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**1. HYPOXIA AND HYPERCAPNIA DURING RESPIRATION INTO ARTIFICIAL AIR POCKETS IN SNOW**  
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Factors governing survival following complete burial under a snow avalanche are speed of extrication, presence of an air pocket and maintenance of a clear airway. We assessed the effect of breathing into an artificial air pocket in snow on changes in respiratory gases of avalanche victims.

We undertook a prospective randomized 2x2 crossover study in 12 subjects. 28 tests were carried out in which they breathed into air pockets of different volumes (1l or 2l) within snow of different density. The volunteers were sitting in the open-air and were not buried.

The tests showed that during respiration into the air pockets oxygen saturation decreased significantly within 4 min, dependent on snow density, and was inversely proportional to air pocket volume. End-tidal carbon dioxide rose significantly and a respiratory acidosis developed.

Although contributing factors of snow burial like the influence of snow pressure on chest and ventilation, hypothermia and stress were not assessed in this simulatory model, we were able to elucidate an important part of the pathophysiology of avalanche burial.

**3. PHYSIOLOGICAL AND BIOCHEMICAL MECHANISMS OF HUMAN ADAPTATION TO HIGH ALTITUDE HYPOXIA**

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The studies were conducted in acute phase of adaptation of young men with high- (HHR) and low- (LHR) hypoxic resistance at altitude of 3,600 m (Pamirs). Measurements of the arterial pressure, ECG, integral rheocardiography and oxyhaemometry were used for estimating the human functional state in mountain conditions. Spectrometric analysis was used for estimating carbohydrate, lipid and nitrous metabolism. It was shown that in LHR group Central Nervous System (CNS) depression took place that led to a decrease of compensatory cardiovascular reaction to the dosed Flack test, in particular to an inhibition of the cardiac activity, to deceleration of the blood flow rate, to a decrease of the cardiac output and peripheral resistance of the blood vessels, and to predominant cardiac type of blood circulation's self-regulation. The HHR have a compensatory reaction which reveals itself in an increase of the cardiac activity, in the ventricle contraction and in vasoconstriction of the blood vessels. At the same time an excitability of the parasympathetic innervating centers decreased and the new, more "economical" level of the CNS functioning was established. It was shown that the HHR adaptive process is connected with a compensation of the biochemical energy by means of anaerobic glycolysis stimulation which is accompanied by increase of glucose utilization without lactate accumulation, but for the LHR it is connected with a predominance of gluconeogenesis reactions. Also in the LHR group a significant increase of blood cholesterol and signs of blood uremia were recorded. The HHR adaptation is accompanied with small changes in quantity of blood cholesterol and nitrous metabolism products.

**2. PREDICTED HYPOXIA IMAGE AND VO<sub>2</sub>max VALUE IN SKELETAL MUSCLE WORKING UNDER ACUTE HYPOXIA AT DIFFERENT LEVELS OF MUSCLE BLOOD FLOW**

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The aim of the study was to investigate the influence of muscle blood flow F and oxygen partial pressure of arterial blood (PaO<sub>2</sub>), on VO<sub>2</sub>max and to predict the size, shape, and position of hypoxia zone in muscle fiber working under hypoxemia. The computer model of O<sub>2</sub> delivery-consumption in muscle was used for calculation of tissue pO<sub>2</sub> and VO<sub>2</sub> distribution. VO<sub>2</sub>max, end capillary pO<sub>2</sub> and graphic hypoxia images in tissue were investigated as a function of PaO<sub>2</sub> and F (100 < F < 600 ml/min/100g, 30 < PaO<sub>2</sub> < 100 mm Hg). The results showed that an increase of F leads to a rise of VO<sub>2</sub>max. Despite the lower VO<sub>2</sub>max in hypoxia, the venous blood had the lower pO<sub>2</sub> in hypoxia than in normoxia. Muscle oxygen diffusion was found to be one of the most significant factors limiting VO<sub>2</sub>max during acute hypoxemia. This finding was supported by the calculated images of hypoxia in muscle fiber working at VO<sub>2</sub>max.

**4. WHO REACHES THE SUMMIT OF ACONCAGUA ?**

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919 mountaineers were interviewed on returning from Aconcagua to establish factors associated with reaching the summit. Complete data-sets were obtained from 705 subjects. Susceptibility to AMS was assessed by scoring symptoms on previous exposures, mountaineering activity by previous max. altitude and days spent above 3000 m per year, pre-acclimatization by days above 3000 m in the last 4 weeks. Factor analysis revealed 3 groups with the following characteristics:

| Parameter                        | Group1 | Group 2 | Group 3 | p      |
|----------------------------------|--------|---------|---------|--------|
| total number of subjects         | 254    | 268     | 183     |        |
| summit reached                   | 90%    | 76%     | 14%     | <0.001 |
| max. altitude reached previously | 6659   | 6246    | 5051    | <0.001 |
| days above 3000m/year            | 44     | 17      | 13      | <0.001 |
| days above 3000m last 4 weeks    | 2,7    | 1,0     | 0,7     | <0.001 |
| score of AMS history             | 2,0    | 5,3     | 2,7     | <0.001 |
| AMS on Aconcagua                 | 4%     | 72%     | 37%     | <0.001 |
| took acetazolamide               | 8%     | 31%     | 9%      | <0.001 |
| took analgesics                  | 23%    | 48%     | 38%     | <0.001 |
| summit was not the object        | 0%     | 0%      | 19%     | <0.001 |

Age, BMI, gender and hours of training are not significantly different between groups. Each variable in the table correlates significantly with reaching the summit in regression models. Thus previous mountain experience, pre-acclimatization and low susceptibility for AMS are associated with reaching the summit of Aconcagua.

## 5. PRELIMINARY STUDY: EFFECTS OF EXTREME ALTITUDE ON ERYTHROPOIETIN AND ERYTHROPOIESIS

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We evaluated the effects of extreme altitude on erythropoietin (EPO) and erythropoiesis. Three subjects (two experienced mountain guides and one novice climber) underwent climbing expeditions in the Himalaya mountain ranges for periods between 3 and 5 weeks. Blood and urine samples were collected for analysis before and after the expeditions. The novice reported a viral illness on return. Haematological parameters of the two guides remained within laboratory reference ranges. The novice climber had prolonged elevation of haematocrit, percentage reticulocytes and soluble transferrin receptor after returning to sea level, suggesting a sustained acceleration of erythropoiesis. Urinary EPO glycoforms, analysed by isoelectric focussing and Western blotting, altered markedly only in the novice climber, to less acidic isoforms, although the pattern differed qualitatively from that seen in recombinant EPO. This pattern is associated with increased receptor binding but decreased serum half-life in vivo. These findings suggest that EPO glycosylation, and therefore bioactivity is modulated as a response to hypoxic stimulus. Further study may confirm the relationship between this modulation, maximum altitude, time at altitude and other stressors.

## 7. ANALGESIA WITH ALMOTRIPTAN AGAINST NAPROXENO, FOR THE TREATMENT OF HEADACHE FOR AMS

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In the Spring of 2000, during an expedition to the Satopanth (7075 mts) a comparative study was carried out on the efficacy of Naxopreno and Almotriptan, used to combat headaches that make their appearance during the height acclimation period, affecting the participants in this type of expedition.

The study covered a period of 19 days at heights over 3500 mts, during which the maximum height reached was 5700 mts. The number of participants was 9, (8 men, 1 woman), none of which had antecedents of frequent headaches. Ages ranged between 27 and 51.

Each participant was given a card on which he or she recorded the intensity level of headache (scored subjectively between 1 and 3) and the degree of relief (scored subjectively between 1 and 5) two hours after administration of the medicine (A or B, respectively) and the presence or absence of accompanying symptoms, i.e. nausea, dizziness . . .).

42 cases of headaches were recorded, of which only 25 were treated. 11 were treated with A (Naxopreno), while 14 were treated with B (Almotriptan). For technical reasons, many other cases of headache were not registered in the study.

Despite the small size of the sample, the results of the study clearly demonstrate ( $p \leq 0,001$ ), significant higher efficacy of Naxopreno over Almotriptan for the treatment of this type of headache.

## 6. CHARACTERISTICS OF HIGH ALTITUDE HEADACHE

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To characterize high altitude headache we obtained questionnaires from 1213 mountaineers 2-6 hours after arrival at 4559m. The history of migraine was assessed by the Kieler Headache Questionnaire and acute mountain sickness (AMS) by the AMS-C-Score of the Environmental Symptom Questionnaire. 589 (49%) subjects had headache and 133 (11%) a history of migraine. Factors-analysis identified 2 types of headache with the following characteristics:

|                                   | Type 1     | Type 2     | p      |
|-----------------------------------|------------|------------|--------|
| Number of subjects                | 417        | 172        |        |
| one-sided                         | 0%         | 58%        | <0,001 |
| both-sided                        | 100%       | 42%        | <0,001 |
| pulsating                         | 20%        | 53%        | <0,001 |
| reduction of activity             | 21%        | 53%        | <0,001 |
| nausea                            | 7%         | 26%        | <0,001 |
| photophobia                       | 18%        | 47%        | <0,001 |
| sonophobia                        | 11%        | 41%        | <0,001 |
| fulfilling criterions of migraine | 0%         | 65%        | <0,001 |
| AMS-C-Score evening               | 0,48(±0,4) | 0,78(±0,6) | <0,001 |
| history of migraine               | 8%         | 26%        | <0,001 |

The frequency of AMS (defined as AMS-C $\geq$ 0.7) and the mean AMS-C scores were not significantly different between mountaineers with and without a history of migraine at low altitude. These data demonstrate that: 1.) a history of migraine at low altitude is not strongly associated AMS and 2.) that headache in severe AMS is often migraine like and that this type of headache occurs in 75% of mountaineers independent of a history of migraine at low altitude.

## 8. NORMAL BMPR-2 GENE IN INDIVIDUALS SUSCEPTIBLE TO HIGH ALTITUDE PULMONARY EDEMA (HAPE-S)

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High pulmonary artery pressure (PAP) is essential for the development of HAPE. HAPE-S have both enhanced pulmonary vasoconstrictor response (PVR) to hypoxia and elevated PAP during normoxic exercise. We demonstrated a similar PVR to hypoxia and normoxic exercise in members of families with primary pulmonary hypertension (PPH) who share the risk haplotype with the index patient. Recent data show mutations in the BMPR-2 gene in PPH patients. Therefore we investigated whether mutations in the BMPR-2 gene also play a role in the development of HAPE. DNA of 11 patients (age 54 $\pm$ 9 y) with well documented history of HAPE (median 2, range 2-4 episodes of HAPE) and increased PAP response to exercise and hypoxia was screened for BMPR-2 mutations by the denatured high performance liquid chromatography method. Compared to HAPE-resistant controls (n=12, age 56 $\pm$ 8 y) systolic PAP in HAPE-S was elevated during normoxic exercise (56 $\pm$ 14 vs. 50 $\pm$ 10 mmHg; p=0.14) and after 2 h at FiO<sub>2</sub>=0.12 (52 $\pm$ 9 vs. 40 $\pm$ 7 mmHg; p<0.01). The exon-wise analysis of the BMPR-2 gene did not show any mutations in HAPE-S. Our results suggest that the genetic background is different between HAPE and PPH but we can not exclude other possible candidate genes, eventually also located on chromosome 2, playing a role in the manifestation of HAPE.

### 9. PREVENTION OF ACUTE MOUNTAIN SICKNESS BY ACETAZOLAMIDE IN NEPALI PORTERS: A DOUBLE BLIND CONTROLLED TRIAL

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Acetazolamide can prevent acute mountain sickness (AMS), but there have been no controlled trials of this drug in mountain porters, some of whom die of AMS every year. We therefore performed a randomised, double blind controlled trial of Diamox (acetazolamide) 250mg daily vs placebo. Nepali doctors stationed at Namche Bazar (altitude 3440m, in the Everest region) enrolled 401 porters, (297 lowlanders, 108 highlanders). Porters were given seven days' supply of trial medication and assessed at three trekking posts, the highest at Lobuje (4930m). Many were partially acclimatised on reaching Namche Bazar, thereafter the rate of ascent (mean 5.31 days), SD 0.966) allowed further acclimatisation.

Only 183/401 (45.63%) porters completed the trial and AMS occurred in only 17/183 (9.29%), 16 lowlanders and 1 highlander. Of these, 10 took acetazolamide (mean AMS score 4.10, SD 0.916) and 7 placebo (mean score 3.43, mean 0.593); the difference between these groups was not statistically significant. The low AMS incidence and lack of benefit from acetazolamide probably resulted from acclimatisation to altitude.

### 11. A NOVEL CONTINUOUS POSITIVE AIRWAYS PRESSURE (CPAP) DEVICE FOR USE AT HIGH ALTITUDE

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Continuous positive airways pressure (CPAP) is used to treat cardiogenic pulmonary oedema and acute lung injury, and has been advocated as a means of treating high altitude pulmonary oedema (HAPE). Until now, logistical and technical constraints have prevented the evaluation of CPAP in the high-altitude environment. One of us (GS), in association with the medical device company Lifevent®, has developed a unique portable CPAP device using very low gas flows. This device was evaluated in 14 subjects after rapid ascent to 3205 m on Aoraki/Mt Cook. One of the subjects developed HAPE within 8 hours of arrival.

This is the first report of CPAP use in the wilderness environment. CPAP was effectively delivered without loss of mask pressure, or re-breathing, with flow rates at times approximating minute ventilation. Peripheral oxygen saturation (SpO<sub>2</sub>) was significantly increased at CPAP of 5,10 and 15 cm H<sub>2</sub>O, while respiratory rate decreased. At ambient pressure SpO<sub>2</sub> = 89.9% (95% confidence interval 87.8% to 92.0%), vs. 94.1% at 5 cmH<sub>2</sub>O (95% confidence interval 92.9% to 95.3%, *p* = 0.0012). The subject with HAPE improved dramatically with CPAP. There was no reduction in apparent cardiac output with increases in CPAP. This device may offer a practical, drug-free solution for treating high altitude illness.

### 10. TREKKERS' AWARENESS OF ACUTE MOUNTAIN SICKNESS (AMS) AND ACETAZOLAMIDE SUBEDI,D., MARAHATTA,R., SHARMA,S., HILLENBRAND,P., SOON,Y., and BMRES. Tribhuvan University Teaching Hospital, Kathmandu, Nepal and Birmingham Medical Research Expeditionary Society.

Trekkers descending from Namche Bazar (altitude 3440 m), at the end of their Himalayan trek were questioned about Acute Mountain Sickness (AMS) symptoms, using the Lake Louise Questionnaire. They were also asked whether acetazolamide masked AMS and whether they had attended lectures on AMS. 150 trekkers participated; AMS occurred in (38.7%), mean score 4.83 (SD 1.94). Females reported significantly more AMS than males (42.3% v 36.7%, *P* = 0.0014). Of the 59 trekkers who had AMS, only 57.6% thought they had suffered AMS; 35.6% attributed their symptoms to other causes and 6.8% were unsure. Acetazolamide ("Diamox") was taken for AMS prevention by 18% and for treatment by 10.7%; the rest, (71.3%) did not take acetazolamide. When asked whether acetazolamide masked AMS, 16.7% believed that it did, 40% did not and 39.3% did not know. Lectures on AMS were attended by 47.4% of trekkers but 20% of these still thought acetazolamide masked AMS. AMS is common in trekkers but often unrecognised and the role of acetazolamide is often misunderstood. There is a need for better education of trekkers.

### 12. MAGNESIUM IN THE TREATMENT OF ACUTE MOUNTAIN SICKNESS: A RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL

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The pathophysiology of acute mountain sickness (AMS) probably involves hypoxia induced cerebral edema from an increased cerebral blood flow in presence of cytotoxic components. The latter may include N-Methyl-D-Aspartate (NMDA) receptor stimulation mediated calcium influx into neurons that leads to cellular swelling. Magnesium is a physiologic NMDA receptor blocker. The aim of this study was to test the efficacy of intravenous magnesium in the treatment of established AMS. In the Capanna Margherita (4,559 m), 25 volunteer subjects with overt AMS (AMS score > 6 with ataxia) were randomized to a 30 min intravenous magnesium sulfate infusion (4 g, 16 mmol) or placebo.

Treatment success was defined as > 50% reduction in the Lake Louise score within 1h. Although 11 of 12 subjects with established AMS who received intravenous magnesium had reduced AMS scores after one hour, only three were treatment successes (25%) compared with none of 13 subjects receiving placebo (*P* = 0.1). With magnesium, mean AMS score had decreased from 11.6 ± 1.7 to 9.9 ± 3.5 (*P* = 0.01); with placebo infusion, AMS scores remained unchanged. With intravenous magnesium, more subjects had a transient flush (75% versus 8%, *P* = 0.001). In subjects with established AMS, intravenous magnesium somewhat reduces symptom severity, but this effect is not clinically relevant. Even though magnesium is not useful for treating AMS a potential role of magnesium in the pathophysiology of AMS cannot be ruled out.

### 13. THE RELATIONSHIP BETWEEN OXYGEN SATURATION AND ACUTE MOUNTAIN SICKNESS IN INDIVIDUALS ASCENDING TO 3080M

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Pulse oximetry (SpO<sub>2</sub>) is an increasingly utilized tool in the diagnosis of altitude related illness such as acute mountain sickness (AMS). While some evidence suggests SpO<sub>2</sub> helps to predict susceptibility, we have inadequate data on the relationship of SpO<sub>2</sub> to the presence of AMS. Additionally there is little data describing normal values for SpO<sub>2</sub> at altitude. We therefore set out to observe AMS and SpO<sub>2</sub> in healthy volunteers who ascended by foot to 3080m (Mt Rainier, USA) from 1640m. A questionnaire-based survey was used to study 89 subjects (20 female 69male). Co-synchronous resting pulse and saturation data were obtained using a finger pulse oximeter after arrival to 3080m. Using the Lake Louise Score, 16% of subjects had AMS at 3080m. Mean SpO<sub>2</sub> was 90% + 4%. No correlation was seen between the presence of AMS and the SpO<sub>2</sub> (Chi Square = 0.55). We conclude that while pulse oximetry is a useful and readily available physiological tool, the SpO<sub>2</sub> does not correlate with AMS as defined by the Lake Louise Score.

### 15. PULMONARY ARTERY PRESSURE CHANGES DURING ASCENT TO HIGH ALTITUDE MEASURED BY ECHOCARDIOGRAPHY

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Hypoxia causes an increase in pulmonary artery systolic pressure (PASP). While this has been documented in normal subjects at high altitude, the evolution of these changes during acclimatization and ascent remains unclear. We set out to observe changes in PASP measured non-invasively using echocardiography in six volunteers during a 3 day ascent to 4317m. Data from 1227m, 3075m, 3779m and 4317m were compared to baseline sea level measurements. Mean PASP of 35mmHg at 3779m was significantly increased, as was 34mmHg at 4317m compared to sea level (mean = 21mmHg, P<0.05). The mean PASP increase to 25mmHg at 3075m was not significant compared to sea level.

This data suggests that significant changes in PASP occur during exposure to 3779m and higher. We were unable to establish whether exposure to moderate altitudes prevents PASP rise at higher altitudes. Further controlled studies are needed to establish whether time at altitude affects the magnitude of PASP rise and the relationship of this to disease states such as acute mountain sickness and high altitude pulmonary edema.

