount Everest region that since 1948 has resulted in an increase in the annual mean summit barometric pressure of $\sim$1.5 mb. Ozone concentrations along the Khumbu Valley during the spring climbing season tend to increase with altitude and above 3500 m, they typically exceed WHO exposure guidelines. We have identified two distinct sources of ozone. The first being stratospheric in origin and the second source was identified as long distance transport of polluted air masses from the Indian subcontinent and South East Asia. **Conclusion:** The increase in summit barometric pressure is of a magnitude to be of physiological importance suggesting that it is becoming easier to climb Mount Everest without the use of supplementary oxygen. Given that the warming that gives rise to this increase has been ongoing since the 1850s, it follows that that early climbers were also exposed to lower barometric pressures as compared to modern climbers thus making their accomplishments all that more impressive. The ozone data shows contributions from both the stratosphere and the long distance transport of pollution. The observed values exceed WHO exposure guidelines and are expected in increase as the industrialization of the Indian Subcontinent continues. Ozone exposure at extreme altitude may represent a new health risk for mountaineers and indigenous populations in the Himalaya. **Acknowledgments:** This research was supported by the Natural Sciences and Engineering Research Council of Canada.

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THE APOPTOSIS OF BONE MARROW CELLS IS DOWNREGULATED IN PATIENTS WITH CHRONIC MOUNTAIN SICKNESS.
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Introduction: Chronic mountain sickness (CMS) is a common disease in the plateau region. Its pathogenesis is closely associated with the enviroment conditions of high altitude, however, it has not been definitely understood up to now. To explore the roles of apoptosis in the pathogenesis of CMS, the apoptosis of bone marrow cells and the expressions of apoptotic factors on the bone marrow mononuclear cells (BMMNCs) in CMS patients were investigated in the present study. **Methods:** The apoptosis of bone marrow cells collected from 5 CMS patients was observed under electron microscope, the apoptotic index of BMMNCs derived from 16 CMS patients (CMS group) were assessed by terminal deoxynucleotidyl transferase-mediated dUTP nick end-labeling (TUNEL) technique and the expression rates of Fas, Fas ligand (FasL), tumor necrosis factor (TNF) and TNF receptor (TNFR) on BMMNCs derived from 35 CMS patients (CMS group) were investigated using flow cytometry. The results of all index were compared with those in the healthy adults lived in the same region (Control group). **Results:** The apoptosis was discovered in the bone marrow of patients with CMS, but the apoptotic index of BMMNCs was significantly lower in the CMS group ($10.13\% \pm 9.80\%$) than that in the Control group ($21.32\% \pm 11.97\%$)($P < 0.01$). There was no significant difference in the expression rate of any apoptotic factor researched in the present study between the CMS group and the Control group, although the increase tendencies in the expression rates of FasL and TNFR and the decrease tendency in the expression rate of TNF were found in the CMS patients. There was a positive correlation between the expression rates of FasL and Fas ($r = 0.409$, $P < 0.05$), but no significant relationship was found between the TNF and TNFR or between Hb and any apoptotic factor mentioned above ($p > 0.05$). **Conclusion:** These results indicated that the BMMNCs apoptosis is downregulated in CMS patients, which might be play a part cooperatively with hematopoietic growth factors in excessive accumulation of erythrocytes in CMS. The mechnism of decreased apoptotic index of BMMNCs in CMS may be involved in the more pro- or anti-apoptotic factors except of Fas/FasL and TNF/TNFR signal systems. **Acknowledgments:** This study was supported by a grant-in-aid from The Talent Development Program of the e Chinese Academy of Sciences (2002-404).

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INTERMITTENT HYPOXIA TRAINING (IHT) INFLUENCES HUMAN HEMATOPOETIC STEM CELLS (HSC) AND IMMUNE SYSTEM.

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Introduction: One of main mechanisms of the adaptation to hypoxia is the response of stem cells. The purpose of this study was to define the IHT effects on human HSC, various factors of natural resistance and main humoral and cellular components of adaptive immunity in peripheral blood. **Methods:** 10 healthy subjects (25-35 years old) were observed twice before and two times after IHT (normobaric rebreathing technique up to $SaO_2 = 75\%$, 5 min hypoxia, 5 min break, 4/day, 15 days). The content of CD45 + CD34 + -, CD4 + - and CD8 + -cells was studied according to standard direct immunofluorescence techniques. Immune indices were determined by routine methods. **Results:** CD45 + 34 + -cells in peripheral blood are found in very small quantity ($1{,}6 \pm 0{,}2$ cells/mkl). As a result of IHT, their level showed the trend to increasing during training period and decreased significantly (by 27%) in a 1 week after IHT. As a result of IHT, the enhancement of natural resistance system occurs, including complement activation, platelet number augmentation, the increase in phagocytic capacity of neutrophils with a decrease in their spontaneous and increase in reserve bactericidity. In such mode IHT doesn't affect the red blood cell status and number of various types of leucocytes, CD4 + and CD8 + T-lymphocytes, basic classes of immunoglobulins and circulating immune complexes. **Conclusion:** Thus, humoral and cellular factors of non-specific resistance are sensitive to such regime of IHT. Their activity increases significantly. It leads to enhancement of natural protection of organism. A decrease in HSC number in peripheral blood is probably associated with the change of their migration capacity. However, it remains unclear whether there is an inhibition of HSC migration into circulation or an activation of HSC escape from circulation. In both cases tissues could accumulate more HSC which in turn could enhance hematopoiesis and general regenerative potential. It assures the HSC transdifferentiation capacity, plasticity and intercellular cooperation. **Acknowledgments:** Supported by STCU grant # 4299.

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ARE UK COMMERCIAL EXPEDITIONS COMPLYING WITH WMS GUIDELINES?

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Introduction: Trekking is becoming an increasingly popular tourist activity, and three of the most popular areas for commercial expeditions are Kilimanjaro, Aconcagua, and Everest Base Camp (EBC). However, with this, comes the risk of acute mountain sickness (AMS), which is believed to be due to the rapid rate of ascent offered by many commercial companies. In an attempt to minimize AMS, the Wilderness Medicine Society (WMS) has recommended that once above 3000 m, the gain in sleeping altitude should be no more than 500 m, and in addition, a rest day should be taken after three or four days of ascent. The aim of this study was to ascertain whether treks to these popular areas, offered by commercial companies in the UK, satisfied the guidelines stated by the WMS. **Methods:** A search of the World Wide Web was conducted in order to identify those UK-based companies that offer treks to the summit of Kilimanjaro and Aconcagua, and to EBC between January 2010 and December 2011. For each route on offer, the ascent profile was compared with the ascent profile recommended by the WMS. **Results:** 10 UK-based companies offering climbs of Aconcagua, and 16 offering treks to EBC were identified. 30 companies offering 90 treks on nine different routes on Kilimanjaro were identified. The average ascent rate on Aconcagua was 250 m/day, and to EBC was 275 m/day. On Kilimanjaro, the ascent rate ranged from 513 m/day to 566 m/day, depending on which route was offered. The ascent rate recommended by the WMS is 400 m/day, and of the companies identified in this study, 10 complied on Aconcagua (100%), 13 complied on EBC (81%), and none complied on Kilimanjaro.

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THE ROLE OF WATER CHANNEL AQUAPORIN 5 IN HIGH ALTITUDE PULMONARY OEDEMA IN MICE.

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Introduction: Aquaporin 5 (AQP5) is a water channel expressed at apical membrane of alveolar type I cell in the lung. Previous studies have shown AQP5 facilitates osmotic fluid transport and cell migration. We hypothesized that AQP5 may play a role in alveolar epithelial barrier function in high altitude pulmonary edema, in which both formation and resolution of lung edema involve fluid transport. **Methods:** AQP5 -/- and wildtype mice were randomLy assigned to normoxic rest (NR), hypoxic rest (HR) and hypoxic exercise (HE) groups ($n = 6$ in each group). The HE mice were trained to walk in treadmill for exercising and chamber pressure was reduced to simulate climbing an altitude of 5000 m for 48 hours. Broncholalveolar lavage (BAL), lung wet-to-dry weight ratio (W/D) and histology were conducted to analyze lung edema. Alveolar-capillary barrier permeability was measured by Evan's blue assay. **Results:** BAL protein concentrations and lung W/D ratio were slightly increased in HE AQP5 -/- mice compared to wildtype mice, but there were no statistical difference. Alveolar-capillary barrier permeability in HR AQP5 -/- mice were slightly but significantly increased compared to controls mice ($P < 0.01$), and alveolar-capillary barrier permeability in HR wildtype mice was higher than that in control mice ($P < 0.05$). Histology analysis showed there was mild to moderate increased lung edema in HR AQP5 -/- mice compared to wildtype mice. **Conclusion:** These results demonstrate that deletion of AQP5 induced slight increase of lung edema and lung injury compared to wildtype mice, which suggested AQP5 play a minimum role in alveolar-epithelium integrity in development of HAPE. **Acknowledgments:** The abstract is Funded by Shanghai Leading Academic Discipline Project #65292; Project Number: B115. Corresponding Author: Chunxue Bai MD, PhD. E-mail: bai.chunxue@zs-hospital.sh.cn.

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THE SURVEY OF NUTRITION AND HEALTH STATUS OF RESIDENTS IN PLATEAU.

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Introduction: To investigate the dietary pattern, nutritional status, the epidemiological feature and trend of the main nutrition-related diseases of residents in plateau. **Methods:** The survey of nutrition and health status was conducted in three regions of different altitude. (The average altitudes were 2260, 2700 and 4100 m respectively). 2. The basic data about population, economy; medical care, the family income, age, education, the prevalence and family history of main chronic diseases were collected. 3. Weighing method was used to get the data of household food consumption within 3 days. 24-hour dietary-recall method was used to investigate the personal dietary intake. **Results:** The food consumption of residents in three regions was different. The residents who lived in the 2260 m had a high intake of rice, milk, eggs, poultry and fresh fruit; and the residents who lived in the region of 2700 m had a high intake of food made of flour, potato and vegetables. Nevertheless, the residents who lived in the region of 4100 m had a high intake of food made of flour, meat and light-colored vegetables ($P < 0.05$). 2. The main source of protein and energy was vegetable food at the altitude of 2260 and 2700 m, while the main source was animal food at the altitude of 4100 m. 3. The protein intake did not meet the recommended standards at the altitude of 2700 m; the vitamin C intake also did not reach the recommended standards at the altitude of 2260 and 4100 m. 4. The prevalence of children's low birth weight was the highest at altitude of 4100 m. The prevalence of overweight and obesity was the highest at the altitude of 2260 m. **Conclusion:** The dietary pattern and nutriment intake were different in the regions of different altitude due to the diversity of life style, living habit and family income. Although the residents that lived in the region of 4100 m consumed more animal food, the prevalence of obesity and chronic disease at the altitude of 4100 m was lower than that at the 2260 and 2700 m, because of the hypoxia and cold, high metabolic rate and energy consumption at the altitude of 4100 m.

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OXYGEN SUPPLEMENTATION EFFECTS ON AMS SYMPTOMS AND FUNCTIONAL CAPACITY OF A 2 KM WALK TEST ON CHAJNANTOR PLATEAU (5050 M, NORTHERN CHILE).