### 14. HEART RATE CORRELATES WITH ACUTE MOUNTAIN SICKNESS IN SUBJECTS AT 3080M

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In spite of many studies of acute mountain sickness (AMS), there are little data on physiological variables that correlate with the presence or susceptibility to AMS. We therefore set out to study the relationship between heart rate and AMS in resting subjects at 3080m.

We observed 191 (33 female, 158 male) recently arrived volunteers at 3080m on Mt Rainier (Washington, USA) according to their own ascent profile. Each completed a questionnaire-based survey; co-synchronous resting pulse data were obtained using a finger pulse oximeter.

AMS was observed in 16% of subjects (Lake Louise Score). Mean resting pulse rate over a 30sec period was 90bpm + 14. Using a Chi Square test, AMS score and pulse were highly correlated (Chi Square 0.013), suggesting subjects with a higher pulse rate were more likely to have AMS. There was no significant difference between males and females.

We conclude that pulse rate offers a simple test, which correlates to the symptoms of AMS. It may prove to be a useful objective tool facilitating AMS diagnosis at moderate altitudes.

### 16. ACUTE MOUNTAIN SICKNESS ON ACONCAGUA (6962 m)

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To assess factors associated with acute mountain sickness (AMS) information was obtained by questionnaires at Laguna de los Horcones (2900 m) from 919 mountaineers returning from climbing on Aconcagua between January 3 and 31, 2001. AMS is defined as a score > 4 of the Lake Louise self report questionnaire, which was filled out retrospectively for the day when subjects had felt worst. AMS prevalence was 39%. No history of AMS, a higher altitude reached on previous exposures, more days spent above 3000 m per year and in the preceding months were associated with a lower AMS prevalence in a bivariate analysis while there were no effects for age, gender, BMI, use of oral contraceptives, smoking tobacco and training hours. Ascent rate was negatively correlated with AMS ( $r = -0.11$ ,  $p = 0.01$ ). Not being susceptible to AMS had the biggest effect in multivariate analysis, reducing the relative risk (RR) by 2.7 (95%-CI: 2.1 to 3.4). Previous climbing above 6000m and spending more than 10 days per year and 5 days in the last 2 months above 3000 m taken together resulted in a further reduction of RR by 2.1(95%-CI:1.3 to 3.4) Our data show that the best predictors of AMS on Aconcagua are susceptibility, previous mountaineering activity and pre-acclimatization. Ascent rate may be slightly slowed down as a consequence of AMS in the setting of staged ascent.

### 17. CHARACTERISTICS OF MOUNTAINEERS ASCENDING ACONCAGUA (6962 m)

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To describe the population ascending Monte Aconcagua information by questionnaires was obtained from 919 returning mountaineers between January 3 and 31, 2001, at Laguna de los Horcones (2900 m). AMS is defined as a score >4 of the Lake Louise self report questionnaire, which was filled out in retrospect for the day when subjects had felt worst. Climbers came from Europe: 54%, South America:27%, North America:14%, Asia and Oceania: 5%. 15 % were women. Further characteristics are: Age (years): <30:27%; 30–39:39%; 40–49:22%, and ≥50:13%. BMI (kg/m<sup>2</sup>): <20:8%; 21–23: 57%; 24–26:22%; >26:13%. Training (h/week):0–4:29%; >10:41%. Days spent above 3000 m per year: 0–4:28% and >20:28%. Previous highest altitude (m): =4000:8%; 4001–6000:44%; 6001–7000:41%; >7000, 7%. 36% took analgesics, 16% acetazolamide, 3% sleeping pills and 1% corticosteroids. 51% abstained from any drugs. The summit was reached by 60%. The prevalence of AMS (individuals taking acetazolamide and corticosteroids excluded) was 39 % (95% CI: 35–43%). Conclusions: There is a large variability regarding previous mountaineering experience, a low percentage of women, and a rather high success rate on Aconcagua. The prevalence of AMS is comparable to data reported in the literature for studies using similar definitions of AMS.

### 19. MAGNESIUM IN THE PREVENTION OF ACUTE MOUNTAIN SICKNESS: A RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL

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The pathophysiology of acute mountain sickness (AMS) probably involves hypoxia induced cerebraledema from an increased cerebral blood flow in presence of cytotoxic components. The latter may include N-Methyl-D-Aspartate (NMDA) receptor stimulation mediated calcium influx into neurons that leads to cellular swelling. Magnesium is a physiologic NMDA receptor blocker. Uncontrolled observations suggest that oral magnesium may prevent acute mountain sickness. The aim of this study was to test this hypothesis with a randomized, double blind, placebo-controlled trial. Methods: Seventy volunteers were randomly allocated to oral magnesium-citrate 400 mg (16.5 mmol) or placebo. Treatment taken every 8 hours for 72 hours, from the beginning of the ascent to the end of a stay at altitude. Ascent from 1,130 m to 4,559 m lasted 24±2 hours and the following 48 hours were spent at 4,559 m. AMS was assessed 12-hourly using the Lake Louise score. Results: There were 9 dropouts. With magnesium, 12/30 subjects (40%) were prevention failures (score at any time point =6 and/or ataxia) compared with 11/31 (36%) with placebo (RR 1.13, 95%CI 0.59 to 2.15). Onset time, incidence and severity of AMS was similar in both groups. 50 of all subjects (82%) had a score > 3 at any time-point during the study period; 32 (52%) had a score > 6. With magnesium, significantly more subjects had diarrhea (32% vs 12%). Conclusions: In a setting of unacclimatized subjects rapidly ascending to high altitude a high oral intake of magnesium does not prevent nor attenuate nor delay AMS.

### 18. HIGH ALTITUDE INCREASES SERUM MIF

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Macrophage migration inhibitory factor (MIF) is an endogenous glucocorticoid regulator. MIF counter-regulates the actions of endogenous cortisol, is induced by hypoxia and is important in inflammatory responses such as sepsis. We asked whether MIF was increased on acute exposure to high altitude and whether higher levels were associated with the occurrence of AMS. Methods: 38 healthy subjects ascended rapidly to 4300m. Half the subjects took ginkgo biloba 120mg orally as AMS prophylaxis and half took placebo. AMS was measured by the Lake Louise score (LLS) and the Environmental Sickness Questionnaire—C score (ESQ-c). Serum was drawn for MIF analysis before and after ascent. Serum MIF was analyzed by ELISA. Results: MIF increased in all subjects (1.26±0.14 vs. 2.3±0.31 ng/ml p<.01). Treatment with Ginkgo had no effect on MIF levels before or after ascent (1.39±0.25 vs 1.08±0.17 ng/ml, placebo vs. ginkgo before, p=NS and 2.59±0.47 vs 2.05±0.42 ng/ml after, p=NS). There was no correlation between MIF levels and the severity of AMS by LLS or ESQ-c.

Conclusions: Acute high altitude exposure increases serum MIF. Ginkgo biloba does not prevent AMS by altering MIF levels. Further studies are needed to elucidate the role of MIF in adaptation to high altitude exposure.

### 20. MIDAZOLAM IMPROVES SLEEP AND DOES NOT EXACERBATE ACUTE MOUNTAIN SICKNESS DURING RAPID ASCENT TO 4559m

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To investigate whether the intake of 15mg midazolam may precipitate acute mountain sickness (AMS) during the ascent to 4559m within 24 hours. Forty-six healthy mountaineers were randomly assigned to receive midazolam (M) or placebo (P) for two consecutive nights (3650m and 4559m). AMS score, sleep quality (0 = excellent, 3 = very poor) and efficiency, breathing patterns and peripheral SO<sub>2</sub> were measured. The results (mean±SEM) obtained at 4559m are in the table.

|  | Placebo     | Midazolam   | P value |
|--|-------------|-------------|---------|
| Subjective sleep quality               | 1.74 ± 0.14 | 1.17 ± 0.17 | 0.02    |
| Sleep efficiency (% time asleep)       | 76 ± 3      | 84 ± 2      | 0.04    |
| Apnea index (Apneas/h sleep)           | 78 ± 16     | 54 ± 12     | 0.24    |
| SaO <sub>2</sub> < 70% (% time in bed) | 52 ± 9      | 37 ± 8      | 0.19    |
| AMS-c score                            | 0.60 ± 0.12 | 0.31 ± 0.08 | 0.06    |

In conclusion midazolam at the dose of 15mg improves sleep quality and does not enhance the development of AMS in healthy mountaineers during rapid ascent to high altitude.

## 21. CHARACTERISTICS OF NOCTURNAL BREATHING PATTERNS AT HIGH ALTITUDE IN PEOPLE DEVELOPING ACUTE MOUNTAIN SICKNESS

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To investigate whether acute mountain sickness (AMS) after rapid ascent to high altitude is associated with sleep and breathing disturbances during night. In 25 healthy mountaineers during the first night at 4559m we recorded sleep efficiency, breathing patterns and pulse oximetry (SpO<sub>2</sub>). AMS (score >4) was defined using Lake Louise criteria. Values are medians (quartiles).

|   | Controls. (n=11)    | AMS (n=14)           |
|---|---------------------|----------------------|
| AMS score (morning)                     | 3 (2 to 4)          | 7 (7 to 9) *         |
| Sleep efficiency (%)                    | 86 (80 to 89)       | 70 (60 to 81) *      |
| Respiratory rate (min <sup>-1</sup> )   | 17 (16 to 20)       | 19 (14 to 22)        |
| Tidal volume (L)                        | 0.36 (0.31 to 0.40) | 0.46 (0.36 to 0.60)* |
| Ventilation (L/min)                     | 5.8 (5.2 to 6.3)    | 9.1 (6.3 to 10.5)*   |
| Apnea/Hypopnea Index (h <sup>-1</sup> ) | 41 (13 to 93)       | 92 (34 to 134)       |
| SpO <sub>2</sub> (%)                    | 74 (68 to 78)       | 60 (53 to 73)*       |

\* p<0.05 vs controls.

We conclude that subjects with AMS, compared to controls, have a lower SpO<sub>2</sub>, this despite increased but unstable ventilation, which may reduce sleep efficiency.

## 23. RESPIRATORY CHANGES RELATED TO EPITHELIAL ION TRANSPORT AT ALTITUDE

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Methods: Nasal potential difference (NPD); lung water (LW) measured by electrical impedance tomography; cough threshold (CT) to inhaled citric acid; forced vital capacity (FVC) and pulmonary artery pressure (PAP) estimated by Doppler echocardiography were measured at 700m (BL) and during 2 weeks at 3800m (HA) in the Tien Shan mountains in 20 healthy volunteers. Results: On ascent to HA, NPD hyperpolarized from  $-13.7 \pm 1.6$  to  $-17.5 \pm 1.5$  mV (mean  $\pm$  SEM,  $p < 0.05$ ); LW increased and FVC and CT decreased (all  $p < 0.05$ ). There was only a mild increase in PAP ( $12 \pm 1$  to  $20 \pm 1$  mmHg) which would be insufficient to cause increased capillary filtration. All changes were most prominent during the first 2 days at HA, and thereafter tended to return to normal. The amiloride-inhibitable portion of NPD did not change.

Conclusion: These results suggest that altitude causes a subclinical increase in LW accounting for decreased FVC and CT, potentially explained by increased respiratory epithelial anion secretion.

## 22. POSITIVE ASSOCIATION OF THE ENDOTHELIAL NITRIC OXIDE SYNTHASE GENE POLYMORPHISMS WITH HIGH-ALTITUDE PULMONARY EDEMA

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In order to elucidate the genetic background of the defective nitric oxide (NO) synthesis in the lung of high-altitude pulmonary edema (HAPE), we examined the Glu298Asp variant and 27-basepair (bp) variable numbers of tandem repeats (VNTR) polymorphisms of the endothelial NO synthase (eNOS) gene using polymerase chain reaction followed by restriction fragment length polymorphism in 41 HAPE-susceptible subjects (HAPE-s) and 51 healthy climbers (control group) of a Japanese population. The Asp.allelic frequency of the Glu298Asp variant was 51.2% in HAPE-s and 15.7% in controls, which was significantly different between the two groups ( $P = 0.000266$ ). The eNOS4a allelic frequency of 27-bp VNTR was 41.5% in HAPE-s, significantly higher than that of 11.8% in controls ( $P = 0.001067$ ). The frequency of combining both the Asp and eNOS4a alleles was 26.8% in HAPE-s, but none of the controls were genotyped the two polymorphisms simultaneously, with more powerful significant difference between the two groups ( $P = 0.0000587$ ). Both polymorphisms of the eNOS gene were significantly associated with HAPE. A genetic background may underlie the impaired NO synthesis in the pulmonary circulation of HAPE-s. These polymorphisms could be as genetic markers for predicting the susceptibility to HAPE.

## 24. DEXAMETHASONE PREVENTS THE MICROCIRCULATORY INFLAMMATORY RESPONSE TO SYSTEMIC HYPOXIA

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Dexamethasone is effective in the treatment of AMS, suggesting an inflammatory component in this condition. We have shown that systemic hypoxia produces an inflammatory response characterized by increases in reactive oxygen species (ROS) generation, leukocyte-endothelial adhesive interactions, and vascular permeability in various microcirculatory beds of rats. The objective of this study was to determine if dexamethasone prevents these responses. The mesenteric microcirculation of rats was studied using intravital microscopy. Hypoxia (FIO<sub>2</sub> = 0.10) increased the number of leukocytes adhering to venules (leukocytes / 100 $\mu$ m) from  $0.5 \pm 0.2$  in normoxia to  $10.7 \pm 0.7$  after 10 min of hypoxia ( $p < 0.05$ ). This was accompanied by a  $61 \pm 10$  % increase ( $p < 0.05$ ) in the fluorescence intensity of dihydrorhodamine (DHR), an ROS probe. Pretreatment with dexamethasone (2 mg /kg subcutaneously 24 h before hypoxia) completely blocked the increase in leukocyte adherence and in DHR fluorescence.

These results indicate that dexamethasone prevents the inflammatory response to hypoxia in the mesenteric microcirculation and suggest that its effect on AMS may be due to its anti-inflammatory properties.

### 25. LACK OF ASSOCIATION OF HIGH ALTITUDE PULMONARY EDEMA AND POLYMORPHISMS OF THE NO PATHWAY

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Recent findings suggest that low NO levels in pulmonary vessels contributes to the enhanced hypoxic pulmonary vascular response in individuals susceptible to high altitude pulmonary edema (HAPE). Therefore we hypothesized that nitric oxide synthase (NOS)-3 gene polymorphisms like G894T or CA-repeats in intron 13 associated with a decreased synthesis of NO may contribute to susceptibility to HAPE, while the C242T polymorphism in the p22phox gene (important component of the NAD(P)H oxidase) may be associated with decelerated degradation of NO and thus resistance to HAPE. Therefore we assessed these genotypes in 51 mountaineers susceptible and in 52 mountaineers not susceptible to HAPE. The frequency of the TT genotype of G894T polymorphism was 14% in HAPE-susceptible and 8% in HAPE-resistant individuals, the frequency of the T-allele was 37% vs. 30%, the frequency of CA-repeats  $\geq 38$  was 10% vs. 8%. The frequency of the TT-genotype of p22phox C242T polymorphism was 10% vs. 10%, and for the T-allele 33% vs. 36%. None of the differences in the frequencies proved to be significant. We conclude that there is no evidence for a major role of the examined gene polymorphisms in the pathophysiology accounting for susceptibility to HAPE.

### 27. ACUTE MOUNTAIN SICKNESS AND ACETAZOLAMIDE: WHAT DO TREKKERS KNOW?

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Ascending trekkers were interviewed after spending one night at Namche Bazaar (3440m) in Nepal. Questionnaires were used to record Acute Mountain Sickness (AMS) scores (Lake Louise), use of Acetazolamide (AZ) and subject demographics. There were 89 subjects, 55 (62%) male and 34 (38%) female. Ages ranged from 18 to 60 years, with most being 21–30. The majority (73%) were travelling independently but 27% were on commercial treks. Only 11 (12%) were taking AZ but 28 (31%) had AMS scores of three or more. Independent travellers were less likely ( $p < 0.05$ ) to have any knowledge about prophylactic use of AZ in AMS. Trekkers with knowledge of AZ use were more likely to be carrying AZ for emergencies ( $p < 0.01$ ). More than a third of young independent trekkers had significant AMS, which was not reduced by prior knowledge about or use of AZ. Commercial treks provide information and emergency AZ but this does not reduce the incidence of AMS. We found no individual factor associated with reduced incidence of AMS.

### 26. ACUTE MOUNTAIN SICKNESS (AMS) PRESENTING TO THE KUMTOR MINE SITE, KYRGYZ REPUBLIC (CIRCA 4000 M)

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The AMS incidence rate (IR) among general visitors to high altitude is substantial. This cross sectional study estimates AMS IR among shift workers and explores a role of occupational factors for AMS. Convenience sampling was used. Respondents were regarded as AMS (-) and AMS (+). A score of  $\pm 3$  points (by Lake Louise score) was a threshold for AMS. For statistical analysis SPSS for Windows 10.0 (1999) was used. Total 200 workers (79% M, 21% F). Mean age and BMI of them  $36.6 \pm 8.37$  and  $24.8 \pm 3.33$  respectively. 46% workers live at sea level, 54% of them live at an altitude of 1700 m. The mean work duration was  $3.9 \pm 1.51$  years. Physical workers are represented 59.5%, office workers 40.5%. Smokers 41.5% and non-smokers 58.5% AMS IR was 25%. Physical workers are more likely to develop AMS (Odds Ratio 0.48; 95% confidence interval, 0.24–0.96). There was relationship between chronic diseases and AMS (Odds Ratio 2.24; 95% confidence interval, 1.09–4.58).

No associations between age, gender, BMI, altitude of residence, previous experience of work at high altitude, years of work at the mine site with AMS was found.

### 28. SUBLINGUAL GLYCERYL TRINITRATE-INDUCED HEADACHE AS A PREDICTOR FOR INCIPIENT ACUTE MOUNTAIN SICKNESS

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The most common symptom associated with Acute Mountain Sickness (AMS) is headache. The headache may be caused by meningeal irritation as a result of blood vessel dilatation. Glyceryl trinitrate is known to dilate cerebral vasculature and causes headaches similar in quality to the headache associated with AMS.

This study evaluated the relationship between GTN-induced headache and AMS scores. Nine subjects were studied at sea level and on every day of ascent to the summit of Kilimanjaro (5896m). Each day, sublingual GTN was administered and headache score shift between pre and post dose was rated by the subjects. Subjects also rated their daily AMS score. The data was analysed using the Fisher test. A positive correlation ( $p = 0.003$ ) was demonstrated between GTN induced- headache score shift and shifts in AMS score observed on further ascent of between 400–1000m in the next 24hour period. The likelihood of a large AMS shift carries a relative risk of 5.42 for a large headache score shift. Sublingual GTN may be useful as a predictor for incipient AMS. Further studies may be useful to test this hypothesis.



### 29. RESPUESTA AL ESTIMULO ANDROGENICO DE LAS GLÁNDULAS COAGULANTES EN RATAS EXPUESTAS A LA ALTURA (MOROCOCHA 4,540 m)

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Las glándulas coagulantes de la rata al igual que la vesícula seminal en el hombre producen fructosa bajo estímulo androgénico. En trabajos previos hemos reportado que la exposición aguda a la altura, tanto en ratas como en humanos produce un aumento de testosterona sérica. El presente trabajo se realizó con el objeto de conocer si las glándulas coagulantes de ratas expuestas a la altura responden al estímulo androgénico de forma similar que al nivel del mar. 50 ratas macho nacidas en Lima (150m) fueron llevadas a Morococha (4,540 m) y divididas en dos grupos: 25 sin tratamiento y 25 recibieron Sulpiride (Dogmatil-Spedrog) a fin de disminuir los valores de testosterona sérica. 50 ratas fueron trabajadas en Lima (control) en grupos similares. Se analizó testosterona por RIA y fructosa por el método de Roe modificado por Foreman. Los resultados indicaron que en la altura la respuestas al estímulo androgénico es la misma que al nivel del mar.