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Introduction: We evaluated the effects of oxygen supplementation on the functional capacity and acute mountain sickness (AMS) symptoms in 26 young healthy subjects that performed a test of 2 km fast walk at sea level and at Chajnantor plateau at 5050 m of altitude. **Methods:** The 16 men and 11 ladies were randomLy distributed into four groups according the following arrangement: M1: 8 men who received by mask supplementary oxygen at a rate of $1LO_2$ min-1; group M3: 7 men who received $3LO_2$ min-1. W1: 5 ladies who received $1LO_2$ min-1 and W3: 6 ladies receiving $3LO_2$ min-1. A previous walk test at sea level was carried out in a flat land track of 100 m of length that was covered in 10 U-returns. First walk at altitude was made carrying the supplementary oxygen system but without functioning. Second test was performed in the following day with actual oxygen supply through a facemask. **Results:** Our results showed that supplementary oxygen administration in a 2 km walk test significantly improved the walking time at 5050 m in men but not in women groups.

Also we observed a significant improvement in AMS symptoms in men groups. The women had bad tolerance to breathe as mask; three of them left the test for bad tolerance the mask. Nevertheless, instead of supplementary oxygen in men, a reduced performance persists in comparison to the test values at sea level. **Conclusion:** This study has practical application in people who develop specific tasks at high altitude, during a whole working day (6-8 hours). Our findings indicate that they could benefit from the administration of supplementary oxygen, in continuous or intermittent form, with the objective of diminish the AMS incidence and to improve its working physical condition. In the same way, our results could be applied to improve the performance in workers who must develop static activities at altitude, but requiring great concentration capacity, such as vehicle driving, decision making, or fine manipulation, in which the speed of reaction is vital and a mechanism guarantying a suitable brain oxygen supply it can be a key safety factor not only during the ascent and altitude stay as in the descent to lower altitude. **Acknowledgments:** Authors are grateful to Chiledeportes II Region by their sponsorship to research projects in the area of the Altitude Physiology and Medicine through the modality of Sports Sciences; and to ALMA Project (European Southern Observatory) authorities for their support to the present study.

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CHOLESTEROL AND TRIGLYCERIDES' CHANGES IN PLASMA AND LIVER IN EXPOSED RATS TO CHRONIC HYPOBARIC HYPOXIA (4600 M).

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Introduction: The aim was to determine the changes of lipid profile in plasma and liver and some metabolic pathways in rats exposed to Chronic Hypobaric Hypoxia (CH). **Methods:** 30 adult male Wistar rats, were randomLy assigned to two groups and were studied for 30 days: chronic hypoxia (CH;n = 15) and normoxic (NX;n = 15). We simulated high altitude in a hypobaric chamber at 428 Torr (4600 m). NX rats received the same amount of food that CH rats currently ate in the chamber. The following variables were assessed (Weight, BP, HR, hematocrit and hemoglobin, and lipid profile at Day0, day15 and Day30). After sacrifice at the end of the experiment, lipids were extracted from the liver with chloroform-methanol, according to the Bligh-Dyer method and a Semi-quantitative RT-PCR analysis was performed of SCD-1, HMG-CoA Reductase, and β-actin. **Results:** The results show that both groups lose weight, but it was greater in the CH, $P = 0.01$. The hematocrit and the hemoglobin raised in CH group at day 15 and maintained until the end of the study ($P < 0.001$). There was an increment of total cholesterol and LDL cholesterol and a decreased HDL cholesterol at 15 days in CH $P < 0.05$, whereas the results at day 30 are similar to NX. However, a decreased LDL cholesterol and increased HDL cholesterol was found in both groups at day 30. Triglyceride and VLDL increased at day 15 under CH, until the end of study ($P < 0.01$) and also the Triglyceride value showed a correlation with the Hematocrit $r = .595$, $r^2 = 0.354$; $P = 0.001$. No difference in Hepatic Lipid Profile was seen in both groups. Hepatic HMG CoA Reductase mRNA expression was also similar in both groups, but a lower SCD-1 mRNA level in CH was seen $p < 0.01$. No differences in gene β-actin control were found. **Conclusion:** In conclusion, CH in rats leads to a decrease of weight independently of food intake and cholesterol and fractions seem to have an early influence of hypoxic stress. However, the plasmatic triglycerides and VLDL increase is clearly influenced by hypoxia, probably resulting from lipid degradation, since hepatic synthesis pathways are inhibited. **Acknowledgments:** Universidad Arturo Prat.

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STRUCTURAL CHANGES IN PULMONARY ARTERY OF EXPOSED RATS TO CHRONIC INTERMITTENT HYPOBARIC HYPOXIA.

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Introduction: The aim was to evaluate the structural changes of pulmonary arteries in rats exposed to Chronic Intermittent Hypobaric Hypoxia (CIHH) (2 days hypoxia/2 days normoxia; n = 8), compared to a normoxic group (NX; n = 8). **Methods:** Hypobaric conditions were simulated in a hypobaric chamber at 428 Torr (4600 m) for 45 days assessing some physiological variables. At the end of the study, the right ventricular hypertrophy (RVH) was measured through RV/LV + S ratio. Third order pulmonary arteries were removed and fixed in 10% paraformaldehyde and stained with the nuclear dye DAPI (5ug/ul). Sections and rings were visualized with a Confocal Microscope (EX 405- EM 410-475) and the images quantified with Metamorph software. **Results:** Compared to NX, a weight decrease, a hematocrit and RVH increase were seen in CIHH rats, along with pulmonary artery wall hypertrophy ($P < 0.01$), with no changes in lumen size. Both adventitial and media layer accounted for wall thickness enlargement ($P < 0.05$). Adventitia thickening was accompanied by an increase in cell number and density, while media layer thickening showed no cellular changes. Interestingly, a moderate inverse correlation between weight change and media layer thickness was found ($r = -0.48$; $P < 0.05$). **Conclusion:** In conclusion, under CIHH, there are ongoing structural changes in pulmonary artery characterized by an outward hypertrophic remodeling involving adventitia and media alterations. The adventitia layer showed most changes either in thickness and cell number increase. To explain the results, we suggest that a hypoxia/re-oxygenation phenomenon could play a major role in this model along with inflammation, migration and extracellular matrix deposition processes. **Acknowledgments:** By grants from CEAL-Santander and UNAP.

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ACUTE HIGH ALTITUDE ILLNESS IN PATIENTS URGENTLY TRANSFERRED TO SEA LEVEL PRIVATE HOSPITAL. LIMA, PERU.

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Introduction: With globalization, Peru is becoming an increasingly important attraction for international tourism. Medical problems as Acute High Altitude Illness can arise, especially when tourists visit the Peruvian highlands. The aim of the present study was to describe the clinical characteristics of acute high altitude illness in patients who required urgent transfer to a sea level Private Hospital in Lima-Peru. **Methods:** The medical records of 69 patients with diagnosis of High Altitude Pulmonary Edema (HAPE) and / or High Altitude Cerebral Edema (HACE) who were urgently transferred to the British American Hospital (Clinica Anglo Americana) from 2000 to 2007 were retrospective evaluated. **Results:** The mean age was 51.53 + /- 15.47 years, 47 (72.3%) were males, 65 (98.5%) were tourists. Twenty nine patients come from 3990 m (Cuzco) and 17 from 3918 m (Puno). The most common nationalities were 19 French, 12 Americans, 8 British and 6 Japanese. Sixty three percent of patients started symptoms 1 day after arrival. Fifteen (28.8%) had past medical history and 8 patients had prior acute medical problems before altitude symptoms. Only 5 patients needed intensive care unit. Regarding symptoms 52(75.3%) reported dyspnea, 23 (33.3%) headaches, 22 (31.8%) coughs, and 11 (16%) mental status changes. Fifty five patients (75.3%) developed HAPE, 9 (13%) HACE and 8 (11.6%) HACE and HAPE. Twenty one patients also developed additional acute medical problems. In four patients were necessary oxygen and medical support to discharge. No fatal events related to acute high altitude illnesses were reported during the time of our study. None of the patients took preventive medication. **Conclusion:** HAPE was the most common acute high altitude illness in our study and dyspnea was the most frequent symptom. Acute high altitude illness is a preventable disease, our data suggests that proper advice and prophylaxis will be provided to people who travel to high altitude places. **Acknowledgments:** British American Hospital (Clinica Anglo Americana).

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CRT TREATMENT IN PATIENTS WITH HEART FAILURE AT HIGH ALTITUDE.

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Introduction: The incidents of heart failure are significantly increased around world. A epidemiological survey in China in 2003 showed that the incident of heart failure is 0.9%. Drug therapy has been widely used in clinical practice, however the risk of death is still high (20% to 25%). At the same time cardiac pacing technology (CPT) has constantly improved, and it has become one of the best application prospects for treatment of heart failure. Thus, we used both drugs and CRT to treat the chronic heart failure. **Methods:** Drug therapy for ACEI, spironolactone, β-Blockers, vasodilator therapy. Concurrent CRT implantation, intraoperative test: LV: threshold 3.0 mV, R amplitude 11.8 mV, impedance 956 Ω/5 V; RV: Threshold 0.6 mV, R amplitude 13.6 mV, impedance 712 Ω/5 V. After programmed: LV threshold 5.0 mV, RV threshold 3.5 mV. **Results:** Even after implantation combined with oral medication, CRT one-click optimization, RV ahead of 30 ms, three months after the patient re-admitted to hospital because of upper abdominal fullness, dual-chamber pacing-QRS $<$ 120 ms, echocardiography LV98 $\sim$ 87 mm. EF 26% left ventricle seen in a 0.5$\times$0.5 cm "thrombosis", RV diameter of about 45 mm, the lung A pressure 60 mmHg, in the heart under the guidance of color Doppler ultrasound RV20 ms will give priority to the best optimization of LV. **Conclusion:** The regular expression for the highland areas of right heart dysfunction, the main addition to the above the patient on the current drug treatment, the daily need to use higher doses of diuretics, can only be sustained daily. Progression through the patient's right heart failure are the main clinical manifestations. However, the gradual expansion and echocardiography LV pacemaker for debugging non-response and drug therapy is ineffective, we think this is a typical case of the continued deterioration of cardiac function after CRT cases, that is, the phenomenon of CRT nonresponse. The patient with non-response may be related to high-altitude pulmonary hypertension, which may lead to right heart dysfunction.

133.
MECHANISMS OF HEMOGLOBIN ADAPTATION TO HYPOXIA IN HIGH-ALTITUDE RODENTS.

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Introduction: In high-altitude vertebrates, adaptive changes in blood-oxygen affinity may be mediated by modifications of hemoglobin (Hb) structure that affect intrinsic oxygen affinity and/or responsiveness to allosteric effectors that modulate Hb-oxygen affinity. This mode of genotypic specialization is considered typical of mammalian species that are high-altitude natives. Here we investigate genetically based differences in Hb-oxygen affinity between highland and lowland populations of the deer mouse (Peromyscus maniculatus), a generalist species that has the broadest altitudinal distribution of any North American mammal.: We used a combined genetic and proteomic approach to characterize Hb isoform diversity, and we measured oxygen-binding properties of purified hemoglobins from mice with known genotypes. We also conducted a multilocus population genetic analysis to assess the role of natural selection in shaping altitudinal patterns of nucleotide variation at two tandemLy duplicated alpha-globin genes on Chromsome 8 and two tandemLy duplicated beta-globin genes on Chromosome 1. **Results:** Results revealed that deer mice harbor an extremely high level of Hb isoform diversity which translates into a correspondingly high level of interindividual variation in Hb functional properties. Results of functional experiments revealed that, on average, the Hbs of highland mice exhibit slightly higher intrinsic oxygen affinities and lower chloride sensitivities relative to the Hbs of lowland mice. The experiments also revealed distinct biochemical properties of deer mouse Hb related to the allosteric regulation of oxygen affinity. Combined evolutionary and functional analyses suggest that genetic differences in Hb function between highland and lowland deer mice evolved under the influence of positive directional selection that favors different blood-oxygen affinities in different elevational zones. **Conclusion:** In conjunction with previous findings, our results demonstrate that modifications of Hb structure and regulatory adjustments in the intracellular concentrations of erythrocytic anions both play a role in the adaptive fine-tuning of blood-oxygen affinity. **Acknowledgments:** This work was funded by grants from NIH and NSF.

134.
A CLINICAL-EPIDEMIOLOGICAL STUDY IN CANYON RESCUE.

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Introduction: To determine characteristics, frequency and management of those canyoning injuries that required organized rescue and activation of emergency medical system. **Methods:** A retrospective, descriptive study was done by examining medical incidents in canyoning occurred during a 10-year period. Subjects were selected from the incident reports of the Mountain Rescue Unit database. **Results:** 503 canyoning rescues missions were reviewed, which represented the 22,3% or the total medical incidents in Central Pyrenees. The age of patients was 33.8 $\pm$ 12.1 years old and 58.5% were males. 66.3% of victims had NACA index $\geq$ III. Trauma was the most common reason for calling (82.5%) and 9.2% of subjects were considered not injured. Rescue duration mode was 90 minutes. Mixed rescue techniques (air-land) were needed in 41.4% before the use of winch was established. The most common injury location involved lower extremity (78.1%), and cause of death was traumatic (53.3%). Splinting was required in 74.4%, medical treatment in 34.8% (non steroidal anti-inflamatory drugs, 56.1%), 74.4% of drugs were given intramuscularly. 63.6% of shoulder dislocation were reduced on site. Life support was attempted in 20% of fatalities. **Conclusion:** There are epidemiological changes from previous papers and differences from other mountain sport studies. Severity, on site treatment needs and rescue length justify presence of an emergency medical system at the accident scene.

135.
NEW ASPECTS IN AVALANCHE RESCUE.

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Introduction: On average 150 persons die every year in North America and Europe due to avalanches. **Methods:** **Results:** In 1994, Falk et al presented a novel procedure for calculating the survival probability after burial under an avalanche. As a result, the proposed recommendations governing the comportment of off-piste skiers have gained acceptance and mountain rescue techniques have been adapted. However, it was unknown whether this survival

function is universal and its implications are applicable in areas with different topography and climate. In 2009, a retrospective study by Boyd J et al revealed that fatality patterns in Canada differ significantly from European studies. To confirm the assumption that there are significant variations between the survival curves of Switzerland and Canada, in 2010 Haegeli P et al explored the universality of the avalanche survival curve, comparing avalanche survival data from Swiss (n = 946) and Canadian (n = 301) records between 1980 and 2005. While the updated Swiss survival curve follows the general patterns described in 1994, the Canadian curve was characterized by a much quicker drop in survival at the early stages of an avalanche burial (<35 min) and the much poorer survival in prolonged burials. Furthermore, the study group examined the effect of trauma on the Canadian survival curve. 25 of 134 fatalities (19%, CI 12-26%) died from trauma as their primary cause of death. This explains the quicker drop in the first 10 min of burial. Long-term survival of avalanche victims still remains an unresolved issue, however. In 2008 and 2010 two case reports show that deep hypothermia associated with an air pocket may prevent from neurological sequelae even after prolonged cardiac arrest. In 2010, Paal et al designed an experimental study to analyse the influence of an artificial air pocket on cardiorespiratory param and core temperature during artificial snow burial in a pig model. These tests confirmed a drop of core temperature within 10 minutes burial with a rapid establishment of the previously suspected "Triple-H Syndrome" (Hypoxia, Hypercapnia, Hypothermia) during snow burial. **Conclusion:** Further research is needed to clarify the interactions between hypoxia, hypercapnia and hypothermia in avalanche victims presenting a patent airway and an air pocket.

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THE ROLE OF ADMA IN IDENTIFYING INDIVIDUALS SUSCEPTIBLE TO ALTITUDE SICKNESS.

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Introduction: Since asymmetric dimethylarginine (ADMA) is a nitric oxide synthase (NOS) inhibitor, it should increase pulmonary artery pressure (PAP) and raise the risk of acute mountain sickness (AMS) and high-altitude pulmonary edema (HAPE). With this in mind, we investigated whether changes in ADMA levels at an altitude of 4000 m can predict an individual's susceptibility to AMS or HAPE. **Methods:** Twelve subjects spent two nights in a hypobaric chamber, the first night without exposure to altitude conditions and the second night at a simulated altitude of 4000 m. At identical time points during both nights (after 2, 5 and 11 hours), we determined ADMA serum levels, PAP by Doppler echocardiography and estimated hypoxia related symptoms by Lake Louise Score (LLS). **Results:** Contrary to our initial hypothesis, subjects with altitude sickness showed a decrease rather than an increase in ADMA levels. As expected, however, their PAP rose considerably and in some cases reached a level of more than 40 mmHg. By contrast, subjects without altitude sickness experienced an increase in ADMA and a moderate increase in PAP. **Conclusion:** After two hours of hypoxia, the course of ADMA (increase or decrease) can predict an LLS of > 5 with a sensitivity of 80% and a specificity of 100% and can help assess the risk of an increase in PAP to more than 40 mmHg and thus the risk of HAPE (Phi coefficient: 0.69; $p < 0.05$). **Acknowledgments:** This study was supported by the German Ministry of Defense.

137.

RELATIONSHIP BETWEEN THE GENDER FETAL AND PRE-ECLAMPSIA AT HIGH ALTITUDE.

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Introduction: The preeclampsia is a common hypertensive disorder during pregnancy; this disorder develops progressively with consequences in the mother and newborn. Recent research shows that chronic exposure to testosterone may results in hypertension in the mother. High hemoglobin values have also been associated to pre-eclampsia. The aim of the study is determinate the relationship between gender fetal and the incidence of pre-eclampsia in a Peruvian population at high altitude. **Methods:** This is a cross section study using data of the perinatal informative system (SIP 2000) of 7 hospitals located between 150- 4500 m. The study included 35,447 consecutive deliveries of 22-42 weeks of age without congenital malformations. Preeclampsia and eclampsia were analyzed together. A logistic regression analysis was used to determine the association of gender of the fetus and altitude adjusted by confounders factors (Biological and sociodemographic). **Results:** The ratio Male/Female (M/F) was higher in preeclampsic women (1.24) than in normotensive women; we found a high ratio at high altitude (1.26) compared with the sea-level population (1.13). The ratio M/F in preterm delivery was higher (1.4) than the new born at term (1.2). The adjusted OR at high altitude was 1.17 (IC 95% 1.04-1.33) while at sea level was not significant (OR 1.08; 95% 0.85-1.37). **Conclusion:** In conclusion the population at high altitude, and the gender fetal and other factors increases the preeclampsia/eclampsia risk **Acknowledgments:** This Study was supported by a Grant from the Fogarty (NIH Research Grant # 5-D43TW005746-04 funded by the Fogarty International Center, National Institutes on Environmental Health Services, National Institute for Occupational Safety and Health, and the Agency for Toxic Substances and Disease Registry).

138.

PLACENTAL ADAPTATION TO HIGH ALTITUDE.

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Introduction: The placenta is integral to the development of preeclampsia, its incidence being 3-4 fold greater in high altitude populations. Thus, placentas from healthy and preeclamptic high altitude pregnancies provide an excellent in vivo human model for investigating mechanisms of successful and failed adaptation to hypoxia. **Methods:** Our recent work suggests that placental adaptation to reduced oxygen supply is not accomplished by improving vascularization, rather it involves modification of mitochondrial-mediated response to hypoxia. The goal of our current investigations is to determine mechanisms by which mitochondrial density and activity are altered in placentas from pregnancies that have successfully adapted to high altitude and those that have not (preeclampsia). **Results:** Specifically, acute hypoxic activation of HIF can lead to mitochondrial autophagy (mitophagy) via BNIP3, thus reducing mitochondrial density during chronic hypoxia and mitochondrial density is lower in adapted high altitude placentas. Furthermore, expression of mitochondrial uncoupling proteins (UCP), which act to reduce oxidative phosphorylation and oxygen radical production are also lower

in healthy placentas. However, mitochondrial density and UCP expression do not appear to be lowered in preeclamptic placentas at high altitude. **Conclusion:** Further details of mitophagy and mitochondrial activity in relation to placental adaptation to high altitude will be presented and discussed.

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HYPOXIC EXERCISE INSTANTLY INCREASES SOLUBLE VEGF RECEPTOR − 1 CONCENTRATION IN HEALTHY ADULTS.

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Introduction: It has been shown that acute hypoxia decreases plasma VEGF concentration (1) in healthy subjects at rest. The response of VEGF, other angiogenetic factors and the anti-angiogenic sVEGF-Receptor-1 (sVEGFR-1) to acute hypoxia and exercise (aH&E) remain unclear. **Methods:** To study the cytokine response to aH&E we examined 16 healthy subjects ($VO_{2m}ax > 50$ mL • min-1 • kg-1) of either sex at a simulated altitude of 5500 m (equivalent: Everest Base Camp) by using a chamber with normobaric hypoxia. The experimental sequence included a 360 minute exposure to hypoxia with two 30 minute bouts of stepping (60 steps • min-1) starting at 90 and 270 minutes. Blood samples were taken before and at 90, 180 and 300 minutes in hypoxia and analyzed for VEGF, sVEGFR-1, erythropoietin and platelet derived growth factor (PDGF). **Results:** All subjects tolerated the experiment well. sVEGFR-1 but not VEGF was increased at the 180 and the 360 minute measurements ($P < 0.05$). Both other angiogenic mediators, erythropoietin and PDGF were increased at the 180 and 360 minute measurements ($P < 0.05$). **Conclusion:** While exposure to aH&E caused a vigorous response in sVEGFR-1, VEGF itself was not increased. This result is compatible with an all-over increase in VEGF where the concurrent upregulation of sVEGFR-1 resulted in an unchanged amount of unbound VEGF. 1. Oltmans K. et al. Acute hypoxia decreases VEGF concentration in healthy humans. Am J Endocrinol Metab 2006:290;434-439.

140.