### 31. 3% CARBON DIOXIDE INCREASES CEREBRAL OXYGEN DELIVERY AT 150m & 3549m

CHE Imray, S Walsh, T Clarke, H Hoar, TC Harvey, CWM Chan, PJG Forster, BMRES

The role of supplementary carbon dioxide at altitude has yet to be determined. The effect on oxygen delivery to the brain was calculated based upon previously collected data. 12 subjects were studied at 150m and a month later at 3549m. Air, 3%CO<sub>2</sub>, 35%O<sub>2</sub>, and 3%CO<sub>2</sub>/35% O<sub>2</sub> were used. Pulse oximetry (SpO<sub>2</sub>) was measured using a Propac Encore Monitor; regional cerebral oxygenation (rSO<sub>2</sub>) was measured using a Critikon 2020 monitor; middle cerebral artery velocity (MCAV) was assessed using a Logidop 3 machine. Oxygen delivery (DO<sub>2</sub>) was calculated (MCAV X SpO<sub>2</sub>).

#### Results:

|                       | SpO <sub>2</sub> % | MCAV        | RSO <sub>2</sub> | DO <sub>2</sub> |
|-----------------------|--------------------|-------------|------------------|-----------------|
| 150m Air              | 97.5(1.5)          | 58.8(14.2)  | 69.9(2.6)        | 5773            |
| 3549m Air             | 91.3(3.0)          | 63.1(18.6)  | 65.6(2.8)        | 5761            |
| 150m CO <sub>2</sub>  | 98.5(1.0)*         | 68.1(13.3)* | 70.6(2.5)*       | 6707*           |
| 3549m CO <sub>2</sub> | 93.3(3.0)*         | 68.6(19.2)* | 66.7(3.2)*       | 6414*           |
| 150m O <sub>2</sub>   | 99.3(0.7)*         | 54.0(16.5)* | 70.3(2.6)*       | 5362            |
| 3549m O <sub>2</sub>  | 99.6(0.8)*         | 58.1(16.5)* | 68.8(2.9)*       | 5786            |
| 150m Mix              | 99.5(0.2)*         | 64.8(13.4)* | 71.0(2.6)*       | 6447*           |
| 3549m Mix             | 100(0.0)*          | 62.0(20.8)  | 70.2(3.8)*       | 6200*           |

Statistics: Paired t test \* p<0.05 vs Baseline

Conclusion: DO<sub>2</sub> remains constant on air. Supplementary 3% CO<sub>2</sub> and the mix increases oxygen delivery at both altitudes.

### 30. 3% CARBON DIOXIDE INCREASES CEREBRAL OXYGEN DELIVERY WHEN BREATHING HYPOXIC GAS MIXTURES

CHE Imray, AW Wright, C Chan, AR Bradwell and the Birmingham Medical Research and Expeditionary Society

Oxygen delivery to tissues is critical in determining performance and illness at all altitudes. 17 subjects (3 female, age 22–56) were studied at 50m. Once a steady state had been achieved, supplementary CO<sub>2</sub> was then added to the 12% oxygen. Minute volume (MV) was measured. Pulse oximetry (SpO<sub>2</sub>) and end tidal CO<sub>2</sub> (PetCO<sub>2</sub>) were measured using a Propac Encore Monitor; regional cerebral oxygenation (rSO<sub>2</sub>) was measured using a Critikon 2020 monitor; middle cerebral artery velocity (MCAV) was assessed using a Logidop 3 machine. Oxygen delivery (DO<sub>2</sub>) was calculated (MCAV X SpO<sub>2</sub>). Baseline studies were followed by 1 minute of voluntary forced hyperventilation (FHV).

#### Results

|                                 | PetCO <sub>2</sub> | SpO <sub>2</sub> | rSO <sub>2</sub> | MCAV        | DO <sub>2</sub> | MV        |
|---------------------------------|--------------------|------------------|------------------|-------------|-----------------|-----------|
| Baseline                        | 39(3.1)            | 97.6(1.2)        | 69.7(2.8)        | 53.1(8.1)   | 5182            |           |
| 12% oxygen                      | 36.0(3.5)*         | 79(3.1)*         | 63.7(3.1)*       | 58.9(10.3)  | 4653*           | 7.8(1.9)* |
| O <sub>2</sub> /CO <sub>2</sub> | 46.2(6.3)**        | 93.6(5.6)**      | 69.0(3.0)**      | 62.4(8.5)** | 5840**          | 11.0(5.1) |

Statistics: Paired t test \* p<0.05 vs Baseline, \*\* p<0.05 vs 12% oxygen

Conclusion: 12% oxygen results in a fall in SpO<sub>2</sub>, PetCO<sub>2</sub>, DO<sub>2</sub> and cerebral rSO<sub>2</sub>. The oxygen carbon dioxide mix increased DO<sub>2</sub> to above baseline levels.

### 32. CEREBRAL OXYGEN DELIVERY FALLS WITH VOLUNTARY FORCED HYPERVENTILATION AT ALTITUDE

CHE Imray, H Hoar, M Beazeley, AD Wright, AR Bradwell, C Chan, BMRES

Hyperventilation profoundly affects PeCO<sub>2</sub>, and in turn cerebral blood flow. This study aimed to further investigate effects on cerebral oxygen delivery at altitude. 8 subjects were studied at 0m, 2400m and 5050m. Pulse oximetry (SpO<sub>2</sub>) and end tidal CO<sub>2</sub> (PetCO<sub>2</sub>) were measured using a Propac Encore Monitor; regional cerebral oxygenation (rSO<sub>2</sub>) was measured using a Critikon 2020 monitor; middle cerebral artery velocity (MCAV) was assessed using a Logidop 3 machine. Oxygen delivery (DO<sub>2</sub>) was calculated (MCAV X SpO<sub>2</sub>). Baseline studies were followed by 1 minute of voluntary forced hyperventilation (FHV).

#### Results:

|                        | 0m         | 0m FHV      | 2400m      | 2400m FHV  | 5050m      | 5050m FHV   |
|------------------------|------------|-------------|------------|------------|------------|-------------|
| SpO <sub>2</sub> %     | 98.7(1.5)  | 99.5(1.7)*  | 94.6(1.5)  | 99.7(0.5)* | 73.6(4.9)  | 95.5(0.9)*  |
| PetCO <sub>2</sub>     | 37.4(1.9)  | 21.9(2.8)*  | 36.4(2.8)  | 19.4(1.8)* | 29.4(1.8)  | 7.0(2.6)*   |
| MCAV cms <sup>-1</sup> | 54.5(10.2) | 37.2(16.1)* | 55.9(14.8) | 25.1(9.6)* | 61.8(12.4) | 19.6(11.3)* |
| rSO <sub>2</sub> %     | 69.2(2.7)  | 67.2(3.1)*  | 68.5(2.1)  | 68.3(2.1)  | 62.1(1.6)  | 66.9(1.34)* |
| DO <sub>2</sub>        | 5379       | 3701*       | 5228       | 2492*      | 4548       | 1824*       |

Statistics: Paired t test/ANOVA \* p<0.005 FHV vs Baseline at 0m, 2400m, 5050m.

Conclusion: At 5050m SpO<sub>2</sub>, PetCO<sub>2</sub>, rSO<sub>2</sub>, and DO<sub>2</sub> fell, whilst MCAV rose compared to 0m. FHV reduced PetCO<sub>2</sub> and increased SpO<sub>2</sub> at all altitudes. At 0m, the reduction in MCAV overrode the small increase in SpO<sub>2</sub>, resulting in a drop in cerebral oxygenation and DO<sub>2</sub>; however at 5050m the increase in SpO<sub>2</sub> was so great that despite the reduction in MCAV there is an increase in rSO<sub>2</sub> and there was a fall in DO<sub>2</sub>.

**33. ENHANCEMENT OF CEREBRAL AUTOREGULATION IN NEWCOMERS TO HIGH ALTITUDE**

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Cerebral autoregulation (CA) is the capacity of the brain to maintain constant blood supply within a wide range of mean arterial blood pressure values. CA is generally thought to be altered in newcomers to high altitude suffering from high altitude cerebral edema, a severe form of acute mountain sickness.

Twenty young males volunteers were evaluated at low altitude (Bishkek, 760 m), at days 1, 2, 5, 10 and 15 at high altitude (Kum-Tor, 3800 m), and at day 1 after return to low altitude. We evaluated dynamic CA by computing the autoregulation index (ARI) by analyzing the change in cerebral blood flow velocity measured by transcranial Doppler during hypotension induced by reperfusion of the lower limbs after 3 minutes of acute ischemia. None of the subjects suffered from acute mountain sickness. ARI increased within the first days at high altitude and reached a maximal value (+ 30 %) at day 5 compared to low altitude value (from  $3.9 \pm 0.3$  to  $5.1 \pm 0.3$ ,  $p < 0.005$ , mean  $\pm$ SE). This increase at day 5 was partially attenuated after correction of hypocapnia ( $4.8 \pm 0.4$ ) but not after correction of hypoxemia ( $5.1 \pm 0.2$ ). In conclusion: CA seems to be enhanced in newcomers to high altitude in the absence of acute mountain sickness. This increase in CA results partially from hypocapnia due to hyperventilation.

**35. POSSIBLE DISSOCIATION BETWEEN ATTENTION AND MEMORY IMPAIRMENTS RELATED TO MODERATE HIGH ALTITUDE**

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A multiple baseline design (lowland1-altitude1-lowland2-altitude2) were used with five young climbers (22.4 years) without previous experience in mountains higher than 3500 m. They carried out two ascents to peaks higher than 4500 m resting a week after the first climbing. They stayed six days upper than 4000ms the first time and four days in the second case. All the days in which the research took place the subjects completed the digit span subtest of the Weschler scale and a time estimation test for short periods three times a day. The digit span was considered a short-term memory (STM) measure while the time estimation test was considered an attention measure. There was no significant difference between the two baseline phases (lowland1-lowland2) neither between the two experimental phases (altitude1-altitude2). There were no effects in time estimation test average or standard deviation for the different conditions. A slight but significant effect was found in the memory task ( $7.82 \pm 1.53$  vs.  $5.87 \pm 1.82$ ;  $p < 0.05$ ). The results show that the stay during moderate periods at altitudes near 4000 m produce slight impairment in STM whereas the attention related to time estimation tasks remains unaffected.

**34. 6-HYDROXYDOPAMINE- INDUCED LOCUS COERULEUS LESIONS ALTER THE HYPOXIC VENTILATORY RESPONSE IN CONSCIOUS RATS**

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Upon exposure to hypoxia, the initial and most important response is an increase in alveolar ventilation. There is now growing evidence that the medullary catecholaminergic groups (A1C1, A2C2, A5, A6) participate in the ventilatory response to hypoxia. The present study was designed to assess the involvement of the A6 noradrenergic cell group, located in the locus coeruleus (LC), for the establishment of the ventilatory response to short-term hypoxia. The breathing response to acute hypoxia (10% O<sub>2</sub>) was measured in awake rats 15 days after an unilateral lesion of LC with 6-hydroxydopamine. The 6-hydroxydopamine infused "in situ" caused a major loss of noradrenergic neurons and noradrenalin content in the A6 area. Whereas basal resting ventilation is unaffected by the lesion, tidal volume component of the hypoxic ventilatory response is blunted (- 67%) and the respiratory "roll-off" is reversed. We concluded that i) LC noradrenergic neurons are not essential for breathing modulation under normoxia, ii) under hypoxia, tidal volume is controlled by central nervous mechanisms, iii) noradrenergic neurons of the LC are involved in this regulation.

**36. PILOT STUDY: MATRIX OF CORRELATION OF PHYSIOLOGICAL AND PERCEPTIVE VARIABLES RELATED TO MODERATE HIGH ALTITUDE**

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Two groups of young climbers (n1=4 y n2=5) ascended independently the Mont Blanc (4808 m.). They spent four and three days respectively till the return to lowland. From the day before the ascent till the day after the descent the following variables were monitored three times a day. Blood Pressure (diastolic, systolic and average: DBP, SBP, ABP), Peripheral Temperature (PT), Heart Rate (HT) and the rest time before the recording (DESC) as physiological variables. The somnolence measured by the Stanford Somnolence Scale (SSS), time estimation measured by the Time Estimation Test (MET and DTET) as perceptive variables and the altitude (MS) recorded by GPS Garmin 12 or by map as environmental variable. The correlation matrix obtained is presented. The results show significant association between PT and MS ( $r = 0.72$ ;  $p < 0.01$ ), DESC and SBP ( $r = 0.62$ ;  $p < 0.05$ ), SSS and PT ( $r = -0.63$ ;  $p < 0.05$ ) and between SSS and DESC ( $r = 0.62$ ;  $p < 0.05$ ). There were no significant relations with the time estimation measures. Should be noted the strong association found between altitude and peripheral temperature and how the peripheral temperature is also related with the perceived somnolence.

Table 1. Correlation matrix of physiologic and perspective variables.

| MS | DBP   | SBP  | ABP    | HR    | PT     | DESC  | SSS    | MET   | DTET  |      |
|----|-------|------|--------|-------|--------|-------|--------|-------|-------|------|
|    | 0.66* | 0.30 | 0.24   | 0.60  | 0.72** | -0.30 | -0.28  | -0.10 | 0.26  | MS   |
|    |       | 0.03 | 0.76** | 0.20  | 0.44   | -0.27 | -0.36  | -0.07 | 0.41  | DBP  |
|    |       |      | 0.67*  | 0.19  | 0.59   | 0.62* | -0.26  | 0.34  | 0.09  | SBP  |
|    |       |      |        | -0.40 | -0.39  | 0.07  | 0.04   | 0.26  | 0.25  | ABP  |
|    |       |      |        |       | 0.73** | -0.30 | -0.13  | 0.05  | 0.26  | HR   |
|    |       |      |        |       |        | -0.48 | -0.63* | -0.07 | 0.45  | PT   |
|    |       |      |        |       |        |       | 0.62*  | 0.47  | -0.14 | DESC |
|    |       |      |        |       |        |       |        | 0.39  | -0.23 | SSS  |
|    |       |      |        |       |        |       |        |       | 0.28  | MET  |
|    |       |      |        |       |        |       |        |       |       | DTET |

\* p < 0.05 \*\* p < 0.01.

### 37. SIMULATION OF FUNCTIONAL WORKING STATES OF THE BRAIN IN HYPOXIA CONDITIONS

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A computer procedure automatically allows us to watch functional working states of the brain (FWSB) during hypoxia, and central nervous system activation during sensori-motor loading (first signal positive and brake stimuli). The program defines the main properties of the nervous processes, parameters of the vegetative nervous system, wave frame of the rhythm-cardiogram at implementation of three following FWSB.

1. Hard work of a brain. It is characterized by the greatest possible steady mode with fulfillment of minimum (5%) errors (probability of correct sensori-motor activity  $P=0,95$ ). The program defines a level of function mobility of nervous processes, force of nervous processes, efficiency of a brain, balance of nervous processes.

2. Operation of a brain with maximal mobilization of forces. It is a pre-stressful mode when the quantity of errors makes 25% ( $P=0,75$ ).

3. A stressful mode of a brain with 50% level of working failures ( $P=0,5$ ). The given model allows us to define a level of training of information processing in extreme conditions of hypoxia.

### 39. ENDOTHELIUM RELAXING FACTOR (NO) IN CORONARY REHABILITATION WITH HYPOBARIC CHAMBER

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Eight coronary patients 4 infarcted, age average, 67 years 7 coronary bypassed; entered to coronary rehabilitation with hypobaric chamber: (progressive hypoxia exposure). Nitric oxide (NO) was determined previous, during and for 3 months to the culmination 13 hypoxic sessions. NO increases, arriving highest level when they reached maximum height (4000m), subsisting over basal values until the limit of the time settled down by the protocol. NO levels were:

| NO                            | BASAL | Intrachamber 4000m | End Hypoxia | CONTROL            |          |         |
|-------------------------------|-------|--------------------|-------------|--------------------|----------|---------|
|                               |       |                    |             | Sample out chamber |          |         |
|                               |       |                    |             | 10 weeks           | 13 weeks | 1 month |
| $\mu\text{M} / \text{Plasma}$ | 5     | 14                 | 10          | 9                  | 8        | 8       |
| NV: 5-50                      | 4.20  | 12.80              | ---         | ---                | 9.80     | 9.00    |
| P<                            | 0.001 | 0.001              | 0.001       | 0.001              | 0.001    | 0.003   |

Increment of NO is transcendental. He would explain exquisites hypoxic mechanisms that would be taking place in the binomial vascular coronary cardiomyocyte and endothelium—NO.

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### 38. MONOCROTALINE : A PHARMACOLOGICAL MODEL OF CHRONIC HYPOXIA-INDUCED PULMONARY ARTERIAL HYPERTENSION

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The aim of our study was to provide evidence that monocrotaline (MCT), a toxic alkaloid, could be considered as a substitute model of chronic hypoxia-induced pulmonary arterial hypertension. Wistar rats were given a single intraperitoneal MCT injection (60mg/kg, MCT group, 12 rats) or distilled-water (DW group, 8 rats). Twenty two days later, heart, liver, kidney, lungs and plasma were removed after inorganic and trace elements had been measured. Data showed increased zinc ( $0.02\pm 0.002$  vs  $0.02\pm 0.002$  mM/L), sodium ( $13\pm 3$  vs  $12\pm 7$  mM/L), and potassium ( $4.6\pm 0.5$  vs  $3.9\pm 0.5$  mM/L) plasmatic concentrations, as well as decreased vitamin C levels ( $11\pm 3.2$  vs  $14.4\pm 1.73$  mg/L), in MCT compared to DW. Kidney and lung weights were higher in MCT than in DW ( $3.39$  vs  $2.97$  g/kg, and  $9.4\pm 2.7$  vs  $3.7\pm .13$  g/kg, respectively). Right ventricular hypertrophy was evident in MCT compared to DW ( $0.4\pm 0.12$  vs  $0.1\pm 0.02$  g/kg). Results suggested that the MCT model could be used in rats to characterize the pathological processes preceding high altitude pulmonary edema.

### 40. ACUTE MOUNTAIN SICKNESS IN CHILDREN AT 5100 M

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Objective: to compare acclimatization of children and adults to high altitude during an expedition in the Andes. Subjects and methods: 23 children (8 boys and 15 girls of 13–15 years old), and 19 adults were involved in a school project consisting of one month's travel through Chile, Peru and Bolivia, including the ascent of Parinacota (6342 m).

Acute mountain sickness (AMS) was evaluated by the Lake Louise scoring system, and  $\text{SaO}_2$  was measured with a pulse oximeter at sea level, Cusco (3400 m), Sajama village (4200 m), base camp (4700 m) and an altitude camp (5100 m). Data were analysed by Anova.

Results: scores of AMS and  $\text{SaO}_2$  were not statistically different between adults and children. 3 adults and 3 children had severe AMS with some symptoms of cerebral edema at 5100 m. There was no case of pulmonary edema. A portable hyperbaric chamber was used to treat 1 adult and 3 children, in conjunction with dexamethasone in the case of all but one child. Other adults were treated by rest and acetazolamide or by descent. In all cases symptoms disappeared rapidly. Conclusion: acclimatization to high altitude is similar in adults and children aged 13–15 years.