AUSCULTATORY AND ECHOCARDIOGRAPHIC FINDINGS IN DOGS WITH "LONE" TRICUSPID REGURGITATION, AND RESPONSES TO CHANGING PULMONARY ARTERIAL PRESSURE.

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Introduction: Three large, male dogs had multiple catheters placed via a jugular vein through the tricuspid orifice. These produced "lone and pure" tricuspid regurgitation (TR) with systolic murmurs and jugular pulsations. We sought to describe the murmur intensity (mi), and to determine if increasing (with hypoxia) or decreasing (with sildenafil) peak pulmonary arterial pressure (PAP) would affect the mi. **Methods:** Dogs were narcotized lightly and examinations were performed without alterations in PAP, and after PAP was increased as dogs breathed 11% 02, or decreased in response to the PDE5-inhibitor, sildenafil. Mi and point of maximal intensity (PMI) of the murmur on the thorax was recorded by 4 persons who penciled the PMI on a sketch of the left and right sides of the torso. Echocardiograms with Doppler interrogations of the tricuspid orifice quantified severity of TR, and PAP was estimated by the modified Bernoulli's equation. **Results:** All dogs had jugular venous pulsations, and systolic murmurs heard, in general loudest on the right hemithorax at the 3rd intercostal space approximately ¼ of the ventrodorsal distance from the sternum. PAP increased from an average ~35 mmHg to ~54 mmHg during hypoxia and decreased to an average ~30 mmHg after sildenafil. Because the number of dogs included was small, statistical analysis was not performed, but the possibility of these directional changes occurring by chance is 1:6. TR changed ~10%, increasing with hypoxia and decreasing with sildenafil; Mi changed approximately I/VI, decreasing with sildenafil, however Mi could not be quantified due to hypoxic dyspnoea. **Conclusion:** In summary, TR and Mi increased with increased PAP produced by hypoxia and decreased with decreased PAP produced by sildenafil. It suggests that directional changes in PAP may be predicted by mi. However this study must be repeated in dogs with naturally-occurring TR, but will be more complicated since TR occurs most often with mitral regurgitation the murmur of which might obfuscate that of TR. **Acknowledgments:** The Ohio State University Medical Center, Department of Cardiovascular Medicine.

141.

PULMONARY HYPERTENSION (PH) OCCURS BECAUSE OF INCREASED ARTERIOLAR AND/OR ARTERIAL HINDRANCE OF FLOW FROM RIGHT VENTRICLE TO LEFT ATRIUM.

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Introduction: To determine the location of the increased resistance to pulmonary arterial flow hindrance in dogs subjected to FiO_2's of 12% and 10%. **Methods:** Nine dogs were anesthetized with acepromazine-butorphanol-propofol. Pulmonary peak systolic, mean, diastolic, and pulse pressures were monitored continuously using Millar catheters. Dogs ventilated with 21%, 12%, and 10% FiO_2's, and differences in pulmonary arterial pressures and rates of increase and decrease were measured. **Results:** Although we observed the expected hypoxia-induced increase in pulmonary arterial pressure, interesting observations were: (1) the rate of elevation of pressure to decreased FiO_2 appears linear, but the rate of fall in pressure after return to normal FiO_2 is exponential, and (2) the pulse pressure changed more for 10% than for 12%. **Conclusion:** Historesis in differences in "on " and "off" of pulmonary arterial pressure, and differences between pulse pressures for 10% and 12% FiO_2's may indicate that the causative increase in hindrances may be pulmonary arteriolar (i.e., increased pulmonary vascular resistance) or pulmonary arterial (i.e., increased impedance) and depend upon the FiO_2. **Acknowledgments:** We appreciate the support of QTest Labs and Facultad de Medicina Veterinaria, Universidad Nacional de Colombia.

142.

THE ROLE OF PERINATAL HYPOXIA IN THE DEVELOPMENT OF PRECLINICAL CMS.

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Introduction: Chronic mountain sickness (CMS) is a significant public health problem for the more than 140 million persons living at high altitudes (>2500 m) yet its etiology remains incompletely understood, in part, because the effects of normal aging obscure the identification of causal factors. Excessive erythrocytosis (EE, Hb ≥ 18.3 g/dL) is considered to be a preclinical form of CMS. We hypothesized that perinatal hypoxia increases susceptibility to CMS by impairing development of pulmonary structure and/or respiratory control. **Methods:** 30 EE and 29 controls were selected for detailed physiological study from a survey of 820 young (18-25 yr)

male residents of La Paz/El Alto (3600-4100 m). **Results:** Of the 820 males surveyed, 8% had EE. The majority of the 30 EE subjects studied presented with arterial hypoxemia ($SaO_2 < 2$ SD altitude-specific mean) and/or pulmonary hypertension (>35 mmHg, systolic) in the absence of underlying disease. 63% of EE cases experienced perinatal hypoxia as manifested either by being preterm (29%), born to a preeclamptic mother (38%), or neonatal hypoxia diagnosis (38%). In contrast, the frequency of these conditions in controls was 24%, 11% and 6%, respectively. Although EE subjects weighed 378 g less at birth than controls, this difference was not statistically significant. All 59 subjects were normal in terms of body weight, height, and body mass index. Alveolar ventilation and FEF75% values were lower in EE than control subjects, whereas lung diffusion capacity, HVR, FVC, FEV1 and % of FEV1/FVC were equivalent. The majority of EE subjects showed evidence of pulmonary hypertension (62%), and/or right ventricular hypertrophy (67%). **Conclusion:** We concluded that exaggerated perinatal hypoxia may increase the susceptibility to CMS via alterations in pulmonary development and/or respiratory control. Impaired growth in utero has been shown to raise susceptibility to adult disease; these are the first data from a well-controlled study to demonstrate a possible influence of exaggerated perinatal hypoxia on increased the susceptibility to CMS. **Acknowledgments:** We would like to thank the generous participation of our research subjects; Dr. Rob Roach (ARC); Dra. Diva Bellido, Cristina Gonzales, Ana Maria Alarcón, Marta Aguillar, Catherine Romero, Yvonne Contreras (IBBA); Lic. Javier Fuentes (INSEF); Dra. Maritza Vargas and Lic. Walter Amezaga (Normal Superior Simon Bolivar); and financial support provided by NIH (R03TW007957-01A2).

143.

VASODILATORS EFFECTS OF P-HYDROXYACETOPHENONE ISOLATED FROM SENECIO NUTANS FROM NORTHERN CHILE.

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Introduction: The species Senecio nutans (Chachacoma) plant endemic of the altiplane of northern of Chile is widely used by communities altiplanic of Chile, Bolivia, Peru and Argentina as a medicinal tea for acute mountain sickness (AMS). The aim of this study is to determine the vasodilator effects of p-hydroxyacetofenona obtained from Senecio nutans. **Methods:** We obtained aqueus and hydroalcholic extracts from leaves and stems of Senecio nutans. Subsequently, a secondary metabolite was purified from hydroalcholic extract through column chromatography (silica gel) which was eluted with n-hexane-ethyl acetate (10-70%). The purity of the compound isolated was verified by nuclear magnetic resonance spectroscopic and infrared spectroscopy analysis. The vasodilator effects was evaluated through myography in rat aortic rings maintained in Krebs solution (95% O_2, 5% CO_2, pH 7.4, 37 ° C) connected to isometric tension transducers and BIOPAC system. **Results:** The intravenous administration of aqueous and hydroalcoholic extract in rats induce a significant decrease in mean arterial pressure (MAP) from 5 to 10 mg/kg rat, respectively. Also induce dosis-dependent vasodilation in rat aortic rings pre-contracted with phenylephrine (10-6 M). The EC50 determined for aqueous and hydroalcoholic extracts were 56 and 558 ug/mL, respectively. The compound purified from the hydroalcoholic extracts were run in thin layer chromatoghaphy (TLC) in aluminum film with different standards. The retention factor (Rf) was 0.28 similar to the compound 4-hydroxy-3-(2′-isopentenyl) acetophenone. The purified compound (10-4 m) induces a relaxation ~80% in rat aortic rings pre-contracted with phenylephrine. **Conclusion:** Our results suggest that derivatives of p-hydroxyacetophenone obtained from Senecio nutans could be drug with potent vasodilator effects. Future experiments must be conducted to determine effects on blood pressure and the mechanism of action of these compounds. **Acknowledgments:** Supported by FONDECYT 1040294, DI-1339-07, Paredes A and Kuzmicic hold PhD Felowship.

144.

EFFECTS OF HYPOXIA ON NOCTURNAL ERECTION QUALITY: A CASE STUDY FROM THE MANASLU EXPEDITION.

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Introduction: The aim of this study was to evaluate altitude-dependent effects on sleep-related erections (SREs) in order to estimate the role of hypoxia in erection physiology. Penile erections are physiological events based on neuroendocrine and neurochemical mechanisms. SREs occur during REM sleep and their measurement is commonly used to discriminate between psychogenic and organic erectile dysfunction (ED). **Methods:** SREs were recorded by RigiScan on a mountain climber involved in the Manaslu expedition 2008, during 43 consecutive nights at altitudes ranging from 0 to 5900 m. Erections number and duration, event duration (% of session), event rigidity %, time rigidity 0-59% and 60-100%, tumescence activated unit and rigidity activated unit and event tum % > bline (%) were assessed. The subject was equipped with a BodyMedia's SenseWear™ armband in order to exclude disorders on sleep quality. **Results:** No significant differences were observed comparing Total Sleep Times and Rough Sleep Efficiencies approaching to Base Camp (BC) (5050 m), with respect to values detected during BC sojourn. Oppositely, during BC approach to and at BC, the erectile param showed an altitude-correlated reduction trend. During the low ascending the subject had increased trends in all studied NPTR (Nocturnal Penile Tumescence and Rigidity) param, with respect to pre-expedition values relative to sea level. On the opposite, a decline in the physiological erectile function was experienced by the subject at high altitude BC and marked reductions in all the NPTR param were recorded by RigiScan analysis. The return to sea level not only reverted but has improved these functional reductions detected at high altitude. **Conclusion:** Although hypoxia represents a condition related to many co-morbidity ED factors, the literature still does not claim explicitly hypoxia as an etiological ED factor. Our results suggest that oxygen availability and delivery could play an important role in the regulation of local penile erection-related mechanisms and that low oxygen levels might be considered an etiological factor in ED. **Acknowledgments:** This work was supported by the Department of Basic and Applied Medical Sciences, University of Chieti, Italy. We wish to thank all participants in the "Manaslu experimental project". Special thanks to all the Nepalese porters and Sherpas whose roles were crucial to the realization of the scientific project.

145.

INFLUENCE OF ALTITUDE HYPOXIA IN PHYSIOLOGICAL MECHANISMS OF HUMAN MALE FERTILITY.

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Introduction: Spermatogenesis is one of the most delicate processes occurring in reproduction. Many studies suggest that exposure of normoxia-native individuals to hypoxia can affect spermatogenesis. The aim of this study was to evaluate the effect of chronic altitude hypoxia on human male reproductive functions. **Methods:** Seven healthy subjects climbed for 13 days in an acclimatization trek until they reached Manaslu Base Camp (5000 m) for spending 22 days at high altitude. The climbers slept 2 nights in camp 1 (5900 m) and, finally, after some failed attempts to climb to camp 2 (6400 m), returned to Katmandu in 8 days. Before and after the expedition, a number of seminological param (SP) were analysed: volume, total sperm number, sperm count, motility, % of sperm with normal morphology, total number of motile sperm. Before and after the expedition at sea-level (sl), after 10 days at sl and 6 months from the expedition return at sl, the serum levels of T, FSH, LH, PRL, 17β-E2, cortisol, FT3, FT4, TSH were assessed. $P < 0.05$ was considered statistically significant. **Results:** Volume, total number, total number of motile spermatozoa and sperm count was found to be reduced after return to sl. T increased 10 days after, returning to pre-values at 6 months follow-up. FSH increased after return as a result of high altitude experience, with return to pre-expedition value after 10 days. LH increased after return to sl, with recovery 6 months after. The 17β-E2 decreased after return with recover trend 10 days after and with total recovery at 6 months. PRL increased after return, at 10 days, with recovery at 6 months. Decrease of FT3 and increase of FT4 at the end of expedition, with recovery after 10 days. **Conclusions:** Hypoxic experience induced negative effects on male fertility occurring through the reduction of important SP, thus suggesting the influence of oxygen supply in physiological mechanisms of spermatogenesis. Furthermore, this study shows that prolonged altitude exercise is related to an adaptation of the endocrine system. **Acknowledgments:** We wish to thank all expedition volunteers involved in this study. A special thanks to all the Nepalese porters and Sherpas whose role has been crucial for the success of the expedition and to the realization of the scientific project.

146.

EFFECTS OF GLOBALIZATION ON LIVING HABITS IN AN ARGENTINA HIGH ALTITUDE POPULATION.

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Introduction: In order to study growth and nutritional condition of schoolchildren from Antofagasta de la Sierra, a village in height, located at 3223 m in the Puna Argentina, anthropometric measurements were obtained and dietary surveys were applied.

In this paper we analyze the results of dietary surveys. **Methods:** 59 ad hoc surveys were conducted and applied to mothers and guardians of all school-age children from Antofagasta de la Sierra (204 individuals). The data obtained as to do with main meals per day, from Monday to Friday and on weekends separately; frequency of consumption of dairy products, meat, vegetables, water, sugary foods, fried foods and with physical activity. **Results:** Results show that approximately two thirds of children had the four main meals, either from Monday to Friday or weekends. As regards frequency, the findings show relatively low percentages of "healthy food groups" daily consumption, in particular dairy products, fruit and vegetables; high consumption of sugary foods and drinks on a daily basis - more than 58% replacing water intake-, since a third of children do not prefer water as the main beverage. In this group, only 50% of the children exercise physical activity regularly. **Conclusion:** As a conclusion, we found that the surveyed population maintain ancient cultural patterns ingrained in relation to food and recipes consumed because they have lived far from urban centers for centuries until two decades ago. Due to better access roads to this community, there is now a burst in of new food and technologies, Depending on that situation, the results are interpreted as a nutritional, epidemiological, food access and availability transition context. **Acknowledgments:** This work was funded by ANPCYT in the context of the project PICTO 32451 of FONCYT and UNCA.

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EXHALED NO AS MARKER OF INFLAMMATION IN WORKERS WORKING SHIFTS AT HIGH ALTITUDE MINE.

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Introduction: Our previous study in employees of high altitude mine showed obstructive ventilation defect (OVD) to be present in around 9% of sample, not all of which were ever-smokers. The aim of this study is to assess prevalence and role of allergic inflammation in airways as a reason of OVD in mine workers. **Methods:** Employees of high altitude mine (3800-4500 m above sea level) in Kyrgyzstan working either 2- or 3-week shifts undergoing full annual screening were subjected to exhaled NO measurement by means of NiOX MINO device in conditions of low altitude (700 m). Routine spirometry was performed with the use of Micro-Medical office spirometer. Only practically healthy (no diagnosed illnesses) of having any OVD patients were included. NO readings were analyzed in relation to smoking status, work duration, body mass index and other factors. **Results:** By the time of abstract submission, data on 121 subjects were collected (of almost 2500 workers), of whom 90 were healthy and 31 had any form of OVD. NO did not differ between healthy (17.5 ± 9.7 ppb) and having OVD (21.5 ± 10.7 ppb) subjects. There was a small negative ($r = -0.24$) correlation of NO with work duration, some small positive correlation between NO and body mass index ($r = 0.29$), vital capacity ($r = 0.25$), forced volume capacity ($r = 0.27$) and blood hemoglobin ($r = .28$). **Conclusion:** Data presented here are preliminary findings, and the current study is ongoing. Presently same subjected are subjected to NO measurement upon arrival at site, on days 3, 7 and by the end of the shift. Data will be ready and communicated at the congress.

148.

PERIPHERAL OXYGEN DELIVERY ADJUSTMENTS AFTER INTERMITTENT HYPOBARIC HYPOXIA EXPOSURE.

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Introduction: In recent years our group has studied adaptive responses at the level of myocardial and skeletal muscles to intermittent hypobaric hypoxia exposure (IHHE) programs. Although it is clear that the laboratory rat has a lower tolerance to hypoxia than people do, a rat experimental model allows us to perform studies that, for technical or ethical reasons, cannot be performed on humans. **Methods:** Tissue hypoxia is a stressful situation for most animals. To cope with oxygen requirements, organisms are able to make physiological and morphological adjustments to maintain a minimum level of aerobic metabolism under conditions of poor oxygen delivery to the tissues. Intermittent hypoxia exposure patterns follow the training theory; a series of

stressful sessions, followed by sufficient recuperation periods, elicit a better adaptive response. Moreover, according to the symmorphosis principle, structural elements are formed to satisfy functional requirements without excess. As a consequence, it can be expected that some corresponding morphological and metabolic changes in heart and skeletal muscle must be associated with the increase in blood oxygen transport capacity elicited by the hypoxia-induced erythropoiesis. **Results:** Our results showed a significant increase in capillary myocardial density after IHHE, whereas in skeletal muscles these effects seemed to be dependent of the level of activity as well. Associated changes were also detected after IHHE in some muscular enzymes that are markers of oxidative and anaerobic metabolism. In addition, blood viscosity did not increase in proportion with the rise in hematocrit, indicating that some adjustment occurred to maintain adequate blood flow despite the increased corpuscular fraction. Lower plasma protein content and also probably microrheological erythrocyte changes may be the main causes of this phenomenon. We recently demonstrated a significantly increased stem cell (CD34+) proportion in circulating blood after IHHE plus muscle activity. **Conclusion:** These findings provide a basis for future applications of IHHE in potentially fast-growing new biomedical fields.

149.

ACUTE MOUNTAIN SICKNESS (AMS): SOME IDEAS FOR UNRAVELING THE PUZZLE.

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AMS was first described and classified as one of the high altitude illnesses in Peru nearly 100 years ago by Ravenhill. Since then scientists have struggled to understand what causes AMS. In the process, good options have been discovered for treatment and prevention. Yet the underlying pathophysiology remains uncertain. Since the early descriptions of a 'nervous puna' the focus in AMS pathophysiology studies has shifted to investigations of the role of the brain in AMS. We will review a number of factors that may be at play in the pathophysiology of AMS. Some of these factors are clearly described, and others which are 'thought' to be at play, and still others remain completely untested. We will also review procedures to experimentally test AMS and how those procedures, utilized or not, may influence the outcome of studies into the pathophysiology of AMS. In our opinion, to move the study of the fundamental causes of AMS forward, the field needs to consider these issues to formulate advanced studies with potential to reveal the remaining pieces of the puzzle that is the pathophysiology of AMS.

150.

SPORTS TRAINING AT ALTITUDE.

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Introduction: This research was conducted in Arequipa, the second largest city of Peru located at 2360 m, in the High Performance Sports Center in Peru, a space created to enhance physical functional capacity of Sprint, Track and Field, Middle Distance and Long Distance Athletes based on competitive performance. The main research objective was to determine the hematological changes, medical and sports performance training at medium altitude. **Methods:** In terms of methodology, we evaluated the levels of hemoglobin and hematocrit, clinical histories and sports results in a period of 12 months. The sample was consisted 20 elite athletes with an average age of 14 years of both sexes. **Results:** The main results showed that the Centre was home to the best athletes in motion, short and middle distance from across the country, 90% came from the mountains (3500- 4500 m). During the first days of adaptation to altitude of Arequipa, tests were made which included the baselines of hemoglobin and hematocrit. These tests were repeated for the first 15 days and then monthly, to see the trend in a year. At the beginning of the training, athletes from the mountains had an average level of hemoglobin by 18.5 g/dL, while the average for athletes from the coast was 14.0 g/dL. After a month of training in Arequipa, these levels changed the levels of the athletes from the mountains decreased by 1.5 of hemoglobin and athletes from the coast increased by 2 points. After a year, the average hemoglobin level for the group stabilized on 17 g/dL for males and 14.8 g/dL for females, and also their performance and physical capacity of endurance, strength and speed were improved. Regarding the most common medical problems in the early days of adaptation were: headache, fatigue and digestive problems, which were resolved within 10 days. **Conclusions:** An increased hemoglobin level between 1 and 3 g/dL is responsible for a higher uptake of oxygen and improves the capabilities of sports.

151.

CHRONIC MOUNTAIN SICKNESS AND OBSTRUCTIVE SLEEP APNEA: A CASE CONTROL STUDY.

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Introduction: Chronic mountain sickness (CMS) is a clinical syndrome characterized mainly by excessive erythrocytosis. Recent studies have shown that the disturbances in nighttime ventilation of Obstructive Sleep Apnea (OSA) can lower arterial blood saturation and provide an additional stimulus for erythropoiesis. Thus, it is possible that sleep disorders contribute to the development of CMS. This study's goal is to determine the relationship between CMS and OSA in male high altitude dwellers. **Methods:** We conducted a cross-sectional case control study and compared CMS patients with healthy high altitude dwellers (HA) as controls. We recruited 217 male volunteers (96 cases and 121 controls) from Cerro de Pasco, Peru (4300 m). Oral interviews were conducted to determine OSA risk using the Berlin Questionnaire and the Xining Criteria was used to determine CMS diagnosis and severity. **Results:** The average age was 43 (±13.9) years. Twenty-one per cent of volunteers presented a high risk of OSA. By using logistic regression, we determined that participants with OSA presented CMS with an odds ratio (OR) of 2.05 (IC95%: 1.78-6.34; $LL = -84.56$). Likewise, those with OSA presented mild CMS with an OR of 1.95 (IC95%: 1.17-3.26), moderate CMS with an OR of 4.34 (IC95%: 1.97-9.56) and severe CMS with an OR of 6.01 (IC95%: 2.47-14.62). We found a significant ($P < 0.05$) trend between increasing severity of CMS and OSA. Step-wise multivariate analysis showed that BMI and past history of pulmonary, cardiovascular or infectious disease contributed significantly ($LL = -73.12$; log likelihood test: $P < 0.001$) to the relationship between OSA and CMS. **Conclusion:** The results of this study suggest a relationship between OSA and CMS. An increasing severity of CMS appears to be associated with a greater risk of OSA. Future studies should include sleep polygraphy as an objective measurement of OSA.