#### 41. ACUTE EXPOSURE TO 3200 m ALTITUDE OF 109 STUDENTS BETWEEN 9 AND 11 YEARS OLD

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109 students of 9 and 11 years old, (60 girls and 49 boys), who were sea level residents from Antofagasta, ascended in one day to 3200 m. This was part of an educational tour of a mine offered to schools of low economic resources. The children ascended to 3200m over 2 hours, remaining at this altitude for 5 hours during which they had breakfast, lunch and a tour of the mine. Measurements of heart rate and arterial saturation were made before ascent and following return from the mine. In addition a modified Lake Louise Score of Acute Mountain Sickness was carried out. The oxygen saturation fell significantly from a mean of 97% to 90%; heart rate increased significantly from 86 to 112 beats per minute. The most frequent symptoms of acute mountain sickness were: headache (49%); mild otalgia during the descent (47%); nausea (31%) and dizziness (15%). There were 5 cases of vomiting. The children seemed to be more symptomatic than adults during acute ascent to altitude, particularly with regard to headache and mild otalgia during descent.

#### 42. ACUTE MOUNTAIN SICKNESS (AMS) IN CHILDREN

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Children may be more susceptible to AMS than adults but there are few descriptions. A recent trek was undertaken with 3 lowland resident children, aged 15 (male) 11 and 8 (girls). All were taking acetazolamide. Ascent was from Kathmandu to Phaphlu (2,600m) by aeroplane. Namche Bazaar (3,200m) was reached 5 days later with a rest day then ascent to Thangboche (3,600m) and finally Pangboche (4,000m). The 8 year old vomited on the morning following arrival at Thangboche but ate breakfast and felt well. After ascent to Pangboche she was well but the next morning vomited the previous night's food, felt weak and nauseated. There was no headache. The 11yr old girl was well until the evening at Pangboche when she felt nauseated, weak and ate little. Subsequently she vomited and developed a slight headache and slept poorly. She awoke with a bad headache and weakness. Neither child had oedema or pulmonary symptoms and older members of the group were well throughout. Descent was made to Namche Bazaar with complete symptom relief. The two children were very susceptible to AMS, in spite of taking acetazolamide, and sickness without headache is most unusual in adults.

#### 43. COMPARATIVE STUDY OF BODY STATURE AND HEART RATE FOLLOWING EXERCISE BETWEEN CHILDREN OF LOW AND HIGH ALTITUDE RESIDENCE

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Objective: To compare somatometric parameters and heart rate (HR) following 30 seconds of maximal exercise between Tibetan and Catalan children. Methods: We studied 21 Tibetan boys from Tingri at 4500 m and 35 Catalan boys from Terrassa at 400 m. All studies took place in the morning, and were carried out in their respective home towns. Physical exercise consisted in a modification of the Harvard step-test. Results: There was a significant difference between the groups for stature, weight, Body Mass Index, Thoracic Perimeter (T.P.), TP/stature, maximum number of jumps in 30 seconds, HR immediately after exercise and two minutes later. For all variables values were higher in the Catalan group. There was no significant difference in age, resting HR or decrease in H.R. following exercise. Conclusions: Tibetan children from the higher resident altitude have lower somatometric parameter values. Resting HR and change in HR following cessation of 30 s maximal exercise were similar, but Catalan children jumped more times and reached a higher HR.

#### 44. ADAPTATION TO HYPOXIA IN CHILDREN AFTER THREE WEEKS AT HIGH ALTITUDE

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A group of low altitude dwelling children of between 9 and 14 years old was studied during three weeks resident in the mountains at 2000 m. Breathing pattern, alveolar ventilation (VA), total ventilation (VE), alveolar volume and alveolar oxygen tension were measured. At 3 days children had reduced alveolar oxygen tensions (PAO<sub>2</sub> 72 mmHg), decreased alveolar ventilation, alveolar volume, and VA/VE ratio compared to sea level. Total ventilation was increased, predominantly due to an increase in respiratory frequency. Oxygen consumption and heart rate were raised compared to sea level. Following 3 weeks of acclimatization, there was a decrease in respiratory frequency and increase tidal and alveolar volume, resulting in restoration of the VA/VE ratio. However oxygen consumption and heart rate remained elevated.

#### 45. TWO-YEAR FOLLOW-UP OF INFANTS AT 3200–4000M IN LA PAZ, BOLIVIA

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**Objective:** Infant mortality in Bolivia is high and rises with increasing altitude. We asked if premature or low-birth-weight (LBW) babies (1500–2500g) experienced greater mortality/morbidity compared with term infants in La Paz, Bolivia. **Methods:** All infants were born at 3700m within the Caja Nacional de Salud (CNS). Premature (n=35) and term LBW infants (n=47) born in 1998 were compared with a randomized control group of term infants >2500g (n=76). Using CNS clinic records or home visits, we classified infants as healthy, sick (hospitalization or >2 major illnesses), or dead at 2 years. **Results:** Of 158 babies identified, 140 were located. No late deaths occurred among the pretermes; 3 LBW infants died (2 of cardiopulmonary causes); 1 control infant died of cardiopulmonary arrest. Most serious illnesses were cardiorespiratory, including one case of perinatal hypertension. A disproportionate number of sick infants and deaths occurred at > 4000m. **Conclusion:** LBW infants at high altitude merit close follow-up and careful pathophysiologic diagnosis of cardiorespiratory morbidity/mortality in early infancy and childhood.

| Group (n)       | # healthy (%) | # sick (%) | # dead (%) |
|-----------------|---------------|------------|------------|
| Prematures (31) | 28 (90%)      | 3 (10%)    | 0 (0%)     |
| LBW (33)        | 28 (85%)      | 2 (6%)     | 3 (9%)     |
| Controls (76)   | 69 (91%)      | 6 (8%)     | 1 (1%)     |

#### 47. HEMATOLOGICAL KINETICS DURING CHRONIC EXPOSURE TO CARBON MONOXIDE AT ALTITUDE IN SEA LEVEL NATIVE RATS

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Because pollution levels increase in sea level as well as high altitude urban locations, we studied the effects of chronic carbon monoxide (CO) inhalation at high altitude on hematological adaptations.

Dark Agouti rats were randomly assigned for 10 weeks to continuous normoxia (~55 m., N rats), normoxia with CO (~55 m. + 50 ppm CO, CO rats), hypoxia (~4000 m., CH rats), or hypoxia with CO (~4000 m. + 50 ppm CO, CH+CO rats). Hematocrit ratio as well as carboxyhemoglobin (COHb) were evaluated before, during and after exposure. After exposure, using hypoxia or CO alone, polycythemia (N: 39.8±1.9%; CO: 44.1±2.0; CH : 51.2±2.0%) or COHb (N: 1.0±0.5; CO: 4.6±0.6; CH: 1.4±0.4%) levels were consistent with the literature. However, from the 3<sup>rd</sup> to the 10<sup>th</sup> week of exposure, we found that CO potentiated the altitude-induced polycythemia (10<sup>th</sup> week: CH+CO: 66.2±1.5%, p<0.001 vs CH), and that altitude increased the CO-induced enhancement in COHb (CH+CO: 9.3±2.9%, p<0.001 vs CO).

Our data suggest that pollution in high altitude urban areas is responsible for high hematological adaptations levels, and could reinforce the risk of spontaneous vascular thrombosis reported in highlanders.

#### 46. POSTNATAL CHANGES IN THE PULMONARY CIRCULATION AT 3700–4000 M

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**Objective:** The hypoxia of high altitude can impair postnatal changes in the pulmonary circulation. We documented pulmonary artery pressures (P<sub>PA</sub>) and persistence of fetal circulatory patterns among infants born at 3700–4000m in La Paz, Bolivia. **Methods:** Echocardiography was performed at 2 weeks, 1, 3, and 6 months on 16 infants. P<sub>PA</sub> was estimated using pulmonary valve systolic intervals in the regression equation of Wan-zhen. Persistence of the foramen ovale (PFO) and ductus arteriosus (PDA) was noted. **Results:** Twelve of 14 term infants had a PFO diagnosed in the first 3 months. Half of these persisted at 3 months. P<sub>PA</sub> was elevated in the first 3 months and at 6 months approached values considered normal during childhood at 3700m. Two premature infants experienced clinical pulmonary hypertension, one acutely after birth and one subacutely (3 months). **Conclusion:** Postnatal changes in the pulmonary circulation occur slowly at high altitude, with greater vulnerability to incomplete or disrupted transition.

|                            | 2 weeks (n=14) | 1 month (n=11)* | 3 months (n=10)* | 6 months (n=4)* |
|----------------------------|----------------|-----------------|------------------|-----------------|
| PFO, n (%)                 | 10 (71%)       | 5 (45%)         | 6 (60%)          | 2 (50%)         |
| PDA, n (%)                 | 1 (7%)         | 0               | 0                | 0               |
| P <sub>PA</sub> sys (mmHg) | 50 + 9         | 42 + 5          | 42 + 11          | 30 + 5          |
| Mean + SD                  |                |                 |                  |                 |

\*follow-up in progress

#### 48. CARDIAC MORPHOLOGY AND FUNCTION FOLLOWING LONG TERM ALTITUDE TRAINING IN SEA LEVEL NATIVE RATS

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Although effects of altitude training (AT) on maximal aerobic capacity (MAC) have been studied a great deal over the past three decades, the impact of AT on cardiac morphology and function remain poorly understood. Using steel chambers, Dark Agouti rats were randomly assigned for 10 weeks to continuous normoxia (~55 m., N rats) or hypobaric hypoxia (~4000 m., CH rats), including regular training sessions.

Training was conducted during exposure, at 80 % normoxic (N rats) or hypoxic (CH rats) MAC, five 40 to 60-minute sessions per week. Echocardiographic, hemodynamic and hematologic data, collected before, during and after exposures, indicated that normoxic training increased hematocrit ratio, normoxic MAC, left ventricular (LV) end-diastolic diameter, septal and posterior wall thicknesses, LV diastolic function as well as right ventricular (RV) weight. Same increase in normoxic MAC as well as same LV impacts were found in CH rats, but AT increased more RV weight than normoxic training. Results suggested that AT has same LV impacts as training performed in sea level locations. Cardiac function could probably not explain the different normoxic MAC adaptations to AT described in the literature.

#### 49. DETRIMENTAL EFFECTS OF LONG TERM ALTITUDE TRAINING IN POLLUTED ENVIRONMENT ON CARDIAC FUNCTION

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Although cardiac adaptations to chronic atmospheric pollution have already been studied in sea level environments, very little is known concerning pollution effects in altitude locations. Especially, the effects of training performed in such environment have never been studied. Dark Agouti rats were randomly assigned for 10 weeks to continuous normoxia (~55 m.), normoxia with carbon monoxide (CO) pollution (~55 m. + 50 ppm CO), hypobaric hypoxia (~4000 m.), or hypobaric hypoxia with CO (~4000 m. + 50 ppm CO). In the four groups, 5 training sessions per week were conducted in each specific environment using a driven wheel, at 80 % maximal aerobic capacity. Longitudinal echocardiographic and hemodynamic data indicated marked impairment in both left ventricular systolic and diastolic function, and enlargement in end diastolic diameter after training in polluted high altitude environment.

No cardiac function deterioration was found in the three other environmental conditions. Our data suggest that training performed in polluted high altitude locations results in severe hematological adaptations, which could be involved in cardiac dysfunction. Exercise performed in high altitude polluted urban areas should be carefully supervised.

#### 50. LONG TERM ALTITUDE TRAINING IN POLLUTED ENVIRONMENT ALTERS HEART RATE VARIABILITY IN SEA LEVEL NATIVE RATS

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Despite increasing pollution levels in sea level or high altitude urban areas, heart rate variability (HRV) changes following physical training performed in polluted environments have never been studied. Dark Agouti rats were randomly assigned for 10 weeks to continuous normoxia (~55 m.), normoxia with carbon monoxide (CO) pollution (~55 m. + 50 ppm CO), hypobaric hypoxia (~4000 m.), or hypobaric hypoxia with CO (~4000 m. + 50 ppm CO). In the four groups, 5 training sessions per week were conducted in each environment during exposure, using a driven wheel, at 80 % maximal aerobic capacity.

Spectral components of HRV were studied before and after the 10-week exposures, using a Fast Fourier Transform analysis performed in five 256-second recordings. Tachycardia, decreased total spectrum power as well as large increase in low / high frequency power were found in rats trained in polluted high altitude environment, whereas the three other groups showed inverse results. Our data suggest that training in high altitude polluted urban areas could alter sympathetic / vagal balance, which could be involved in altitude-induced pulmonary edema risk factors.

#### 51. UPREGULATION OF ANTI-APOPTOTIC GENE EXPRESSION BY CHRONIC HYPOXIA PROTECTS RAT KIDNEYS FROM ISCHEMIA/REPERFUSION INJURY

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Chronic hypoxia is known to increase renoprotection against sustained ischemia/reperfusion (I/R) injury (Chien et al., Renal Failure, 1995). However, the detailed mechanism of this protection on I/R induced kidney damage is not yet defined. Rats for chronic hypoxia induction were placed in a hypobaric chamber (380 Torr, 5,500 m) 15 h/day. After exposure to hypoxia, the kidneys subjected to 45-min ischemia followed by reperfusion were conducted to analyze apoptosis-related mechanism and to determine reactive oxygen species (ROS) amount in vivo by a chemiluminescence method. Our results showed chronic hypoxia upregulated heat shock protein 70 (HSP-70), Bcl-2 and Bcl-xL expression in renal cortex and medulla in a time-dependent manner. In response to I/R insult, pro-apoptotic and oxidative stress, including increases in Bax/Bcl-2 ratio, caspase 3 expression, poly-(ADP-ribose)-polymerase fragments, ROS release from kidney surface and renal venous blood, and subsequently, severe apoptosis, including the increased DNA fragmentation and apoptotic cell number appeared in the damaged kidney without chronic hypoxia treatment. However, all these oxidative insults were reduced with chronic hypoxia treatment by a mechanism of Bcl-2 and Bcl-xL upregulation. In proximal tubule cultures from chronically hypoxic kidneys, antisense oligodeoxyribonucleotides of HSP-70 and Bcl-2 treatment abrogated protection against hypoxia/reoxygenation injury. Our results suggest that the activation of HSP-70, Bcl-2, and Bcl-xL during chronic hypoxia is important in the acquisition of renal protection against I/R induced oxidative stress.

#### 52. CARDIAC MORPHOLOGY AND FUNCTION FOLLOWING LONG TERM EXPOSURE TO CARBON MONOXIDE AT HIGH ALTITUDE IN SEA LEVEL NATIVE RATS

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Despite increasing pollution levels in high altitude urban areas, cardiac adaptations following chronic exposure to carbon monoxide (CO) at high altitude have never been studied. Dark Agouti rats were randomly assigned for 10 weeks to continuous normoxia (55 m., N rats), normoxia with CO (~55 m. + 50 ppm CO, CO rats), hypobaric hypoxia (~4000 m., CH rats) or hypobaric hypoxia with CO (4000 m. + 50 ppm CO). Left ventricular (LV) morphology and function were evaluated by echocardiography-Doppler before, during and after exposures. Right ventricular (RV) morphology and function were evaluated after exposure, using post mortem weights following catheterization. Although LV weight, systolic and diastolic functions were not altered by environmental conditions in N, CH or CO rats, CO at altitude increased LV weight (+ 24.6±4.3% vs CH after exposure) and systolic function. However, CO intensified the altitude-induced RV hypertrophy (RV/body weight : + 23.2±6.3% vs CH) and RV diastolic function deterioration (-dP/dt : -17.9±4.3% vs CH). Our data suggest that 50 ppm CO at altitude might be more detrimental to cardiac function than CO inhaled at sea level.

**53. LONG TERM EXPOSURE TO CARBON MONOXIDE AT HIGH ALTITUDE : EFFECTS ON HEART RATE VARIABILITY IN SEA LEVEL NATIVE RATS**  
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Heart rate fluctuation analysis provide reproducible markers of sympathovagal balance. Despite increasing pollution levels in sea level or high altitude urban locations, heart rate variability (HRV) changes following long term exposure to polluted environments have never been studied. Dark Agouti rats were randomly assigned for 10 weeks to continuous normoxia (~55 m.), normoxia with carbon monoxide (CO) pollution (~55 m. + 50 ppm CO), hypobaric hypoxia (~4000 m.) or hypobaric hypoxia with CO (~4000 m. + 50 ppm CO, CH+CO rats). Spectral components of HRV were studied before and after the 10-week exposures, using a Fast Fourier Transform analysis performed in five 256-second recordings. Tachycardia, decreased total spectrum power (-37.1±5.8 % vs before exposure) as well as large increase in low / high frequency power (+157.9±27.3 % vs before exposure) were found in rats after exposure to CO at altitude, whereas no significant adaptations were found in the three other groups. Our data suggest that living in high altitude polluted urban areas could alter sympathetic/vagal balance, which could be involved in hypoxia-induced cardiovascular diseases.

**55. PREGNANCY RAISES VENTILATION AND HYPOXIC VENTILATORY RESPONSIVENESS SIMILARLY IN ANDEAN AND FOREIGN RESIDENTS OF HIGH ALTITUDE**

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| Table              | nonpg                    | wk 20                | wk 30                | wk 36                |
|--------------------|--------------------------|----------------------|----------------------|----------------------|
| SaO <sub>2</sub> : | A 92.4 <sub>0</sub>      | 93.1 <sub>1</sub>    | 95.4 <sub>0</sub>    | 94.4 <sub>0</sub>    |
|                    | F 92.4 <sub>0</sub>      | 94.1 <sub>1</sub>    | 94.4 <sub>0</sub>    | 94.4 <sub>0</sub>    |
| PCO <sub>2</sub> : | A 35.9 <sub>±0.6</sub> * | 31.3 <sub>±0.6</sub> | 31.4 <sub>±0.8</sub> | 31.3 <sub>±0.8</sub> |
|                    | F 32.9 <sub>±0.7</sub> * | 30.1 <sub>±1.1</sub> | 31.8 <sub>±0.8</sub> | 30.6 <sub>±0.8</sub> |
| f                  | A 17.1 <sub>1</sub>      | 19.1 <sub>1</sub>    | 18.1 <sub>1</sub>    | 18.1 <sub>1</sub>    |
|                    | F 14.2 <sub>1</sub>      | 12.1 <sub>1</sub>    | 12.1 <sub>1</sub>    | 15.2 <sub>1</sub>    |
| Hvr A              | A 60.2 <sub>8</sub>      | 15.2 <sub>±22</sub>  | 13.2 <sub>±20</sub>  | 15.2 <sub>±26</sub>  |
|                    | F 62.1 <sub>2</sub>      | 17.2 <sub>±35</sub>  | 15.2 <sub>±26</sub>  | 16.9 <sub>±0.3</sub> |
| CaO <sub>2</sub> : | A 17.9 <sub>±0.4</sub>   | 16.8 <sub>±0.3</sub> | 16.9 <sub>±0.3</sub> | 17.9 <sub>±0.5</sub> |
|                    | F 18.3 <sub>±0.5</sub>   | 17.4 <sub>±0.6</sub> | 17.9 <sub>±0.5</sub> | 13.2 <sub>±0.2</sub> |
| Hgb                | A 14.4 <sub>±0.3</sub> * | 13.3 <sub>±0.2</sub> | 13.2 <sub>±0.2</sub> | 14.0 <sub>±0.4</sub> |
|                    | F 15.0 <sub>±0.3</sub> * | 13.6 <sub>±0.4</sub> | 14.0 <sub>±0.4</sub> |                      |

\* p<.05 compared with pg values, p<.05 A vs F

(IUGR). We asked whether the Andeans' heavier birth weights were due to higher levels of arterial oxygenation during pregnancy. Design: Women of foreign (F, n=8, European) or Andean (A, n= 25, Aymara) ancestry residing in La Paz, BO (3600 m) gave informed consent to studies conducted at wks 20, 30 and 36 of pregnancy and 3 mo postpartum for a measurement in the nonpregnant state. We monitored arterial O<sub>2</sub> saturation (SaO<sub>2</sub>) by pulse oximetry, ventilation by end-tidal O<sub>2</sub> and CO<sub>2</sub> (PetO<sub>2</sub>, PetCO<sub>2</sub>) and volume by flowmeter, and the isocapnic hypoxic ventilatory response (Hvr) by a rebreathing method. Results: Pregnancy raised alveolar ventilation in the A and F groups as indicated by a fall in PetCO<sub>2</sub> and rise in SaO<sub>2</sub>. HVR doubled in both groups. The pattern of breathing differed with F women having lower frequency (f) and higher tidal volume than the A women. Arterial O<sub>2</sub> content (CaO<sub>2</sub>) was maintained in the A women, since their fall in hemoglobin concentration was offset by the rise in SaO<sub>2</sub>, whereas CaO<sub>2</sub> tended (p=.06) to be lower during pregnancy in the A women. Conclusion: Lower birth weights in F than A women are unlikely to be due to differences in arterial oxygenation during pregnancy. We speculate that differences in O<sub>2</sub> delivery due to alterations in uteroplacental blood flow are involved. (NIH TW01188).