152.
ARTERIAL OXYGEN SATURATION WAS NOT A PREDICTOR OF ACUTE MOUNTAIN SICKNESS NOR SUMMIT SUCCESS.
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Introduction: The purpose of this study was to determine if arterial oxygen saturation (SaO_2), as measured by a finger pulse oximeter upon rapid arrival to 4260 m, could be predictive of acute mountain sickness (AMS) or summit success on a climb to 5640 m. **Methods:** In total 73 climbers volunteered to participate in the study. After excluding those taking drugs to counteract the effects of AMS and those with missing data, 48 participants (45 male, 3 female) remained. The average age of participants was 34.5 ± 10.2 y. Climbers were transported from 2650 m to the Piedra Grande hut at 4260 m on Pico de Orizaba within 2 h. After a median time of 9.88 h at the hut, they climbed toward the summit (5640 m) and returned with a median trip time of 13.25 h. The Lake Louise Self-assessment Questionnaire (LLSQ) for AMS, heart rate, and SaO_2 from a finger pulse oximeter were collected upon arrival at the hut and repeated immediately before the climbers departed for their summit attempts and immediately upon their return. The presence of AMS was defined as a LLSQ ≥ 3 with a headache and at least one other self-reported symptom. **Results:** 64.3% of the participants successfully reached the summit. Average SaO_2 for all participants at 4260 m prior to their departure for the summit was $84.4 \pm 3.6\%$. 54.8% of participants met the criteria for AMS during their ascent. There was not a significant difference ($p > 0.05$) in SaO_2 between those who experienced AMS ($SaO_2 = 84.3 \pm 4.3\%$) and those who did not ($SaO_2 = 84.2 \pm 3.3\%$) during the ascent; neither was there a difference in SaO_2 between summiteers ($84.8 \pm 3.7\%$) and non-summiteers ($83.3 \pm 4.0\%$). **Conclusion:** SaO_2 does not appear to be predictive of AMS or summit success. **Acknowledgments:** American Alpine Club, Mazamas, and Wilderness Medical Society.

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BLOOD AND BODY COMPOSITION CHANGES BEFORE AND AFTER ASCENTS OF ACONCAGUA AND EVEREST.
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Introduction: Both Mt. Aconcagua (6962 m) and Mt. Everest (8850 m) are highly prized summits by mountaineers. Ascents of these peaks place a physiological strain on the human body resulting in adaptation. The purpose of this case study was to compare the pre- and post- blood chemistry and body composition of a mountaineer who ascended both peaks. **Methods:** The male subject was 41 y during the Aconcagua ascent (February 2008) and 43 y during the Everest ascent (May 2009). He was moderately fit ($VO_{2m}ax = 54$ mL/kg/min), residing at 1382 m, and had a history of more than a dozen ascents above 6000 m over the previous 10 years. Baseline blood draws and body composition measurements were done within a couple days of departure for both expeditions. The blood draw consisted of a complete blood count (CBC), and body composition was assessed by air displacement plethysmography (Bod Pod®). **Results:** The post-Aconcagua measurements were taken 10 d after reaching the summit. They revealed a 2.0 kg drop in body mass and a reduction in body fat (15.5% to 12.1%). Blood chemistry remained largely unchanged (RBC = 5.09 million/mL to 4.95 million/mL, Hgb = 15.6 g/dL to 15.4 g/dL, Hct = 46.4% to 45.7%, MCHC = 33.7 g/dL to 33.8 g/dL). The post-Everest measurements were taken 14 d after reaching the summit. Body mass was reduced from 65.0 kg to 60.5 kg with a drop in body fat from 17.3% to 10.2%. Despite no change in RBCs (4.90 million/mL to 4.86 million/mL) there were increases in Hgb (15.7 g/dL to 17.7 g/dL), Hct (45.8% to 48.0%), and MCHC (34.3 g/dL to 37.0 g/dL). **Conclusion:** It took the subject 12 d to reach the summit of Aconcagua whereas it took 50 d to reach the summit of Everest. The longer duration at higher altitude resulted in more dramatic physiological changes.

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COMPARISON OF ASSESSMENT SCALES OF ACUTE MOUNTAIN SICKNESS.
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Introduction: The purpose of this study was to compare three assessment scales of acute mountain sickness (AMS) on climbers making a rapid ascent of a 5640 m peak. **Methods:** The three scales administered were the Lake Louise Self-assessment Questionnaire (LLSQ), the 11-item Environmental Symptom Questionnaire (ESQ-III), and a 100 mm visual analog scale (VAS). Each questionnaire was administered three times: when climbers first arrived at the base camp hut (4260 m), immediately prior to their departure for the summit, and post-hoc immediately upon return to the hut following their summit attempt. **Results:** Sixty-four climbers completed the questionnaires. After staying in the hut for a median time of 9.88 h prior to departing for the summit, the mean AMS scores were LLSQ = 1.8 ± 1.8, ESQ-III = 0.2 ± 0.3, and VAS = 3.9 ± 6.1. All of the scales correlated ($r = 0.67$ to 0.77, $p < 0.01$). The median roundtrip time to the summit and back to the hut was 13.25 h. Post-hoc reporting of AMS revealed a large increase in the scores during the ascent (LLSQ = 5.5 ± 3.3, ESQ-III = 1.1 ± 1.0, VAS = 20.8 ± 27.5). All of the scales were highly correlated ($r = 0.78$ to 0.87, $p < 0.01$). Also, the relationships among scales for high altitude headache were high ($r = 0.88$ to 0.91, $p < 0.01$). The criterion of LLSQ ≥ 3 with a headache and one additional symptom resulted in 41 of 64 climbers being diagnosed with AMS compared to 32 climbers with a more stringent criterion of LLSQ ≥ 5 and 33 climbers using the ESQ-III cut point of 0.7. There was a differential diagnosis between ESQ-III and LLSQ about 16% of the time regardless of which LLSQ cut point was used. **Conclusion:** Cut points and the sensitivity and specificity of the VAS were determined relative to the established criteria of the other scales. Although participants will likely need to be educated on how to properly complete the VAS, this scale may bring some added clarity to the assessment of AMS. **Acknowledgments:** American Alpine Club, Mazamas, and Wilderness Medical Society.

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IGF-I PROTECTS RETINAL GANGLION CELLS FROM HYPOXIA-INDUCED APOPTOSIS BY ACTIVATING ERK-1/2 AND AKT PATHWAYS.
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Introduction: Hypoxia-induced retinal ganglion cell (RGC) apoptosis has been implicated in many optic neuropathies. Insulin-like growth factor-I (IGF-I) is important in maintaining neuronal survival, proliferation and differentiation. However, whether IGF-I can protect RGC from hypoxia-induced apoptosis and its precise mechanism remain unclear. The purpose of this study is to explore the possible

neuroprotective roles of IGF-I in hypoxia-induced RGC apoptosis. **Methods: Results:** In our study, we observed that hypoxia could induce the apoptosis of primary cultured RGC isolated from SD rats by TUNEL, JC-1 and caspase-3 activation assays, while IGF-I treatment would significantly inhibit the hypoxia-induced apoptosis of the RGC. Surprisingly, we also found that pretreatment of the specific inhibitor of IGF-I receptor (AG1024), Erk-1/2 (U0126) and Akt (LY294002) may markedly attenuate the effect of IGF-I treatment. Furthermore, the Western Blot results confirmed the possible involvement of Erk-1/2 and Akt pathways in IGF-I-reduced apoptosis of RGC in response to hypoxia. **Conclusion:** Our data indicated that IGF-I might rescue primary cultured RGC from hypoxia-induced apoptosis by activating Erk-1/2 and Akt pathways, suggesting the IGF-I treatment as a potential therapy approach to hypoxia-associated retinal neurodegenerative diseases.

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OBSERVATION OF BONE MINERAL DENSITY IN PERIMENOPAUSAL WOMEN AT DIFFERENT ALTITUDES.

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Introduction: Osteoporosis is the world's intractable diseases, more and more attention, and the many factors that lead to osteoporosis has also been more in-depth research. At different altitudes on the plateau, whether bone mineral density in Han women with perimenopausal have different with one in plain areas, it has not been reported in China. we would observe and compare bone mineral density in perimenopausal women at different altitudes, to study a correlation between bone mineral density in perimenopausal women and altitude. **Methods:** The perimenopausal women who living in different altitude were divided into two groups: perimenopausal women with 180 cases at high altitude (elevation 4200 m) for the A group. perimenopausal women with 180 cases moderate altitude (elevation 2260 m) for the B group. The two groups were all Han Chinese with a mean age (46 ± 1.5) years old, not yet menopausal,with an average age of menarche (14.01 ± 1.60) years, and exclude hereditary and bone metabolism diseases.The reference of 180 cases data that published in Chinese Osteoporosis in 2002 as plain control group. Age, body mass index of perimenopausal women at moderate altitude groups have not different with high-altitude group($P > 0.05$). Bone mineral density of lumbar spine, greater trochanter and femoral neck in two group were determind by CHRONOS French dual energy x-ray absorptiometry. **Results:** Bone mineral density of 2-4th lumbar spines, trochanter, femoral neck in A group have no significant difference with B group ($P > 0.05$), two compared with the plain $P > 0.05$, there was no significant difference in. Conclusion: The plateau regions at different altitudes of perimenopausal women with bone mineral density and the plain areas without distinction. **Conclusion:** We believe this phenomenon and adapt to the highland environment, habits related to the plateau of living longer, the body has to adapt to high altitude environment, nutrition intake and metabolism is basically balanced.

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MEASUREMENT OF BODY CORE TEMPERATURE BY HEAT FLUX DOUBLE SENSOR IN HYPOTHERMIC PIGS DURING ARTIFICIAL AVALANCHE BURIAL.