**54. LONG-TERM PRENATAL HYPOXIA IMPAIRS THE MATURATION OF CENTRAL CATECHOLAMINERGIC SYSTEM AND BEHAVIOUR IN THE RAT**

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In order to estimate the effects of hypoxia during the gestation on the maturation of catecholaminergic structures involved in motor and cognitive functions, pregnant rats were subjected to hypoxia (10% O<sub>2</sub>) lasting 2 weeks. The tyrosine hydroxylase (TH) activity, the rate limiting enzyme in catecholamine synthesis, was quantified in the Locus Coeruleus (LC), Prefrontal Cortex (PFC), Hippocampus (Hipp) and striatum at birth, 3, 7, 14, 21 and 68 postnatal day (P0, P3, P7, P14, P21, P68). The locomotor novelty reactivity and the circadian activity were measured in an actimetry box at P21 and P68.

Exposure to prenatal hypoxia increased the TH activity in the LC at P3 (+29%) and P21 (+30%). In the PFC, the TH activity was increased at P3 (+370%) and at P7 (+35%) and was decreased at P21 (-80%). In Hipp, the TH activity was decreased at P3 (-42%) and P21 (-43%). We noticed at P21, a locomotor hyperreactivity to the novelty and a nocturnal hypoactivity.

Prenatal hypoxia alters the maturation of the central catecholaminergic structures involved in the behaviour. It could constitute some cellular basis of the installation of behavioural disorders observed during development. Thus prenatal hypoxia might contribute to behavioural alterations in some children.

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**56. COMMUNITY PERSPECTIVES ON CHRONIC MOUNTAIN SICKNESS AT 3100 M IN NORTH AMERICA: A MULTIFACTORIAL ANALYSIS**

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Chronic Mountain Sickness (CMS) is a poorly understood malady affecting some long-time high altitude residents. This community-based study was designed to improve understanding of population health in Leadville, CO, USA (n = 288, M=140, F=148, age range 20 -88 years). Data on 25 variables were gathered on all participants. Results support previously established age distribution of CMS cases in men and women, but don't support gender differences in susceptibility. Three family clusters among the 48 CMS cases suggest a genetic component to susceptibility. Also, CMS cases were significantly (p > .001) more likely to have been born at high altitude than their normocythemic counterparts, suggesting that some characteristics of birth or infancy at high altitude may predispose individuals towards CMS. The 'Barker Hypothesis' suggests that low birth weight and respiratory disease during childhood may be the origin of such a predisposition. CMS appears to be multi-causal, a product of interactions between genetic, developmental and behavioral characteristics of high altitude residents.

### 57. TOXIC LEVELS OF CARBON MONOXIDE AMONG RESIDENTS OF 3100 M IN NORTH AMERICA

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Blood specimens drawn on 253 residents of Leadville, CO (3100m) as part of a community-based survey of CMS yielded carboxyhemoglobin levels ranging from 0.0 to 8.7 g/dl. The ratio COHgb/Hgb \* 100 is used to evaluate toxicity; at sea level, non-smokers average 1%, moderate smokers 2–15%. Ratios greater than 20–25% indicate toxicity. Ratios were below 20% for 226 participants, but 27 participants had ratios greater than 20% (maximum 48.5%). Twenty-five of these individuals were smokers, but the high CO levels were a surprise. At sea level the half-life of COHgb is about 6 hours; at 3100 m the half-life may be longer, contributing to higher concentrations and the risk of toxicity. When CO displaces O<sub>2</sub>, and shifts hemoglobin dissociation left, nervous system function is impaired and cellular toxicity develops. Symptoms are similar to those of CMS; CMS scores correlated positively with COHgb levels among normocythemic smokers in this population. The role of chronic CO toxicity in high altitude response is unknown, but unlikely to be benign.

### 59. PULMONARY HYPERTENSION-RELATED HIGH ALTITUDE HEART DISEASE IN TIBET

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High-altitude heart disease (HAHD) is a form of chronic mountain sickness, which is characterized by right ventricular enlargement and right heart failure that develops primarily to severe pulmonary hypertension by high altitude exposure. The prevalence is higher in children than adults and in men than women, but is lower in both sexes of Tibetan high-altitude residents compared with acclimatized newcomers, such as Han Chinese. Its occurrence may have a familial (genetically based) inheritance. Clinical symptoms consist of headache, dyspnea, cough, irritability, and sleeplessness. Physical findings include a marked cyanosis, rapid heart and respiratory rates, edema of the face, liver enlargement, and rales. Echocardiography of the patients with HAHD indicated a marked rise in the right ventricular (RV) outflow and an increase in the internal diameter of the RV, which was compatible with pulmonary hypertension. Chest radiography revealed bilateral pulmonary infiltrates and a prominent pulmonary artery. Autopsy demonstrated a dilated pulmonary artery trunk, atheromas and thrombosis of the pulmonary artery, and hypertrophy and dilation of the RV and right atrium. The histologic examination of the lung revealed that small pulmonary arteries had severe medial hypertrophy with crenation of the elastic laminae. The vessel walls were extremely thick. Right ventricular enlargement, pulmonary hypertension, and remodeling of pulmonary arterioles are hallmarks of HAHD. Most patients have complete recovery on descent to a lower altitude, but symptoms recur with a return to high altitude.

### 58. EFFECTS OF 55 DAYS EVEREST EXPEDITION CHRONIC HYPOXIA EXPOSURE

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To investigate the effects of chronic hypoxia exposure on cardiovascular function, eight members of Mt. Everest (8848m) expedition (1995) were examined before and after their successful climbing. Following tests were undertaken: (1) hematological measurements: red blood cell (RBC), hematocrit (Hct%) and hemoglobin (Hb), (2) body weight, (3) incremental exercise testing (IET) in normoxia (sea level), and hypoxia (FIO<sub>2</sub>=10%, 5145m): maximum oxygen uptake (VO<sub>2</sub>max), heart rate maximal (HRmax), maximum oxygen pulse (O<sub>2</sub> pulse), maximum ventilation (VE), tidal volume, and oxygen equivalent (VE/VO<sub>2</sub>max). The results revealed that: (1) body weight decreased (2) RBC increased 32%, Hct% increased 21% and Hb increased 17% (3) VO<sub>2</sub>max, O<sub>2</sub> pulse and VE in normoxia IET test decreased but not significantly. (4) VO<sub>2</sub>max increased 18.9%, exhausted time increased 21%, O<sub>2</sub> pulse increased 15.4% in hypoxia IET, (5) during hypoxia IET, respirator frequency decreased, tidal volume increased, and VE/VO<sub>2</sub>max decreased. The results suggests that the enhancement of VO<sub>2</sub>max in hypoxia situation after chronic hypoxia exposure may be caused by peripheral effects of hematological changes and central effects of respiratory and cardiac function improvement.

### 60. DOPAMINERGIC METABOLISM IN CAROTID BODIES AND HIGH ALTITUDE ACCLIMATIZATION IN FEMALE RATS

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We tested the hypothesis that ovarian steroids stimulate breathing through a dopaminergic mechanism in the carotid bodies (CB). In ovariectomized female rats raised at sea level domperidone, a peripheral D2 receptor antagonist, increased ventilation in normoxia (Ve : + 55 %) and acute hypoxia (+ 32 %). This effect disappeared after 10 daily injections of ovarian steroids (progesterone + oestradiol). At high altitude (HA—3600 m, IBBA, La Paz, Bolivia), neutered females had higher CB tyrosine hydroxylase activity (the rate limiting enzyme for catecholamine synthesis : + 129 %) and dopamine utilization (+ 150 %), lower Ve (- 30 %) and hypoxic ventilatory response (- 57 %), higher hematocrit (+ 18 %) and hemoglobin concentration (+ 21 %), than intact female rats. Consistent signs of arterial pulmonary hypertension (right ventricular hypertrophy) also appeared in ovariectomized females. None of these parameters were affected by gonadectomy in males. Our results show that ovarian steroids stimulate breathing by lowering a peripheral dopaminergic inhibitory drive. This process may partially explain the de-acclimatization of postmenopausal women at high altitude.



### 61. EFFECTS OF EXERCISE TRAINING ON ACCLIMATIZATION TO HYPOXIA: SYSTEMIC O<sub>2</sub> TRANSPORT DURING MAXIMAL EXERCISE

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Acclimatization to prolonged hypoxia results in downregulation of myocardial  $\beta$  adrenoreceptors ( $\beta$ -AR), reduced maximal heart rate ( $H_{r,max}$ ) and cardiac output ( $Q_{max}$ ) and little or no change in maximal O<sub>2</sub> uptake ( $VO_2$  max). Hypoxia-induced  $\beta$ -AR downregulation is attenuated by exercise training (ET). This study tested the hypothesis that the attenuation of  $\beta$ -AR downregulation by ET would result in higher  $H_{r,max}$ ,  $Q_{max}$  and  $VO_2$  max in trained than in sedentary, acclimatized rats. After 3 weeks of treadmill training, male rats either underwent acclimatization to  $PI_{O_2}$  70 Torr for 10 days (AT), or remained in normoxia (NAT). Controls were sedentary acclimatized (AS) and non acclimatized rats (NAS). All rats exercised maximally in normoxia and in hypoxia ( $PI_{O_2}$  70 Torr). During normoxic exercise,  $VO_2$  max (ml/min/kg) was  $95.8 \pm 1.0$  in AT;  $87.7 \pm 1.7$  in NAT ( $p < 0.05$ );  $72.5 \pm 1.2$  in NAS ( $p < 0.05$ ) and  $74.2 \pm 1.4$  in AS ( $p < 0.05$  AS vs NAS). A similar distribution of  $VO_2$  max values occurred in hypoxic exercise. ET prevented the decrease in  $H_{r,max}$  and helped maintain  $Q_{max}$  after acclimatization:  $Q_{max}$  was similar in AT and NAT, intermediate in NAS, and lowest in AS. The preservation of  $Q_{max}$  of AT, coupled with higher arterial blood content ( $CaO_2$ ), resulted in AT having the highest rate of convective blood O<sub>2</sub> delivery ( $TO_2$  max =  $Q_{max} \cdot CaO_2$ ) and contributed to the elevated  $VO_2$  max of this group. In conclusion, the results indicate that attenuation of  $\beta$ -AR downregulation by ET contributes to preserve  $Q_{max}$  and  $VO_2$  max after acclimatization, suggesting that  $\beta$ -AR downregulation plays an important role in limiting  $VO_2$  max after acclimatization.

### 63. EXERCISE PERFORMANCE OF BOLIVIAN AYMARA IN 3 CONDITIONS: AT LA PAZ 3510 M, BREATHING A HYPOXIC MIXTURE SIMULATING CHACALTAYA AND AT CHACALTAYA 5200 M

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The work capacity of 17 male Aymara natives of La Paz, was evaluated and compared under three conditions: (LP) La Paz 3510 m,  $PB = 495$  Torr,  $PI_{O_2} = 94$  Torr. (SC) Simulating Chacaltaya in IPPA's glass chamber, with a  $PI_{O_2} = 74$  Torr and (CH) in Chacaltaya's Glass Pyramid Laboratory, at 5200 m  $PB = 398$  Torr and  $PI_{O_2} = 74$  Torr. ECG,  $V_E$ ,  $PEO_2$ ,  $P_ECO_2$ ,  $SaO_2$  were measured on-line in a computerized system that calculated  $VO_2$ ,  $VCO_2$  and RQ. Software performed automatic calibration. Data analyses at rest (R) and maximum exercise (E) indicate that:

| R  | $VO_2$ L/min | $VCO_2$ L/min | RQ   | $SaO_2$ % | Pulse /min |      |      |     |      |      |
|----|--------------|---------------|------|-----------|------------|------|------|-----|------|------|
| LP | 0.46         | 0.12          | 1.07 | 0.14      | 90.4       | 1.7  | 72.5 | 6.0 |      |      |
| SC | 0.37         | 0.20          | 0.51 | 0.17      | 1.35       | 0.31 | 84.4 | 3.4 | 84.9 | 13.7 |
| CH | 0.17         | .08           | 0.22 | .07       | 1.25       | 0.15 | 82.1 | 5.0 | 92.0 | 11.4 |

| E  | $VO_2$ L/min | $VCO_2$ L/min | RQ   | $SaO_2$ % | Pulse /min |      |      |     |       |      |
|----|--------------|---------------|------|-----------|------------|------|------|-----|-------|------|
| LP | 3.76         | 0.50          | 4.29 | 0.71      | 1.14       | 0.15 | 86.5 | 1.8 | 142.3 | 11.9 |
| SC | 3.16         | 0.68          | 4.29 | 0.53      | 1.35       | 0.33 | 76.2 | 3.3 | 151.2 | 13.9 |
| CH | 1.37         | 0.49          | 1.83 | 0.27      | 1.33       | 0.17 | 76.2 | 6.1 | 152.4 | 11.5 |

In conclusion, although  $SaO_2$  levels were the same between SC and CH,  $VO_2$  and  $VCO_2$  were significantly lower ( $p < .0001$ ) than the LP in the CH and not so in the SC group. Work capacity was the same during the 3 different conditions. Simulated altitude laboratory studies are not completely similar to the real altitude environments.

### 62. EXERCISE PERFORMANCE IN A WOMAN WITH CMS, FOLLOWING TRIPLE HYPOXIA SYNDROME TREATMENT

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MG, a 69 year old female patient resident of Oruro (3800 m), complained of shortness of breath, chest pain, one leg edema, cough and blood streaked sputum. She had been diagnosed elsewhere of hypertension and was on anti-hypertensives, digitalis and diuretics. Her condition worsened over one month. Laboratory tests revealed a hematocrit of 75% and 8.5 million/mm<sup>3</sup> red blood cells,  $PaO_2 = 35$  Torr and  $SaO_2 = 68$  %. She was diagnosed as suffering from Triple Hypoxia Syndrome secondary to pulmonary embolism. Treated as an outpatient, she was discontinued of previous medication, and given treatment for pulmonary embolism. One week later, she improved and returned to the 2<sup>nd</sup> hypoxia (CMS) and had a hematocrit of 69 %,  $PaO_2 = 49$  Torr and a  $SaO_2 = 84$  %. A stress test revealed that she was able to perform sub-maximally 4 levels (sedentary females reach level 5) and was stopped as a precautionary measure.  $SaO_2$  descended to 76% in 2<sup>nd</sup> stage but later increased to 80% in 4<sup>th</sup> stage of exercise. Ventilation was not different from normal but heart rate was significantly higher, going from 84 at rest to 160 bpm at the end of exercise.  $VO_2$  and  $VCO_2$  were also lower during all stages of exercise when compared to normal females. In conclusion, following the triple hypoxia syndrome secondary to pulmonary embolism, she recovered and returned to her normal life, and although she suffers from CMS with a hematocrit of 69% is able to perform even sub-maximal exercise uneventfully. This is further proof of the concept of considering CMS an adaptation to disease at high altitude.

### 64. BOLIVIAN AYMARA THAT PLAYED SOCCER AT 6542 M. MAINTAIN HIGHER OXYGEN SATURATION AND LOWER OXYGEN UPTAKE DURING MAXIMAL EXERCISE

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Maximal oxygen uptake ( $VO_2$ max) was determined on a treadmill in 2 groups at 3510 m,  $PB = 495$  Torr, in chronic hypoxia. The Sajama Group (SG) were 7 healthy male mountain guides, Aymara natives (Age:  $32.2 \pm 5.7$ ) born and living in the Sajama village at 4200 m. The La Paz group (LP) were 17 healthy Aymara male natives (Age:  $21.3 \pm 6.5$ ) of the Bolivian army, born and living in La Paz (3500 m). Hematocrits and weights were not significantly different. ECG,  $V_E$ ,  $PEO_2$ ,  $P_ECO_2$ ,  $SaO_2$  were measured on-line in a computerized system that calculated  $VO_2$ ,  $VCO_2$  and RQ. The results show that the SG maintained the resting level  $SaO_2$  during the first 3 stages of exercise (90.0% TO 89.3%), whereas in the LP,  $SaO_2$  progressively dropped. Furthermore, the SG has significantly lower oxygen consumption and carbon dioxide production than the LP at every stage ( $p < 0.0001$ ). The SG ascended in 7 hours from 4300 m to 6542 m, prepared the soccer field, played 40 minutes intensely and returned to celebrate to the Sajama Village, all in 16 hours. In conclusion, the Sajama Group maintains a level of saturation equal to the value at rest during the initial stages of exercise and also consumes significantly much less oxygen than the La Paz control group. This remarkable work capacity at extreme altitude with complete cardio-pulmonary, metabolic, genetic and phenotypic adaptation, made possible their extraordinary performance of soccer at 6542 m on the plateau summit of the Sajama Mountain, the highest in Bolivia. [NOTE: the video of the actual game will be projected at the meeting.]