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Introduction: If an avalanche victim is completely buried by snow prolonged survival is only possible if breathing is possible due to an air pocket surrounding his airways. Hence, two thirds of buried victims die from obstructive asphyxia within 35 min (10-11, 15), but one third will survive for more than 35 min depending on the size of an air pocket and snow density (2). Therefore, in victims with an air pocket hypothermia becomes an important co-morbidity. It is known that hypothermia can have a protective effect on highly oxygen dependent brain and heart in reducing oxygen metabolism by $\sim 6\%$ per $^{\circ}C$ body core temperature (13), but it may also provoke cardiac arrest below the critical level of $32^{\circ}C$ (4, 6, 12, 15-16). Deep hypothermia has a mortality rate between 30 and 80% (1, 5). Previous studies found core temperature cooling rates of $1.2^{\circ}C$/hour (7) in contrast to some recent case reports with $\approx 9^{\circ}C$/hour (15). To this day, onsite temperature measurement is still unreliable with epitympanic, not practicable with rectal probes, and semi-invasive method with an esophageal or invasive with pulmonary artery probe, which are only applicable in intubated patients (3). Core temperature is predictive of survival and hence essential in guiding on-site treatment (11). Thus, a reliable, fast and non-invasive method for body core temperature measurement is warranted to optimize onsite treatment of avalanche victims. **Methods:** In a prospective, randomized study, officially approved by the Veterinary Study Committee of the Science Ministry of Austria, and conducted in the Oetz Valley, Austria, at 1,900 m of altitude, avalanche burial was simulated by burying intubated, continuously anesthetized and spontaneous breathing pigs (weight 25-42 kg) beneath avalanche snow. From a total of eight pigs, randomized in group A ($n = 3$) and B ($n = 2$) having a closed air pocket of 1L and 2L respectively, the control group C ($n = 3$) with an open air pocket to the outside permitting to breath into ambient air was used to assess agreement between the different methods of core temperature measurement. Pigs were monitored continuously and body core temperature (Tc) was measured and recorded manually by pulmonary artery (TcPA) and esophageal probes (TcOE). In comparison to those, Tc was measured with the non-invasive, heat flux Double Sensor (8-9), placed on the head (submandibular; Tchead) and sternum (Tcster) and recorded continuously every 2sec by HealthLab-System (Koralewski, Hambühren, Germany). Statistical analyses were done with PASW statistics 18.0 and Matlab 2009, significance level $P < 0.05$. **Results:** Because survival times in group A and B were short and we could not find a correlation between TcPA/OE and Tchead/ster temperature due to concomitant hypoxia, we present only results of group C to demonstrate long term temperature sequences without hypoxia. Survival in the control group ranged from78 to 178 min with a mean survival of 137 min (± 48.8 min). Mean decrease in body core temperature from baseline to the endpoint per piglet was $-10.5^{\circ}C$ (± 3.9) with TcPA, $-11.5^{\circ}C$ (± 3.9) with TcOE, $-14.12^{\circ}C$ (± 6.2) with Tcster, and-$17.3^{\circ}C$ (± 2.0) with Tchead. A Bland-Altman analysis revealed significant negative correlations between the difference and mean of TcPA to TcOE ($r = -.58$, $p < .001$) as well as Tcster ($r = -.87$, $p < .001$) and Tchead ($r = -.76$, $p < .001$), indicating that TcOE, Tcster and Tchead are lower than TcPA with lower core temperatures. After correcting for this measurement bias mean decrease in body core temperature was, $-10.7^{\circ}C$ (± 3.7) with TcOE,-$9.3^{\circ}C$ (± 4.1) with Tcster, and $-10.6^{\circ}C$ (± 1.2) with Tchead. Using those corrected values 95% confidence intervals for agreement are $\pm .75^{\circ}C$ for TcOE, $\pm 1.73^{\circ}C$ for Tcster and $\pm 3.1^{\circ}C$ for Tchead with intraclass correlation coefficients (ICC(3,1)) of .99, .97 and .92 respectively. **Conclusion:** Brain temperature, cerebral cooling rate and absolute temperatures are decisive for the outcome of avalanche victims (14). Various techniques have been

developed to measure body core temperature but an optimal method has not been found yet. This study shows a possibility to measure Tc non-invasively by heat flux DoubleSensor with a quick response rate and in good agreement as compared to standard pulmonary artery or esophageal methods. Although mean Tcster was not statistically significant different from Tchead it seems to produce better results than Tchead possibly related to the location of the sensor. Moreover, with DoubleSensor we did notice in two pigs an initial increase in Tchead followed by a steep drop thereafter not seen in PA or OE. The same could be observed in one pig with Tcster. It has to be figured out if it is related to physiological or methodological reasons. Nevertheless, our results on three piglets do suggest that DoubleSensor measurement will most probably be reliable for the on-site as well as in hospital measurement of core temperature in avalanche and other hypothermic patients.

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STRATEGIES FOR IMPROVING HUMAN PERFORMANCE AT HIGH ALTITUDE.

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Introduction: Increasingly, people are ascending to high altitude to work. How can their performance be improved in this hypoxic environment? The advantages obtained by gradual ascent and the resulting acclimatization are well known. However many people have misconceptions about acclimatization. Although it reduces the incidence of high altitude diseases such as Acute Mountain Sickness, it certainly does not return the body to the sea level state. As Barcroft noted in 1925 "all dwellers at high altitudes are persons of impaired physical and mental powers." Incidentally this statement apparently incensed the eminent Peruvian physician Carlos Monge Medrano. One strategy for working at high altitude is to commute, spending for example a week at altitude and a subsequent week at sea level. Partial acclimatization occurs and this pattern is employed in some mines in Chile. Another strategy for improving performance at high altitude involves pre-exposure to an intermediate altitude for several days. For example continuous residence for 6 days at an altitude of 2200 m improves work performance after a rapid ascent to 4300 m (Muza et al., 2010). Interestingly this regime also resulted in a lower pulmonary artery pressure when the subjects ascended to a simulated altitude of 4300 m (Baggish et al, 2010). A major advance in improving human performance at high altitude has been oxygen-enrichment of room air. This is a relatively simple procedure to carry out and is remarkably effective. For example every 1 percent of oxygen enrichment, for example from 21 to 22 percent, decreases the effective altitude by about 300 m. The technique is now extensively used in mines and telescope facilities, and is a critical feature in the success of the new Chinese train to Lhasa which passes through an altitude of over 5000 m. An alternative to adding oxygen to room air is supplying it with nasal cannulas. A new mine at 4500 m has plans to do this on a large scale to improve sleep but it remains to be seen how well the cannulas will be tolerated.

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ROLE OF CA_2^+ CALMODULIN-DEPENDENT PROTEIN KINASE II IN THE CARDIOPROTECTION OF INTERMITTENT HYPOXIA AGAINST ISCHEMIC-REPERFUSION INJURY.

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Introduction: Cumulated evidence has shown that adaptation to intermittent high-altitude (IHA) hypoxia increases myocardial tolerance to the subsequent severe hypoxic, Ca_2^+ overload or ischemic injury. Attractively, this form of protection is non-invasive, persists longer than ischemic preconditioning (IP) and has less side-effect such as right ventricular hypertrophy compared with the chronic hypoxia. However, much less is known on protective mechanisms of IHA hypoxia compared with the extensive studies in IP. It has been well documented that sarcoplasmic reticulum (SR) plays a central role in the regulation of intracellular free concentration of Ca_2^+ ($[Ca_2^+]i$) and subsequent cardiac contraction and relaxation processes. Dysfunction of cardiac SR Ca_2^+-pump ATPase (SERCA2) during ischemia-reperfusion (I/R) appears to be involved in the Ca_2^+ overload, and thereby affects the extent of contractile dysfunction that follows ischemia, while improvement of Ca_2^+ handling by SR has been indicated to contribute to the beneficial effects of IHA hypoxia in the I/R cardiomyocytes. **Methods:** Here, we used multiple methods from molecular biology to functional analysis to understand the regulatory mechanisms by Ca_2^+ handling proteins on SR and phosphorylation pathways. **Results:** We found that left ventricular contractile recovery, status of SR Ca_2^+/calmodulin-dependent protein kinase II (CaMKII) activity in the SR as well as phosphorylation of phospholamban (PLB) at Thr17, and SR Ca_2^+/calmodulin-dependent SR Ca_2^+-uptake activity were improved, but no changes in the activity of phosphatase during I/R in the hearts from IHA hypoxic rats. **Conclusion:** Our results indicate that preservation of SR CaMKII activity plays an important role in the IHA hypoxia-induced cardioprotection against I/R injury via maintaining SR Ca_2^+-uptake activity. **Acknowledgments:** (Grants: Major State Basic Research Development Program of P.R.China (G2006CB504106) and Knowledge Innovation Program of the CAS (KSCX2-YW-R-75)).

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ASSOCIATION BETWEEN DIFFERENT BIOFUELS USED DURING COOKING AT HOME AND ADVERSE BIRTH OUTCOMES AT HIGH ALTITUDES– PILOT STUDY.

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Introduction: One-third of the world's population burn organic material such as firewood, dung or charcoal (biomass fuel) for cooking, heating and lighting. Maternal exposure to wood fuel smoke may lead to impaired fetal growth due to hypoxia and/or oxidative stress from smoke constituents such as carbon monoxide and particulate matter. We determine if the presence of low birth weight (LBW), Small for gestational age (SGA) or the preterm delivery (PT) is associated to the use of biomass in populations living at high altitudes. **Methods:** We studied 190 residents of high altitude in Abancay (2378 m), and Huancavelica (3680 m). 95 cases (54 low birth weight ($<$2500 g), full term delivery ($\geq$37 weeks), and 41 preterm ($<$37 weeks) and 95 controls (Born Children with a weight $\geq$ 2500 grams, full term delivery) alive attended in public hospitals during the 18 months prior

to the start of the pilot study, all the deliveries were attended in the public hospitals. The group "exposed" was a woman who uses biomass fuel for cooking and the group "none exposed" was a woman who use gas for cooking. Clinical records were obtained from the public hospitals for each delivery. A questionnaire that included socio-demographic, reproductive, social habits and fuel used for cooking was assessed. The variable SGA that includes LBW, n = 79 (36.7%) was created. A conditional logistic regression model adjusted for confounding variables were performed. **Results:** We observed an increased risk to have an infant with LBW in mothers who use wood (OR 2.69, CI 95% 1.03 – 7.03) compared with mothers who used gas, the model was controlled by adjusted by maternal age, Body mass index, parity, status marital, education, smoke. We observed an increased risk to have an infant with SGA in mothers who use firewood (OR 3.04, CI 95% 1.19 – 7.77) compared with mothers who used gas. Infants born to wood users averaged 106.3 g lighter than infants born to gas users. **Conclusion:** Women using biomass to prepare their food had a significantly higher risk of delivering LBW infant and SGA than those that used gas. Cooking with wood fuel during pregnancy was associated with LBW compared with using gas. In average birth weight reduction associated to biomass fuel use was 106.3 g a value that is higher than those observed in populations at sea level (82 g). **Acknowledgments:** This Study was supported by a Grant from the Fogarty Program of The National Institutes of Health of the United States.

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HIGH-ALTITUDE SLEEP DISORDERS IN ROAD MAINTENANCE WORKERS.

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Introduction: Investigation prevalence of high altitude sleep disorders(HASD)of road maintenance workers during high altitude chronic acclimatization, reveal the characteristic changes,physiological and pathological association of Rbc and symptoms in HASD. **Methods:** 177 road maintenance workers at the elevation of (2800–2900), (3600–3740)m, (4250–4300)m were random sampled. Testing instrument is to adapt the the diff-2 full-automatic blood cell analytical instrument, and physical examination. **Results:** The prevalence of high HASD is 41.8% in total groups, male is higher than female ($p \leq 0.05$). The prevalence of high altitude polycythemia is 60.8% in HASD.Compared with control group, correlation and linear regression analysis: HASD has correlation with the performance of multi-system of nerve, spirit digestive, respiratory, heart, weight, hematological etc, the most closely relationship is the thinking disorders flustered, anorexia, weight loss, higher Rbc. **Conclusion:** In the high altitude hypoxia environment, road maintenance workers who does labor intensity has higher prevalence of HASD, HASD participates in the high altitude acclimatization, it is the syndrome of bad acclimatization at plateau.

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ASTROCYTE-CONDITIONED MEDIUM REDUCES HYPOXIA/ISCHEMIA INJURY TO NEURONS.