**65. EXERCISE PERFORMANCE IN CHRONIC MOUNTAIN SICKNESS (CMS) PATIENTS AT 3510 M**

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Work capacity was evaluated in 5 CMS male patients with cardiac and pulmonary disease of different etiopathogenesis, but adapted to chronic hypoxia. They had increased polycythemia (Ht = 69.2 % ± 5.9) and were compared to exercise results of 17 normal N (Ht = 50 % ± 2.1). The SaO<sub>2</sub> response during the exercise was evaluated in our laboratory at 3510 m. ECG, V<sub>E</sub>, PEO<sub>2</sub>, P<sub>E</sub>CO<sub>2</sub>, SaO<sub>2</sub> were measured on-line in a computerized system that calculated VO<sub>2</sub>, VCO<sub>2</sub> and RQ. They all were able to reach maximum exercise comparable to normal. Results for rest (R) and maximum exercise (E) were as follows:

| R   | SaO <sub>2</sub> % | Pulse /min | VE L/min  |
|-----|--------------------|------------|-----------|
| N   | 90.4 1.7           | 72.5 6.0   | 9.54 1.8  |
| CMS | 85.6 1.8           | 73.4 11.5  | 6.69 1.4  |
| E   | SaO <sub>2</sub> % | Pulse /min | VE L/min  |
| N   | 86.5 1.7           | 142.3 11.9 | 61.9 10.1 |
| CMS | 80.6 1.8           | 133.3 29.4 | 54.3 12.2 |

The resting SaO<sub>2</sub> in these patients was lower than normal (p <0.001) and decreased from 85.6 to 80.6% at maximum exercise. Ventilation and pulse were not significantly different from normal. The results in moderate cases of CMS look like those of a normal subject, living at a much higher altitude. The VO<sub>2</sub>max, VCO<sub>2</sub> max, studied in one case were similar to normal. The work capacity remains unchanged traducing that the oxygen transport mechanism is effective even in increased polycythemia with low arterial oxygen tension. Adaptation of stable CMS patients at high altitude is thus confirmed, once more.

**67. MEASUREMENT OF CIRCULATORY TIME USING PULSE OXIMETRY DURING BREATH HOLDING IN CHRONIC HYPOXIA**

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Pulse oximetry during breath holding (BH) in normal residents at high altitude (3510 m) gives a characteristic graph.

Following a deep inspiration to total lung capacity (TLC) and subsequent breath holding, at around 18 seconds, a descent of saturation (SaO<sub>2</sub>), is observed. This down pointed peak, prior to the elevation of SaO<sub>2</sub> to sea level values, as previously described, corresponds to the blood circulation time from the alveoli to the finger where the pulse oximeter probe is placed. Such a simple maneuver corroborates the measurement of circulation time by other methods.

This independent phenomenon is even observed when the subject breathes 100% oxygen. (PIO<sub>2</sub> = 403 mmHg for a barometric pressure of 495 mmHg). BH time is, as expected, prolonged under these circumstances.

The possible explanation is as follows: Once BH is initiated, there is no renewal of alveolar air. Oxygen consumption, due to inspiratory muscles contraction work, is seen as a descent of SaO<sub>2</sub>. However, since oxygen incoming from the TLC inspiration arrives, saturation begins to rise. This corresponds to the vertex of the graph formed by the descent and subsequent rise of the SaO<sub>2</sub> detected by the pulse oximetry. Thus the time delay of blood circulation from the pulmonary alveoli to the finger is measured.

This phenomenon is observed at different levels of inspiratory oxygen pressure in the lungs traduced by the percentage of saturation, in both natives and normal residents at this altitude.

**66. BREATH HOLDING AND PULSE OXIMETRY AS A DIAGNOSTIC TOOL AT HIGH ALTITUDE**

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Since the time of Haldane, Douglas and Fitzgerald (1913), when they used a tube and a simple gas analyzer to study the changes in alveolar concentration of CO<sub>2</sub> and O<sub>2</sub> during breath holding (BH), modern technology makes this a simple but very effective method of studying several additional aspects of respiratory physiology. Now with pulse oximetry together with fast O<sub>2</sub> and CO<sub>2</sub> analyzers along with the adequate software, a computer shows the changes on-line during breath holding. This procedure can be used to diagnose pulmonary and circulatory disease at high altitude. Breath holding, a simple maneuver, can be studied at different altitudes and during different functional states, and oxygen concentrations.

The computer graphs, allow us to: 1) evaluate pulmonary diffusion. 2) measure circulation time of blood from the alveoli to the fingers. 3) differentiate the normal SaO<sub>2</sub> in natives and residents from low SaO<sub>2</sub> in heart and pulmonary disease as for example in chronic mountain sickness. 4) detect pulmonary shunts breathing 100 % oxygen prior to BH. 5) observe chronic hypercapnia in end tidal CO<sub>2</sub>.

Finally, we think that in the future, unpredictable approaches to other aspects of pulmonary function will surface with the use of this technique.

**68. LACTATE DEHYDROGENASE CHANGES IN DIFFERENT TISSUES IN A CHRONICAL HYPOXIA ADAPTED RAT STRAIN**

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We have previously shown that the maximal anaerobic power of highlander-bolivian children is more affected by their nutrition status rather than by altitude.

To further link these observations to molecular measurements, lactate dehydrogenase (LDH) was studied in an animal model (Sprague Dawley rat strain) adapted to chronic hypoxia in La Paz (Bolivia, 3700 m, PB = 490 mmHg). This strain food intakes are naturally 30 % reduced compared to "normoxic" animals.

Then, two controls groups of low altitude-living rats were performed: one free fed (*ad libitum*) and another (pair-fed) nourished with the food intakes measured for the hypoxic group. The body weight growth curves were similar for both hypoxic and pair-fed groups. These observation remain unexplained although IGF-1 receptor mRNA levels exhibits variations. In white muscle, and right and left hearts, LDH specific activities drop dramatically in the pair-fed group compared to *ad libitum* one. This decreased which is partially compensated in chronic hypoxia conditions and this modifications cannot be explained by changes in the LDH isoenzyme patterns. This data support that anaerobic metabolism variations observed in altitude result in a confrontation of two mechanisms: hypoxia and reduced food intake.

**69. PERUVIAN CONTRIBUTION TO THE STUDY ON HUMAN REPRODUCTION AT HIGH ALTITUDE: FROM THE CHRONICLES OF THE SPANIARD CONQUEST OF PERU UP TO DATE**

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The chronicles show that infertility may be possible by acute exposure to altitude, but it is not presented in all members of a species and it is from short duration. However, fertility in natives at high altitude was normal. Neonatal survival rate in offspring from newcomers at high altitude was reduced. Father Cobo (Century XVII) refers a relationship between magnitude of admixture between Spaniards and natives and rate of neonatal survival at altitude. Offspring from natives survive more than Spanish offspring or half-breed born in these lands. Father Acosta in 1590 and thereafter, Father Cobo in 1653 were the first that claimed the thin air as cause of symptoms of acute mountain sickness. Scientific studies related to the effect of high altitude on reproduction began on the decade of the forties in the last century. These studies demonstrated that acute exposure to high altitude resulted in infertility, but this was transient. Although many authors have suggested that high altitude hypoxia acts as a stress that reduces fertility in both, animal and human populations, data revealed that altitude may affect fertility during acute exposure to high altitude. In natives at high altitude evidences demonstrate the opposite situation. Own studies performed in women at Cerro de Pasco (4340 m) concluded that reproductive efficiency was higher at high altitude than at sea level. The increased efficiency occurred, in spite of a delayed menarche and an earlier age at menopause. The high overall fecundity rate observed at high altitude might be due to a very short between births interval. Lactational amenorrhoea method is more frequently used at altitude than at coast or jungle. However, breastfeeding does not seem to be an efficient contraceptive factor at high altitudes. This seems to be an effect of low serum prolactin concentration observed in women at high altitude. The incidence of newborns at pre-term was 12% at high altitude and 4% at sea level. Demographic data from the National Institute of Statistics in Peru (2000) show that neonatal and post-neonatal mortality rates were higher at altitude places than in the coast or jungle. This situation is observed independent of prenatal care. Actually, Perinatal mortality rate is still higher at altitude places than at the coast or jungle of Peru (INEL, 2000). Stillbirth rates (51.52 per 1000) and Neonatal Mortality Rates (39.39 per 1000 newborn) of migrants living in Puno (3800 m) were higher than those observed in urban or rural natives from Puno. These data suggest that population with longest antiquity in Puno (3800) have more probability to survive in such environment. Controlling socioeconomic effect, Infant Mortality rate was higher at moderate and high altitude than at low altitudes. In conclusion, high perinatal and neonatal rates are still observed in these places in the Century XXI, five centuries after the Spaniard Conquest. These data may suggest that altitude has at this time more negative influence than before conquest on newborns increasing risk of death. It is probably that admixture with Spaniard gene had affect adaptation process at high altitude.

**71. RESPUESTA AL ESTIMULO ANDROGENICO DE LAS GLANDULAS COAGULANTES EN RATAS EXPUESTAS A LA ALTURA (MOROCOCHA 4,540 m)**

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Las glándulas coagulantes de la rata al igual que la vesícula seminal en el hombre producen fructosa bajo estímulo androgénico. En trabajos previos hemos reportado que la exposición aguda a la altura, tanto en ratas como en humanos produce un aumento de testosterona sérica. El presente trabajo se realizó con el objeto de conocer si las glándulas coagulantes de ratas expuestas a la altura responden al estímulo androgénico de forma similar que al nivel del mar. 50 ratas macho nacidas en Lima(150m) fueron llevadas a Morococha (4,540 m) y divididas en dos grupos: 25 sin tratamiento y 25 recibieron Sulpiride (Dogmatil-Spedrog) a fin de disminuir los valores de testosterona sérica. 50 ratas fueron trabajadas en Lima (control) en grupos similares. Se analizó testosterona por RIA y fructosa por el método de Roe modificado por Foreman. Los resultados indicaron que en la altura la respuesta al estímulo androgénico es la misma que al nivel del mar.

**70. ADRENOPAUSE OR DECLINE OF SERUM ADRENAL ANDROGENS WITH AGES IN WOMEN AT SEA LEVEL AND AT HIGH ALTITUDE**

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The present study aimed to determine adrenopause or reduction of serum adrenal androgens with age at high altitude and at sea level. This is a cross-sectional study performed in 210 women residents at high altitude (4340 m) and 123 women living in Lima (150 m) aged 20–70 years. Fasting early morning blood samples were obtained. Serum dehydroepiandrosterone (DHEA), DHEA sulphate (DHEAS), androstenedione (A), testosterone and estradiol were measured by radioimmunoassay. Serum testosterone concentrations were higher in women living at high altitude than in those living at sea level. Serum concentrations of DHEA, DHEAS and androstenedione (A) were lower in women living at high altitude than at sea level. The DHEAS/DHEA ratio was significantly higher, whereas A/T ratio was lower in samples from women living at high altitude than at sea level. Since 50 years of age, a higher decline in serum levels of DHEA was observed in women living at high altitude than in those at sea level. At 60–70 years of age, serum levels of DHEA at high altitude were 46.9% of values in women of the same age at sea level. Decay of DHEAS at sea level and at high altitude occurred since 40 years of age. Decline was faster at high altitude than at sea level. At 60–70 years, serum values of DHEAS at high altitude were 56% of the value at sea level. Serum levels of A at 60–70 years in high altitude natives was 27.34% of the value at sea level. At sea level, serum testosterone levels did not change with age from 20 to 70 years. At 20–39 years and 50–59 years, serum T levels were higher at high altitude than at sea level ( $P < 0.05$ ). At 60–70 years, serum T levels were similar in women living at sea level compared to those living at high altitude. At sea level and at high altitude, serum testosterone/estradiol ratio increased with age ( $P < 0.0034$ ,  $P < 0.0001$ , respectively). This ratio increased early at high altitude (40–49 years) than at sea level (50–59 years). Multivariate analysis showed that altitude ( $P < 0.0001$ ) and higher chronological age ( $P < 0.001$ ) were associated to lower serum DHEAS levels. DHEAS was related to chronological age ( $P < 0.0001$ ). Low serum androstenedione levels were related to high altitude at birth and higher chronological age ( $P < 0.0001$ ). In conclusion Adrenopause is attained earlier and of major magnitude at high altitude than at sea level.

**72. IMPAIRED CIRCADIAN SYNCHRONISATION AND RESPONSE OF THE BIOLOGICAL CLOCK TO LIGHT IN ADULT RATS AFTER PRENATAL HYPOXIA**

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Prenatal hypoxia (PNH) is associated with numerous situations and induces long lasting consequences. Our hypothesis was that PNH leads to consistent changes of the circadian rhythm of activity and its entrainment by light. Pregnant female rats were placed in an hypoxic chamber from gestational day 5 until delivery. Adult PNH rats had significant alterations in their circadian rhythm of locomotor activity (freely accessible running wheels). Under 12/12 light-dark (LD) cycle they show a phase advance (88 minutes vs. controls) of the onset of activity and they were far less active than controls. After an abrupt 6-hours delay in the LD cycle, PNH rats needed more time to resynchronize their activity ( $9.2 \pm 0.5$  days) compared to controls ( $6.0 \pm 1.5$  days,  $p < 0.05$ ). In constant darkness the response of the circadian clock to a light pulse 3 hours after activity onset was reduced in PNH rats. Prenatal hypoxia produces long lasting consequences on the functional output of the biological clock. Since classic syndromes of depression are also associated with alterations of the biological clock the present results may be relevant to human health.

### 73. SHORT-TERM MOUNTAIN LIVING IMPROVES GLUCOSE TOLERANCE

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Previous *in vitro* study has shown that acute hypoxia could induce an increase in membrane permeability to glucose across plasma membrane in skeletal muscle. The current study was to investigate the effect of high-altitude mountain living on glucose tolerance (as an indicator of diabetes development). The effect of mountain hiking activity on glucose tolerance was also determined in this study. A significantly impaired glucose tolerance but normal fasting glucose level was observed in the subjects with the BMI value equal or greater than 25. Three-day mountain living (altitude approximately 2400 meters) without exercise significantly improved glucose tolerance of the subjects, including those high BMI individuals. Moreover, hiking in a relatively flat plateau area caused a better improving effect on glucose tolerance, in compared with hiking in the mountain containing many hills in a comparable altitude. Although three days of mountain living did not significantly alter BMI and fasting glucose level of the subjects, we have found that living in altitude for three days could significantly improve glucose tolerance. Furthermore, the effect of hiking on improving glucose tolerance appears to be influenced by the geographic environment.

### 75. MECHANISMS OF DEVELOPMENT AND CORRECTION OF HYPOXIA IN DIABETIC PATIENTS

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Carbohydrates and oxygen participate in main energy processes, therefore between their exchanges there is close interrelation. We inspected 70 patients with different degree of insulin insufficiency (1983, 1988). First of all we established that the regulation of the level of blood glucose may depend on ecological factors. In patients with diabetes, marked changes in coagulability and viscosity of blood, activation of free-radical processes, lowering of arteriovenous difference and percentage of consumption oxygen by tissues, development of metabolic acidosis, a shift of the oxyhemoglobin dissociation of curve to the left, derivation of glycosilated hemoglobin, disturbances of microcirculation were all observed. Transition of patients with insulin dependent diabetes to mountains during 3 weeks at height 2100 m, 7–10 days of adaptation with short-term rises up to heights of 3700 m resulted in an increase of insulin production (by 73 %) and C-peptide, decrease of glycemia (by 68 %) and amounts of glycosilated protein, rise in antihypoxic and antistressful reserves, buffer capacity of blood, amount of insulin receptors on erythrocytes and leucocytes (at lowering of medical doses of antidiabetic drugs). Our experience yields the basis to consider the mountain climate beneficial climatotherapy for patients, first of all with prediabetic status and insulin dependent diabetes.

### 74. EFFECTS OF ACUTE EXPOSURE AT 3000 M ON CORTISOL AND CATHECOLAMINES IN TYPE 1 DIABETIC PATIENTS AT REST AND DURING EXERCISE

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6 uncomplicated type 1 diabetic patients (T1D), and 7 normal adults (N), were investigated at sea level and after an overnight stay at 2950 m. Blood glucose, lactate, and cortisol were assessed in fasting condition, before (I), immediately (II), 5' (III) and 15' (IV) after exercise. Urinary catecholamines were assessed overnight and before and after the exercise. At altitude, plasma cortisol (mcg/dl) was significantly higher than at sea level after exercise, both in T1D (II:  $21.3 \pm 4.2$  vs  $12.8 \pm 4.1$ ,  $p < 0.04$ ; III:  $22.8 \pm 2.2$  vs  $15.6 \pm 5.3$ ,  $p < 0.04$ ; IV:  $25.0 \pm 2.6$  vs  $16.1 \pm 5.6$ ,  $p < 0.03$ ) and N (II:  $20.6 \pm 7.5$  vs  $11.6 \pm 4.2$ ,  $p < 0.04$ ; III:  $24.3 \pm 8.3$  vs  $13.6 \pm 4.9$ ,  $p < 0.01$ ; IV:  $22.1 \pm 6.9$  vs  $15.1 \pm 4.7$ ,  $p < 0.01$ ), whereas catecholamines were in the normal range, both at sea level and at altitude. No significant variations in blood glucose and lactate were observed. Even at 3000m, exercise increases plasma cortisol more than at sea level. T1D patients should frequently monitor their blood sugar during exercise at moderate altitude.

### 76. SENSIBILIDAD A LA INSULINA EN ALTURA Y A NIVEL DEL MAR

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Se ha demostrado que la altura incrementa el metabolismo de la glucosa; los sujetos de altura (SA) usarían con mayor avidez la glucosa periférica con relación a los sujetos de nivel del mar (SNM), lo cual indicaría que la sensibilidad a la insulina de los tejidos es mayor en SA que en SNM; que explicaría la menor glicemia en SA.

Se utiliza el clamp euglicémico hiperinsulinémico. Se estudiaron 10 SNM varones de Lima y 19 SA varones de Huancayo, entre 20 y 30 años, con un IMC de 20–25 Kg/m<sup>2</sup>.

Los resultados muestran glicemia menor en SA con relación a SNM, con un promedio de  $52.68 \pm 9.63$  vs.  $60.37 \pm 7.37$  mg./dl. ( $p < 0.05$ ). Los SA tuvieron mayor consumo de glucosa que los SNM expresado en mg/kg/min. En conclusión, la glucemia en SA es menor que en SNM; con un consumo de glucosa mayor en SA. Agradecimiento a la Fundación Alexander von Humboldt y Universidad de San Marcos.

### 77. CONTINUOUS BLOOD GLUCOSE MONITORING AT MILD HIGH ALTITUDE

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It is known that the high altitude dweller (HAD) has a lower basal glycemia than the sea level dweller (SLD) . We demonstrated that HAD Cusco ( 3400 m) has a higher glucose uptake than SLD Lima (150 m) . We studied 20 healthy males , 10 SLD Lima and 10 HAD Huancayo (3250 m),  $24.4 \pm 1.8$  ;  $22.2 \pm 3.2$  years and  $BMI 22.8 \pm 1.2$  ;  $22.9 \pm 2.6$  kg/m<sup>2</sup> (mean  $\pm$  S.D) . Glucosensor Unitec Ulm used for continuous glucose monitoring. HAD showed a lower glycemia during all the 12 hours monitoring  $52.4 \pm 6.8$  mg/dl (mean  $\pm$  SD) than by SLD  $73.0 \pm 12.6$  mg/dl ( $p < 0.001$  ). Triglycerides were higher in HAD. HAD has a lower glycemc level and a higher triglycerides concentration than SLD . This work was supported by Alexander von Humboldt-Foundation and Fundación Instituto Hipólito Unánue.

### 79. EQUIPMENT FOR PARTIAL OXYGEN PRESSURE MEASUREMENT DURING INTERMITTENT HYPOXIC TRAINING (IHT)

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IHT has become popular in Russia and Ukraine, and special devices have been developed for its administration. One of the most important aspects of such devices is accurate and dependable measurement of oxygen partial pressure in expired air while transcutaneously measuring oxygen partial pressure (PO<sub>2</sub>) in arterial blood. Two novel elements of this work are (1) the application of pulse methods of oxygen sensor polarization in the technology for optimal PO<sub>2</sub> sensor design and (2) improvement of processing output signals to improve the metrological characteristics. Application of this novel polarization method causes minimal sensor influence on the steady-state processes in biological objects, thus increasing the measurement accuracy and ensuring prompt reaction of the device to changes in external factors. Owing to high operation speed, the device can be used for measuring lung ventilation parameters and blood vessel response to irritation. In using pulse polarization techniques, an optimal device design, device-manufacturing technology, and a relevant mathematical processing of measurement results is selected. The apparatus has the potential to be widely used in many areas of experimental and clinical medicine that require PO<sub>2</sub> values.