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Introduction: Astrocyte plays an important role in brain injuries caused by hypoxia/ischemia. Astrocyte-conditioned medium (ACM) was employed to explore mechanisms underlying the protection of neurons in hypoxia/ischemia model in our experiments. **Methods:** Cortical neurons were treated with 3-hour oxygen-glucose deprivation (OGD) to induce cell death. Neuronal viability was evaluated with MTT assay. **Results:** The result showed that more neurons survived after being pretreated with ACM for 24 h (about 40%) compared with control group (10%), which indicated astrocyte may secrete some molecules to protect neurons in OGD injury. Inhibitors of PKC, PKA, P38 MAPK, AMPAR, NMDAR, and L-type calcium channel (LCC) were used to study the further mechanism. However, none of them could block the ACM effects. These results suggested that PKC, PKA, P38 MAPK, AMPAR, NMDAR or LCC were not involved in the protection of ACM. Excitotoxicity was a leading cause of brain injury in ischemia. By hoechst (33342) staining, we found in cultured hippocampal neurons, more apoptotic cells were observed in glutamate (200 μM, 4 h) treated group (about 30%) than control group (6%). Interestingly, the immunofluorescence experiment showed that one subunit of AMPARs, GluR2, was upregulated by 50% in ACM-pretreated group, while the hoechst staining result showed ACM could significantly decrease neuronal apoptosis. **Conclusion:** All the data above suggested a mechenism of neuronal protection from astrocyte in ischemia: regulating the expression of GluR2 in cultured hippocampal neurons. **Acknowledgments:** This work was supported by National Key Basis Research Program of Ministry of Science and Technology of China (973 grant number: 2006CB504105) and National Natural Science Foundation of China (grant number: 30871287).

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GGA PRECONDITIONING PROMOTES HYPOXIC TOLERANCE AND FACILITATES ACCLIMATIZATION TO ACUTE HYPOBARIC HYPOXIA IN MOUSE BRAIN.

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Introduction: It has been shown that induction of HSP70 by administration of geranylgeranylacetone (GGA) leads to protection against ischemia/reperfusion injury. The present study was performed to determine the effect of GGA on the survival of mice and brain damage under acute hypobaric hypoxia. **Methods:** The present study was performed to determine the effect of GGA on the survival of mice and brain damage under acute hypobaric hypoxia. **Results:** The data showed that the mice injected with GGA survived significantly longer than control animals (survival time of 9.55 ± 3.12 min, $n = 16$ vs. controls at 4.28 ± 4.29 min, $n = 15$, $P < 0.005$). Accordingly, the cellular necrosis or degeneration of hippocampus and cortex induced by sublethal hypoxia for 6 h could be attenuated by pre-injection with GGA, especially in the CA2 and CA3 regions of hippocampus. In addition, the activity of NOS of hippocampus and cortex was increased after exposure of sublethal hypoxia for 6 h, but could be inhibited by the pre-injection of GGA. Furthermore, the expression of HSP 70 was significantly increased at 1 h after GGA injection. **Conclusion:** Conclusions: These results suggest that administration of GGA improved survival rate and prevents brain from acute hypoxia damage, the underlying mechanism was involved in inducing HSP70 expression and inhibiting the NOS activity. **Acknowledgments:** This work was supported by a grant from the National Basic Research Program of China (No. 2006CB504100) *Correspondence to: linglingzhu@hotmail.com.

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EFFECTS OF INTERMITTENT HYPOXIA ON THE PROLIFERATION AND MIGRATION OF NSCS IN DENTATE GYRUS IN THE JUVENILE MOUSE.

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Introduction: The present study aims to investigate whether the intermittent hypoxia can affect the proliferation and migration of neural stem cells (NSCs) in dentate gyrus (DG) of juvenile mouse, and whether Notch1 pathway is involved in the above process. General Notch1 heterozygous deficient (N1 + /-) mouse are used to study the effect of Notch1 pathway. **Methods:** The mouse are placed in the intermittent hypoxia (2000 m) environment for 4 h everyday, which lasts for 4 weeks, since the second day after birth. The mouse are injected with brdu and perfused after intermittent hypoxia. The number of brdu positive cells are counted and analyzed. **Results:** The results show that the intermittent hypoxia (2000 m) for 4 weeks can promote the proliferation of NSCs in DG. The number of brdu positive cells in the intermittent hypoxia group is about 1.6 times more than that of normoxia control group (Nor group: 109.5 ± 9.7/slice vs. IH group: 175.25 15.5/slice, $P < 0.001$). In addition, The brdu positive cells of wild type mouse is more than that of Notch1 +/- mouse after intermittent hypoxia (IH WT group: 175.25 ± 15.5/slice VS. IH Notch1 +/- group: 127.75 ± 23.2/slice; $P < 0.05$). In the aspect of migration, we found that the migration of NSCs in WT mouse is nornmal after the intermittent hypoxia, but is interfered in the Notch1 +/- mouse, which the brdu positive cells distributed in the hilus of WT mouse is less than that of Notch1 +/- mouse (IH WT group:12.08 ± 1.04 % VS. IH Notch1 +/- group:19.33 ± 3.55%; $P < 0.01$). **Conclusion:** In conclusion, the intermittent hypoxia can promote the proliferation of NSCs in DG of the juvenile mouse, and the Notch1 pathway is involved in the proliferation and migration of NSCs in DG. **Acknowledgments:** This work was supported by a grant from the National Basic Research Program of China (No. 2006CB504100).

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ADAPTATION PERIOD CARACTERISTICS IN HIGH - ALTITUDE NEWBORN.

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Introduction: Birth is a mandatory environmental change for the fetus when turning into a newborn. The adjustment processes that occur in the minutes following childbirth are crucially important for the baby's survival in the extrauterine environment. High-altitude environmental conditions, particularly hypobaric hypoxia, make this adjustment period different from what occurs in babies born in a normoxic envirronment. **Methods:** This is a prospective, longitudinal and analytical study, where 81 female and male newborns selected according to inclusion and exclusion criteria were assessed. The study was performed in EsSALUD Hospital in Juliaca, a city located at 3828 m above sea level. **Results:** Oxygen saturation progressively increased, from an average 69.1 percent at 5 minutes, 79.6 percent at 15 minutes, and 88 percent at 30 minutes, stabilizing at 120 minutes, where the value was 90.5 percent on average. Cardiac rate was on average 167.7 beats per minute at 5 minutes, and it progressively decreased, to 162.9 at 15 minutes, and it stabilized from three hours of age on. Respiratory rate was 68.3 at 5 minutes, 65.8 at 15 minutes, 60 at 30 minutes, and it stabilized in 54.6 breaths per minute at 120 minutes. **Conclusion:** The adjustment period for high-altitude newborns is longer compared to that reported in low-altitude newborns. Both respiratory and cardiac rates stabilize around 6 hours of age. Oxygen saturation, which is low at birth becomes stabilized after 6 hours of life.

166.
BLOOD SUGAR BASAL AND TEST OF TOLERANCE TO THE GLUCOSE IN HEALTHY SUBJECTS SUBMITTED TO ACUTE HIPOXIA.

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Introduction: L a Rinconada located to 5435 m at sea level in the Puno district. This altitude, at which the barometric pressure ($BP = 400$ mmHg), and the partial oxygen pressure ($PpO_2 = 80$ mmHg) are almost half from sea level values ($BP = 760$ mmHg; $PpO_2 = 159$ mmHg), is considered the border line at which permanent human life is possible **Methods:** we studied to 10 healthy resident subjects of Puno's city, located to 3,827 m whose submitted to acute hypoxia in the Centro Poblado Menor de la Rinconada located to 5435 m, the same ones that after 4 hours of arrived at extreme height were evaluated by the test of tolerance to the glucose, simultaneously they were evaluated to 10 healthy resident subjects of the Centro poblado Menor de la Rinconada **Results:** Blood sugar (mg/dL) Group Control Group of study Blood sugar basal 57.33 ± 6.08 91.5 ± 15.11 Blood sugar to 1 h 82.33 ± 15.04 103.75 ± 11.5 Blood sugar to 2 h 66.33 ± 4.62 124.25 ± 29.1 Blood sugar to 3 h 60.44 ± 3.5 80.75 ± 18.95 **Conclusion:** The levels of blood sugar basal were significantly more low in the settlers of the Centro Poblado Menor de la Rinconada the absorption period is delayed under acute hipoxia.

167.
PREVALENCE OF CHRONIC MOUNTAIN SICKNESS AND SIGNS OF LACK OF ADAPTATION TO THE ALTITUDE IN THE SMALL TOWN CALLES LA RINCONADA (5435 M-PUNO- 2007).

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Introduction: To determine the prevalence of Chronic mountain sickness in the small town called La Rinconada (5435 m) **Methods:** This is a prospective, descriptive and transverse study done in the small town called La Rinconada at an altitude of 5435 m, province of San Antonio de Putina, department of Puno. **Results:** From the group of studied people; 11.3% are females and 88.7% are males, they were from 18 years old to 56 years old. The average of the age was 31.22 years old with a standard deviation of 8.72. La prevalence of CMS is 47.42%. 97.7% of the patients had headache as the most frequent symtomc followed by parestesias in 54.6%, respiratory difficulty in 54%, cyanosis 37.4%, tinnitus

34.5% and insomnia 20.7%. **Conclusion:** The prevalence of CMS is 42%. • The most frequent symptoms were headache, parestesias and cyanosis.

168.

SIXTY PERCENT (60 %) MEAN HEMATOCRIT IN AN ANDEAN HUMAN POPULATION PERMANENTLY EXPOSED TO EXTREME LIFE CONDITIONS.

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Introduction: Located over 5435 m, La Rinconada in the district of Puno, Peru is the highest urban centre in the world. This altitude, at which the barometric pressure (BP = 400 mmHg), and the partial oxygen pressure (PpO_2 = 80 mmHg) are almost half from sea level values (BP = 760 mmHg; PpO_2 = 159 mmHg), is considered the border line at which permanent human life is possible. However, La Rinconada dwellers are furthermore gold mine workers, thus exposed to additional mine hypoxia and chemical mercury toxicity **Methods:** In the present work we aimed to determine the basal physiological param of La Rinconada residents. Hematocrit (hct), pulse, arterial oxygen saturation (SaO_2), as well as the prevalence of chronic mountain sickness (CMS; international criteria Xining China, 2004) was evaluated in 346 subjects (39 women and 307 men). The collected data was subdivided in eight groups from 18 to 58 years old. **Results:** Interestingly, despite the sex and extensive age differences, the data showed very regular values of hct (57.34 ± 0.43 %), pulse (86.00 ± 0.62 beats/minute) and SaO_2 (80.93 ± 0.24 %). Moreover, contrary to the expected, CMS was absent in women and its prevalence was 52.2% in the male population. Not one case of severe CMS was reported **Conclusion:** These findings suggest that La Rinconada dwellers show an outstanding capability to cope with critical life conditions. Consequently, these data support the investigation of additional physiological and genetic param in this gold mine Andean population. **Acknowledgments:** To the engineer Cesar Pampa and his wife for his valuable help.

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