### 78. MOUNTAIN RESCUE IN SLOVENIAN ALPS—A RETROSPECTIVE STUDY IN YEARS 1995–2001

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Mountain Rescue Association of Slovenia (GRS Slovenija) has almost 90 years of experience of organized rescue work, though, it was differently organized in its lifetime. Its service improved a lot by the use of helicopter and by the direct access of medical staff (doctor) to the accident scene. Doctors are trained in emergency medicine as well as in climbing and alpine technique and are skilled to quickly help the patient at the site of accident, especially when brought there by a helicopter.

Our presentation is trying to make a brief analysis of the past work in mountain rescue in Slovenia, aiming especially toward analysis of benefits of helicopter versus classical rescue techniques, emphasizing advantages of short response time and presence and action of doctors at the scene. The data may be used as supporting-point for future organisation.

### 80. SHORT INTERMITTENT EXPOSURE TO SIMULATED ALTITUDE INDUCES ERYTHROPOIESIS IN RATS

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In order to delve deeper into the study of the basic mechanisms of adaptive responses during intermittent periods of hypoxia previously described in humans by our group, we have applied different protocols to laboratory rats. Three protocols of different duration (days) and exposure (hours) at a simulated altitude of 5000m were compared. Protocol A had 25 days of duration with an exposure of 33 hours on alternate days. Protocol B was 5 consecutive days with 25 hours of exposure, and protocol C had 10 hours of exposure in one day. Protocol A showed a significant increase ( $p < 0.05$ ) in packed cell volume at the 12th day (18 hours of exposure), hemoglobin concentration at 15th day (21 hours), reticulocyte count at 9th day (15 hours) and 2,3-BPG at 3rd day (9 hours). Protocol B showed a significant increase ( $p < 0.05$ ) in packed cell volume at the 5th day (25 hours), hemoglobin concentration at 5th day (25 hours), and reticulocyte count at 5th day (25 hours) and 2,3-BPG at 3rd day (9 hours). Protocol C did not show significant increases in these values. We conclude that the results we found in humans were reproduced in rats, thus allowing a useful animal model for intermittent simulated altitude studies. The two first protocols of intermittent exposure to hypobaric hypoxia were effective to induce haematological changes. Protocol B shows to be the most efficient per day of exposure, and protocol A shows to be the most efficient per hours of exposure.

**81. EFFECT OF REPETITIVE HYPERCAPNIC HYPOXIA (HHx) ON BP, HR AND [Hb] IN RATS**

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Twenty-four male S-D rats were divided into 4 groups: controls, 3 weeks, 4 weeks and 5 weeks exposure group. With the use of a timed solenoid valve, a mixture of CO<sub>2</sub> and N<sub>2</sub> was flushed into the chamber for 1 min, reducing FIO<sub>2</sub> to 7% and raising FICO<sub>2</sub> to 8%; then air was flushed allowing return of gas fractions to ambient levels for 3 min. Each cycle was repeated for 6 h/day. In all groups, HHx decreased Pao<sub>2</sub> to 44–46 and increased Paco<sub>2</sub> to 48–49 Torr. There was no difference in baseline BP, HR and [Hb]. among groups. However, BP increased and HR decreased during HHx, and the magnitude of the changes was highest in the 5 weeks group. [Hb] increased transiently during HHx in the exposure groups. In conclusion, this level of repetitive HHx does not produce hypertension and polycythemia but induces acute BP elevation, bradycardia and a transient increase in [Hb], which is dependent on the exposure period.

**83. EFFECT OF CHRONIC INTERMITTENT HYPOBARIC HYPOXIA ON THE BETA ADRENERGIC RECEPTOR-ADENYLATE CYCLASE SYSTEM IN RAT HEART**

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The study purpose was to determine the effect of chronic intermittent hypobaric hypoxia (CIHH) on alterations in the beta-adrenergic receptor-adenylate cyclase system. Wistar rats were exposed to CIHH in alternating periods of hypoxia (Hx) and normoxia (Nx) in a hypobaric chamber (428 torr; 4,600 m) in shift of 4 days Hx/2 days Nx (HI1) and 4 days Hx/4 days Nx (HI2) during 4 months. Rats staying at Nx and chronic hypoxia (CR) were used as control. Beta-receptor binding properties were measured with [<sup>125</sup>I] iodocyanopindolol and adenylyl cyclase activity (ACC) by radioimmunoassay. The CIHH caused no changes in beta-receptor Bmax and Kd in the two different shifts compared to Normoxic control. The ACC decreased during stimulation with isoproterenol 10<sup>-5</sup> M (HI1:17.9, HI2:17.2, CR: 13.3, Nx: 59.15; p<0,01 hypoxia vs normoxia). These results do not show the induction of down regulation of beta adrenergic cardiac receptor exposed to HHCI as observed in rats exposed to CR. However the hypoxia causes a strong decrease of normal response of signal-transducing system compared to normoxia (sea level). Grant Apertus 2000 Laboratorios Andromaco

**82. MECHANISMS OF TISSUE HYPOXIA DEVELOPMENT UNDER INTERMITTENT HYPOXIA TRAINING**

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Experimental studies were performed to investigate the mechanisms of intermittent hypoxic training (IHT). The IHT protocol provided for a daily 5-hour stay of rats in a barochamber at imitated "altitude" of 5,000 m in the course of 7, 14, or 42 days. On completion of the IHT course, both trained and untrained (control) animals underwent a test with inhaling a gaseous mixture with 7% O<sub>2</sub> for 30 min. It was shown that beginning from day 10–14 of IHT, acute hypoxia caused a lesser decrease of pO<sub>2</sub> in skeletal muscle in the trained compared to the untrained rats; a lower lactate accumulation in liver, brain and heart tissues; a lesser reduction of cytochrome c-oxidase and succinyl dehydrogenase activities in mitochondrial membranes of the liver and brain; as well as a less marked decrease of the membrane Na<sup>+</sup>, K<sup>+</sup> -ATPase activity in the liver and Ca<sup>++</sup>, Mg<sup>++</sup> -ATPase activity in the sarcoplasmic reticulum of skeletal muscle. The IHT protocol led to normalization of free radical processes and correction of antioxidant imbalances in tissues.

**84. INTERMITTENT HYPOBARIC HYPOXIA: AN ALTERNATIVE METHOD TRAINING AT SEA LEVEL TO COMPETE AT ALTITUDE**

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Thirty four juvenile sportsmen, 23 males; 11 ladies; between 14 and 18 years were exposed to intermittent hypobaric hypoxia in a Hypobaric Chamber three hours daily three times per week during one month in Antofagasta city at sea level previous to competing in Oruro at 3600m. in The Trans Andean Games—2001, Bolivia. We used venous blood to evaluate changes in hematological parameters. We did submaximal test by cycle ergometer to 50 and 100 watt to a standard altitude of 4500m., before and after a month of exposure to progressive intermittent hypobaric hypoxia. A test of Cooper was applied to quantify changes in the aerobic capacity at sea level. A slight but significant increase in the blood hemoglobin happened in the ladies who also improved their performance in the test of 12 minutes. The percent of hemoglobin saturation, the perception of the effort according to Borg RPE scale and cardiac double product improved significantly in the load of 100 watt in ladies and males. Symptoms of acute mountain sickness according to Lake Louise Score during the competition in Oruro were: 20.7%; 27.5%; 24.2% and 3.5% days 1, 2, 3 and 4 respectively. The exposure to intermittent hypobaric hypoxia at sea level can be an alternative to improve the acclimatization and the performance to compete in altitude.

### 85. BLOOD PRESSURE IN INTERMITTENT HYPobaric HYPOXIA: A COMPARATIVE CROSS-VIEW AMONG EPIDEMIOLOGICAL AND EXPERIMENTAL RESULTS

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The aim of this study was to have a cross-view of blood pressure behavior of workers and rats undertaking the same exposure condition to intermittent hypobaric hypoxia. During a two year period, 636 spontaneous in-field worker's consultations at a mining settlement over 3800 m were gathered. Forty rats were exposed to a similar shift during 4 months in a hypobaric chamber at 4000 m. Both were compared to a control group. Epidemiological results: High Blood Pressure accounts for an incidence rate of 5.9/1000 and a ratio of 3.1; compared to the control group with an incidence rate of 1.9. Animal model: Systolic High Blood Pressure was present in 100 % of the exposed rats (base $124\pm 8$ ) compared to 0 % in control group. This rise has a peak ( $156\pm 11$ ) at 2 months of exposure and goes down to a close normal value ( $135\pm 7$ ) at 4 months. Incidentally, we appreciated the white collar effect. This comparative cross-view demonstrates that the exposure to intermittent hypobaric hypoxia would have an influence in blood pressure in human beings as well as in rats exposed to it.

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### 87. ACUTE MOUNTAIN SICKNESS, ARTERIAL HYPERTENSION AND HEADACHES AND ASSESSMENT PARAMETERS ASSOCIATION: A LOGISTIC REGRESSION MODEL

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The aim of this study was to search for an association between Acute Mountain Sickness (AMS), Arterial Hypertension (HBP), Headaches and clinical and laboratory parameters, based on the epidemiological study about incidence and disease risk associated with intermittent work at high altitude (over 3,800 m) in workers at a mining settlement. The HBP, AMS, Headaches cases and other diseases and the chosen control group came from the same data base. A logistic regression was performed on these cases and these independent variables: Heart Rate (HR), O<sub>2</sub> Saturation, Systolic Blood Pressure (SBP), and Diastolic Blood Pressure (DBP), at 95% of confidence. High association between AMS and low O<sub>2</sub> saturation, mean  $86.4\pm 0.8$ , (p-value=0.000), was found. High association between HBP and SBP, mean  $159.8\pm 5.6$ , (p=0.005), was found. High association between HBP and DBP, mean  $104.3\pm 3$ , (p<0.001), was found. High association between Headache and HR, mean  $87.5\pm 1.6$ , (p=0.002), was found. These findings, among other future leads, could be a corroboration that the presence of a low O<sub>2</sub> saturation is a sine qua non for appearance of AMS. FONDEF D97 I 1068 UNAP DI-02/2001

### 86. ACUTE MOUNTAIN SICKNESS (AMS) AND HEADACHE EPIDEMIOLOGICAL CHARACTERISTICS IN INTERMITTENT WORK AT HIGH ALTITUDE

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The aim of this study was to obtain the epidemiological characteristics of the illnesses associated with exposure to intermittent work at high altitude (over 3.800 m) in workers at a mining settlement.

During a two year period, 4.403 in-field consultations for these symptoms were analyzed. Lake Louise score was obtained to qualify for AMS and data gathered were simplified by using just a single episode per worker per shift. Headaches were compared with a control group at sea level. AMS represented 3.9% of total consultations, with a rate of 19.3/1000 and an increase during the winter months in both years.

Headache represented 4.6% of total consultations, with a rate of 23.7/1000 and a ratio or excess of consultations of 9.5 fold over the control group. Although AMS appears in this group with an incidence rate lower than previously reported, the higher rates of consultations and the excess consultation for headache, makes headache an outstanding health problem at high altitude. By grant of FONDEF D97 I 1068

### 88. BLOOD RHEOLOGICAL BEHAVIOUR IN RATS AFTER SHORT INTERMITTENT EXPOSURE TO SIMULATED ALTITUDE

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As in humans, the erythrocyte increase is the most significant of the blood adaptive changes induced by intermittent exposure to simulated altitude in rats. Although this response is oriented to increase oxygen transport capacity, the increasing blood viscosity could impair peripheral and respiratory gas exchange function. Using three protocols of different duration (days) and exposure (hours) at a simulated altitude of 5,000m, apparent blood viscosity ( $\eta_a$ ) and plasma viscosity ( $\eta_p$ ) were measured in a cone-plate microviscometer. In addition, plasma protein content and plasma osmolarity were measured and relative blood viscosity ( $\eta_a/\eta_p$ ) was calculated. Our main finding was that blood apparent viscosity, (especially when measured at high shear rates) did not increase substantially along any of the three different protocols, in spite of significant increases in red cell count, haemoglobin concentration and hematocrit. Relative blood viscosity showed a trend to increase, as a result of the higher amount and percentage of RBC in suspension and possibly also due to the rise of immature cells (reticulocytes) with increased internal viscosity and lower deformability than mature erythrocytes. These data are in agreement with those previously obtained in humans submitted to high altitude pre-acclimation programs based on a series of intermittent sessions of exposure to hypobaric hypoxia.

**89. INTERMITTENT EXPOSURE TO HYPOXIA IMPROVES O<sub>2</sub>-TRANSPORT BUT NOT AEROBIC PERFORMANCE**

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Periodic stays at different altitudes are ordinary in many mountainous countries. However, the effects are only rarely investigated. This study was conducted to evaluate whether intermittent exposure to hypoxia has any influence on physical performance at low and high altitude. Methods: We compared two groups of soldiers from the Chilean army at sea level (0m) and at high altitude (3550m): one group lived at 3550m for a period of six months interrupted every 2 weeks by 3 days at 0m (group IH). The other group lived permanently at 0m (group SL). In all subjects a cycle ergometer test was performed at sea level and on the 2<sup>nd</sup> day at altitude. Results: Already at sea level hematocrit was significantly higher in IH than in SL (IH 46.7±2.0%; SL 43.6±2.5%) and increased in both groups at altitude. At altitude arterial pO<sub>2</sub> was elevated in IH under resting and exercise (IH 60.7±4.3 mmHg, SL 54.2±2.9 mmHg) conditions. At both altitudes ventilation during exercise was remarkably higher in IH than in SL leading to lower alveolar and arterial pCO<sub>2</sub>. VO<sub>2</sub>max (ml/kg·min) did not differ between the groups neither at sea level (SL 46.2±5.4, IH 45.1±5.7) nor at altitude (SL 42.4±4.4, IH 42.0±4.2). Conclusion: Despite higher arterial oxygen content the subjects adapted to intermittent hypoxia do not possess a higher aerobic performance either at altitude or at sea level. We assume muscular catabolism due to direct hypoxia or to reduced training effects is the cause.

**90. RESPIRATORY DISEASES IN INTERMITTENT WORK AT HIGH ALTITUDE: EPIDEMIOLOGICAL CHARACTERISTICS**

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The aim was to obtain epidemiological features regarding the vast magnitude of respiratory system consultations, found in the epidemiological study about incidence and disease risk associated with intermittent work at high altitude (over 3.800 m) in workers at a mining settlement. This finding represents 50% of the total consultations. During a two year period, 26,234 in-field consultations for respiratory system were analyzed and compared to a control group at sea level. A rate of 248/1000 and an incidence ratio of 7.7 compared to control group was obtained. The main sub-group distribution was: Upper airway acute infections (58%), Flu (19%) and Lower airway acute infections (16.5%). Chronic respiratory pathologies were not present. Regarding specific pathologies, the main causes were: pharyngitis (24%), flu (19%) and tonsillitis (19%), all of them acute illnesses. An increasing rate during winter months was observed. Nevertheless, the distribution is similar to the control group, while the higher incidence rates and excess of consultations demonstrate a strong association to this kind of exposure and a huge impact regarding labour health. By grant of FONDEF D97 I 1068

**91. INTERMITTENT WORK AT HIGH ALTITUDE: A NEW EPIDEMIOLOGICAL SITUATION**

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The aim of this study was to obtain an overview of incidence and disease risk associated with intermittent work at high altitude (over 3.800 m) in workers at a mining settlement. During a two year period, 91,500 spontaneous in-field consultations were analyzed and compared with a control group at sea level. We found a high rate of 6 consultations by individual/year and a consultation ratio of 3.1 compared to the control group. The main consultation rates/1000 and ratios to control group were: respiratory (248; 7.7), headaches (23.7; 9.5), gastrointestinal (64.2; 4.9), trauma (32; 2.2), ophthalmic (22; 2.9) and AMS (19.3) respectively. A specific and different epidemiological profile for eye, skin and ear illnesses (acute inflammatory processes) were found in the high altitude group compared to control group. It has been possible to produce, through in-field consultations, the expected health demand in terms of magnitude and their type. The epidemiological features of these pathologies depends on altitude and its environmental factors. Therefore, a baseline has been set, regarding the epidemiology of the diseases and syndromes that occur with this type of exposure. By grant of FONDEF D97 I 1068

**92. EYE, SKIN, AND EAR DISEASES IN INTERMITTENT WORKERS AT HIGH ALTITUDE: EPIDEMIOLOGICAL CHARACTERISTICS**

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The aim was to obtain epidemiological characteristics of consultations for the above illnesses, found in the study about incidence and risks associated with intermittent work at high altitude. During two years, 5,164 in-field consultations were analyzed and compared with a control group at sea level. Eye diseases represent 4% of total consultations, with a rate of 22/1000 and a ratio of 2.9 compared to control; the specific distribution is: conjunctivitis (87%) and actinic keratitis (5%). Skin diseases represent 3.7% of the total consultations, with a rate of 18.9/1000 and a ratio of 1.5; the main specific distribution is: dermatitis (58%) and allergic rash (14%). Ear diseases represent 1.5% of total consultations, with a rate of 7.2/1000 and a ratio of 1.7; the main specific distribution is: otitis (67%), epistaxis (20%) and vertiginous syndrome (13%). Despite the fact that only eye diseases show a high associated risk, the finding of specific and different profiles for the three studied organ systems compared to the control group, highlighting acute inflammatory processes, suggests strong association with the exposure and the environmental factors surrounding it. FONDEF D97I1068.



### 93. CONCEPT OF INTERMITTENT HYPOXIC TRAINING (IHT) IN UKRAINE AND RUSSIA

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Being essentially cut off for perhaps sixty years from the global scientific community, Ukrainian and Russian scientists have developed a new concept for the beneficial use of adaptation to artificial intermittent hypoxia in sports and treating many diseases. In the 1930's the following basic methods were utilized: (1) staying at high-mountain camps for several weeks; (2) regular high-altitude flights in planes; (3) training in barometric chambers; and (4) training by inhalation of low oxygen gas mixtures. In the intervening years, the basic mechanisms underlying the beneficial effects of IHT were elaborated mainly in three areas: regulation of respiration, free radical production and mitochondrial respiration. Findings showed that IHT induces increased ventilatory sensitivity to hypoxia as well as other hypoxia-related physiological changes such as increased hematopoiesis, alveolar ventilation and lung diffusion capacity, and alterations in the autonomic nervous system. Due to IHT, the body's antioxidant defenses increase, cellular membranes become more stable, and improvement of O<sub>2</sub> transport in tissues is evident. IHT induces changes within mitochondria, involving NAD-dependent metabolism, which increases the efficiency of oxygen utilization in ATP production. These effects are mediated partly by NO-dependent reactions. The marked individual variability, both in animals and humans, in the response to, and tolerance of, hypoxia is described.

### 95. INTERMITTENT EXPOSURE TO SIMULATED HIGH ALTITUDE INDUCES OXIDATIVE STRESS

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Free radical-mediated oxidative damage may occur in various conditions including hypoxia due to high altitude. In the present work we studied the effect of intermittent exposure to a simulated high altitude of 5,000 m on the parameters related to oxidative stress. Male Sprague-Dawley rats were used and submitted to two different protocols. One group was exposed to 5,000 m during 25 alternate days of exposure, a total of 33 hours in sessions of 3 hours. Samples were obtained after 9, 18, 27 and 33 hours of exposure and a week after the end of acclimation program. The second group was exposed during 5 consecutive days with a total exposure of 25 hours and samples were analysed at the end of this period and after one week of recovery. The variables studied included the activity of the antioxidant enzymes superoxide dismutase (SOD) and catalase (CAT) in erythrocytes and the level of malondialdehyde (MDA), an indicator of lipid peroxidation, in plasma. Results indicated that the exposure of intermittent hypoxia induced, in both protocols, a significant decrease in the enzymatic activity of the antioxidants analysed. Moreover, a significant increase in the plasma MDA level was observed at 33 hours in the long acclimation (of 21 days) ( $p < 0.001$ ) and at 25 h ( $p < 0.05$ ) in the more intense acclimation (5 days) with return to control values after one week of recovery. In conclusion, lipid peroxidation products appear later than the antioxidant enzyme consumption. A supplementation of antioxidant is recommended in hypoxia acclimation. In this way, our preliminary results showed that vitamin E reduces oxidative damage.

### 94. BENEFICIAL EFFECT OF STAYING IN A HYPOXIC ROOM ON HIGH ALTITUDE CLIMBING

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In order to improve an early phase acclimatization to 4000–5000m which is a key to successful high altitude climbing, sleeping and exercise challenge in a hypoxic room just before climbing was designed. Subjects are five mountain climbers of JAC McKinley 1999. They were exposed to hypoxic condition for 24 hours as below. 2000m/1st day, 3000m/2nd day, 4000m/3rd day. (After a week interval), 4000m/4th day, 5000m/5th day and 6000m/6th day. Arterial blood gases, SpO<sub>2</sub> during sleep, hypoxic ventilatory responses and lung diffusion capacity during exercise at 4000m were monitored or examined.

Result: PaO<sub>2</sub> at 4000m had a positive correlation with HVR at 4000m and negative correlation with the degree of HVR depression (difference between HVR-4000m and HVR-sea level). All climbers including the member who had experienced HAPE at 4200m the year before could reach the top of McKinley without troubles. It was suggested that deoxygenation at high altitude was strongly involved with depression of HVR at altitude and that "Sleeping high and Exercise high" just before might have beneficial effect on high altitude climbing.

### 96. RENAL BLOOD VOLUME REGULATION DURING INTERMITTENT EXPOSURE TO HYPOXIA

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Recently we have shown that total red cell mass of sea level residents intermittently exposed to 3550m for 6 months increased to similar values found in altitude residents. Plasma volume (PV) remarkably decreased during every hypoxic period further improving the O<sub>2</sub>-transport capacity. The aim of the present study was to evaluate whether the renal response to intermittent exposure to hypoxia may contribute to these changes in PV. Methods: 15 young soldiers from the Chilean army who lived at 3550m for a period of six months, interrupted every 2 weeks by 3 days at 0m, entered the study. Bio-impedance analyses were performed and blood and urine samples were taken after 2 days at sea level, immediately after arrival (day 1), on day 2, day 4 and day 10 at altitude. Results: Body weight decreased at altitude from 62.0±5.5 kg to 60.9±5.1 kg. This was associated with a loss in total body water by 1.2±0.7 kg and in extra-cellular water (ECW) by 0.7±0.2 kg. Hematocrit increased from 48.0±2.2% to 50.8±2.6% corresponding to a decrease in PV by 290 ml. Urine minute volume increased immediately after arrival at altitude by about 90% and remained elevated, whereas glomerular filtration rate only temporarily increased at day 1 (from 119±27 to 211±64 ml/min). Na<sup>+</sup> excretion increased until day 10 by about 35%, while K<sup>+</sup> excretion slightly decreased. Conclusion: Even after 6 months intermittent exposure to hypoxia, PV and ECW regularly oscillate during a normoxic/hypoxic cycle which is due to changes in renal sodium and water retention.

**97. NEGATIVE FEEDBACK ON EPO PRODUCTION IN CLIMBERS AFTER RETURN FROM A HIGH ALTITUDE EXPEDITION (6813m)**

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The aim of this study was to analyse haematological alterations in climbers studied at low altitude (LA) after exposure to high altitude (HA). 4 subjects (3men and 1 woman), from 38 to 48 years old, were studied at LA (control C), then 10 (D10) and 102 days (D102) after an ascension above 6813m. Blood samples were taken for measurements of haematocrit (Ht), haemoglobin concentration (Hb), red cell count (RCC) and serum erythropoietin concentration (EPO). At D10, Ht, Hb and RCC increased by  $13,0 \pm 2,4$ ,  $13,6 \pm 3,2$ ,  $13,0 \pm 3,2$  % respectively and EPO decreased by  $69,3 \pm 6,0\%$  comparatively to C. (m $\pm$ SD). At D102, all parameters were near to control values. The haematological response induced by HA exposure observed at D10 were associated to a dramatic fall of EPO, disappearing at D102. These data demonstrate an important negative feedback on EPO production, 10 days after return from a high altitude ascension.

**99. MAXIMAL OXYGEN CONSUMPTION (VO<sub>2max</sub>) IN CHILEAN MINERS AT INTERMITTENT HYPOXIA (IH)**

Jiménez D<sup>1</sup>, Vargas M<sup>2</sup>, León T<sup>2</sup>, Cortés G<sup>2</sup>, Osorio J<sup>1</sup>, Richalet JP<sup>3</sup> Collahuasi<sup>1</sup>, Mutual de Seguridad<sup>2</sup>, Université Paris XIII<sup>3</sup>.

A prospective evaluation was performed on 17 workers (ages  $24.8 \pm 4.3$  years) with no previous exposure to altitude, intermittently exposed to 3800–4000 m (7 days a high altitude, 7 days at sea level). The VO<sub>2max</sub> was evaluated at sea level between the second and sixth day, after 0, 12, 19 y 32 months of IH.

| Month                        | Pre-exposure |        | Exposure |        | 31th  |        |       |       |
|------------------------------|--------------|--------|----------|--------|-------|--------|-------|-------|
|                              | 0            | 12th   | 19th     | 31th   |       |        |       |       |
| Workers n:                   | 30           | 17     | 9        | 17     |       |        |       |       |
| Charge, Watts                | 205.3        | 33.3   | 197.7    | 24.29  | 183.3 | 32.5*  | 175.0 | 25.5* |
| VO <sub>2</sub> max (ml/min) | 2599.7       | 2221.4 | 2180.4   | 2083.9 | 173.7 | 12.43* | 175.5 | 13.1* |
| Heart Rate max               | 188.4        | 13.83  | 176.1    | 9.96*  | 175.5 | 13.1*  |       |       |
| Sat O <sub>2</sub> (%)       | 92.3         | 3.3    | 93.4     | 3.2    | 93.7  | 2.57   | 95.6  | 2.75* |

\* p < 0.05 vs Pre-exposure

We conclude that at the end of 31 months of IH the drop in VO<sub>2</sub>max and max heart rate could be due to sedentary work conditions and/or desensibilization of cardiac receptors. The increase of O<sub>2</sub> Sat at maximum exercise could be an indicator of adequate acclimatization. Supported by grant from FONDEF D97I1068 Chile, Arturo Prat University.

**98. OXIDATIVE STRESS INDUCED BY ACUTE HYPOXIA FOLLOWED BY REOXYGENATION IN HEALTHY SUBJECTS**

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After 30 min lung washout, sixteen healthy volunteers (15 women, 1 man, aged 40 to 54 yrs) were exposed to acute hypoxia (12% O<sub>2</sub>, simulated altitude 4,800 m) for 30 min followed by reoxygenation (21% O<sub>2</sub> or 100% O<sub>2</sub>) for 2 hrs. Flow pentane chosen as indicator of lipoperoxidation was measured at T0, T15, T30, T45, T60, T90, T120, T150, T180 and T190 min. Malondialdehyde, activities of superoxide dismutase and glutathion peroxidase were determined simultaneously at T30, T60, T120 and T180. During hypoxia, flow pentane increased 15 min after the start of hypoxia (+33%, p<0,01) and remained at this level until the end of hypoxia for all subjects. During reoxygenation, pentane returned to the basal value 30 min after the end of hypoxia and did not vary until the end of the protocol. Malondialdehyde and enzymatic activities were not significantly different from T30 during all the protocol. These results suggest that acute hypoxia is able to activate oxidative stress which in turn may induce biochemical mechanisms to limit oxygen toxicity during reoxygenation.

**100. ACTIGRAPHY IN ACCLIMATIZED WORKERS IN INTERMITTENT HYPOXYA (IH) AT 4300 M**

Vargas M, Hudson C. Instituto de Salud Pública-Chile

Actigraphy was realized (Sleep Watch Ambulatory-monitoring Inc) during a continuous cycle of 7 days of work at 4300 meters and 7 days of resting at sea level, to 27 workers of Cia Minera Quebrada Blanca. The sleep assessment is through the proposed methodology by RJ Cole and DF Kripke, 1988

| Interval (hrs) | Sea level       | Altitude        | P     |
|----------------|-----------------|-----------------|-------|
| A. 20:00–24:00 | 0.37 $\pm$ 0.53 | 0.81 $\pm$ 0.75 | 0.000 |
| B. 24:00–07:30 | 5.4 $\pm$ 1.7   | 5.03 $\pm$ 0.99 | 0.01  |
| C. 07:30–20:00 | 1.52 $\pm$ 1.61 | 0.08 $\pm$ 0.23 | 0.000 |

In the A interval there is a significant increase in the sleep hours in the altitude, due to the individuals go to bed early; in the interval B and C it is appreciate a significant diminish of the sleep hours in altitude. Interesting is the finding of sleep in altitude during the C interval, coincident with the hourly of the labor journey. We concluded that through actigraphy, that at 4300 meters the average sleep of the 7 nights (5.93 $\pm$ 1.44 hours) is significantly less than the average of 7 nights (7.30 $\pm$ 2.55 horas) at sea level (p<0.001 Newman Keuls). Supported by Grant from Cia Minera Quebrada Blanca-Aur Resources Chile

**101. AUTOPERCEPTION AND LIPIDIC PROFILE IN ACCLIMATIZED WORKERS TO INTERMITTENT HYPOXIA (IH)**

Vargas M<sup>1</sup>, Cortés G, Hudson C, León A, International Centre Altiplanic Studies, Universidad Chile

36 workers, age 40,1 years, weight 78,6kg, height 1.70m from Cia Minera Quebrada Blanca with IH, (5,22 years),.7 days working/sleeping at 4300m commuted by 7 days resting at sea level (SL), are monitored.. Blood samples are taken at SL, 5–6th day, and autoperception of Acute Mountain Sickness (AMS) and sleep quality (Spiegel) at HA, 2<sup>nd</sup> to 6<sup>th</sup> day. There is AMS presence on the second day 23%, dropping to 5% on the 4th. The main symptoms are sleeping and fatigue alterations. The Spiegel indicates that on the 2nd day is the worst quality day because of more awakening and tiring sensation.

|                | % MG  | CHOL  | HDL   | CHOL/HDL | LDL   | VLDL  | TRY   |
|----------------|-------|-------|-------|----------|-------|-------|-------|
| Average        | 24,70 | 212,8 | 52,7  | 4,0      | 128,8 | 31,0  | 229,9 |
| SD             | +5,1  | +45,5 | +10,9 | +0,2     | +28,8 | +10,4 | +27,3 |
| Abnormal limit | ≥25   | ≥240  | <=35  | >4,5     | ≥130  | ≥30   | ≥150  |
| % pathologic   | 52,8% | 29%   | 0%    | 0%       | 46%   | 51%   | 54%   |

This population has a high presence of obesity and dislipidemia (29 and 54%), but the HDL levels are high. Supported by Grant from Cia Minera Quebrada Blanca-Aur Resources-Chile

**103. ARTERIAL HYPERTENSION (Arth) PATTERN IN INTERMITTENT HYPOXIA (IH) TO 3800–4200M**

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42 workers (ages 41±9 years) acclimatized to IH (46,6±19,4 months), working 7 days at 3800–4200m (HA) commuted by 7 days resting at sea level (SL) with Arth figures in the medical control at HA, it is proceed to an Ambulatory Monitoring Blood Pressure (AMBP) in HA and SL. According to consensus VI-JNC, are abnormal >40% of the systolic/diastolic >135/85 in vigil, and >120/75 in the night. All cases without previous antihypertensive treatment.

| Arth Patterns        | Total 43   | Arterial Pressure |                |                |
|----------------------|------------|-------------------|----------------|----------------|
|                      |            | SL                | Vigil-Altitude | Sleep-Altitude |
| SL only              | 1 (2,3%)   | Arth              | Normal         | Normal         |
| SL/HA                | 20 (46,5%) | Arth              | Arth           | Arth           |
| Altitude-Vigil only  | 11 (25,5%) | Normal            | Arth           | Normal         |
| Altitude Vigil/Sleep | 10 (23,2%) | Normal            | Arth           | Arth           |
| Altitude-Sleep only  | 1 (2,3%)   | Normal            | Normal         | Arth           |

Identifications of 5 Arth patterns, where the altitude, hypoxia and the work would be preponderant factors. The patterns 3 and 4 would be associate to labour factors and the hypoxia particularly to 5. The antipertensive treatment must contemplate these findings. We conclude that the AMBP is essential to evaluate Arth in IH . Supported by Grant from Cia Minera Collahuasi-Chile.

**102. HEMATOLOGICAL RESPONSE BY AGE IN INTERMITTENT HYPOXIA (IH) AT TWO ALTITUDES**  
Vargas M, Hudson C, Jiménez D<sup>1</sup> Instituto Salud Pública-Chile. Collahuasi<sup>1</sup>

Acclimatized subjects to IH were study in two mining Companies, Collahuasi at 3800–4200 meters 7x7, n=369, with 39,5±21,7 months in IH and Quebrada Blanca (QB) at 4300 meters, 7x7, n=35, with 68,9±28,3 months in IH. The database were analysis through t-test for independent variables.

| Age Groups    | Hemoglobine grs (Hb) |          | Hematocrit % (Ht) |          |
|---------------|----------------------|----------|-------------------|----------|
|               | 3800-4200            | QB-4300m | 3800-4200         | QB-4300m |
| TOTAL         | 15.5±1.2             | 15.7±1.2 | 46.7±3.5          | 46.9±3.5 |
| 1 20-29 years | 15.2±1.1             | 15.0±1.6 | 45.9±3.4          | 44.5±4.9 |
| 2 30-39       | 15.3±1.2             | 15.7±1.2 | 46.0±3.4          | 46.8±3.5 |
| 3 40-49       | 15.7±1.2*            | 15.8±1.2 | 46.4±3.4*         | 47.2±3.7 |
| 4 50 & more   | 15.8±1.2*            | 16.0±1.0 | 47.2±3.5*         | 47.7±3.1 |

\* p<0.05 respect to group 20-29

In spite the QB subjects are having more IH exposure time and are sleeping 500 meters above Collahuasi, there are not significant differences in the same age group, as regards to Ht and Hb, The age increase significantly the Hb and Ht in Collahuasi. Supported by Grant from Cia Minera Quebrada Blanca-Aur Resources & Collahuasi Mining Co.

**104. SLEEP OXYGEN SATURATION (S-SatO<sub>2</sub>) IN CHILEAN MINERS AT INTERMITTENT HYPOXIA (IH), 2700 M AND 3800 M**

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The study of S-SatO<sub>2</sub> in IH is important in order to establish normality ranges by altitude. A evaluation was performed on 96 acclimatized workers intermittently exposed to 2700 m, 4 days working at altitude, 4 days resting at sea level, SL, and 89 acclimatized to 7 days working at 4200, sleeping at 3800 and 7 days resting at SL . The records were at 2700 and 3800 m with pulse oximetry (Nonin 8500M).

| Workers                | Years at IH | Sleep SatO <sub>2</sub> (%) | Heart rate | Barometric Pressure (mmHg) |
|------------------------|-------------|-----------------------------|------------|----------------------------|
| 4x4, n=96<br>2700 masl | 6.3±5.2     | 91.50±1.65                  | 63.23±7.8  | 547                        |
| 7x7, n=89<br>3800 masl | 3.2±1.6     | 85.27±3.24                  | 72.0±8.1   | 480                        |

To more high altitude there are more dispersion of Sat O<sub>2</sub> data. The normal S-SatO<sub>2</sub> limit at 3800 m could be established 1 SD below the mean. The ranges of normality must be defined by studies associated to polysomnography. Grant form Cia Minera Cerro Colorado-BHP-Billiton Chile, and Cia Minera Collahuasi-Chile.

**105. POLYSOMNOGRAPHY (PSG) IN ACCLIMATIZED WORKERS TO INTERMITTENT HYPOXIA (IH). COMPARISON OF SEA LEVEL (SL), ALTITUDE 3800 M (HA) AND OXYGEN SUPPLEMENTARY EFFECT**

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We performed 3 full PSG to 8 miners (age 28±6years) acclimatized to IH (38±10months) working 7 days at 4200 m, commuted by 7 days resting at SL. They slept in comfortable dormitories at Collahuasi-HA. PSG was performed on the 4<sup>th</sup> night, at HA, SL and HA with oxygen supplementary indoor dormitory (equivalent to simulate 2900 m) using Alices III sleep laboratory.

| Sleep parameters            | At 3800m | At 3800m with O <sub>2</sub> Supplementary | Sleep at SL |
|-----------------------------|----------|--|-------------|
| Arousal                     | 28.7±16  | 18.3±9.9                                   | 10.4±8      |
| Periodic Breathing          | 9.8±14   | 2.5±4                                      | 0           |
| Apneas/Hypopneas/hour       | 10.1±7.6 | 7.9±5.2                                    | 5.8±8.7     |
| % REM time/Total Sleep time | 16.6±4.3 | 18.3±3                                     | 23.1±3.5    |
| Latency to REM              | 116.4min | 90.7min                                    | 65.7min     |
| Oxygen Saturation           | 86.7%    | 90.1%                                      | 96%         |

According SL normal limit our acclimatized workers present pathological sleep pattern at HA by alteration on arousals, periodic breathing, apneas/hypopneas, oxygen saturation and REM time. The oxygen supplementary reduced partially the differences SL/HA. To complete evaluation are required sleep patterns from permanent subjects at the same altitude. Supported by Grant from Cia Minera Collahuasi-Chile

**107. SECRETORY PATTERN OF ERYTHROPOIETIN DURING HYPOXIA IN MICE UNDER TREATMENTS TO KEEP THE ERYTHROCYTE MASS FROM RISING**

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Plasma erythropoietin (pEPO) levels markedly increase in response to hypoxia (Hx) to stimulate erythropoiesis. During sustained hypoxia, pEPO declines before an increase in the blood oxygen carrying capacity is evident. To define the role of the size of the circulating red cell mass on the pattern of pEPO changes during exposure to Hx, we have serially measured pEPO in untreated-control mice and in mice whose hematocrits were kept constant by either phenylhydrazine (PHZ) administration or repeated phlebotomies. Animals were placed for 9 d in a hypobaric chamber in which the air pressure was kept at 556 mbar. Hypoxia-stimulated EPO production was derived from pEPO (ELISA, Medac Diagnostika, FRG). Untreated control mice exhibited a steady rise in hematocrit, which remained practically unchanged in the hypoxic groups that were subjected to regular phlebotomies or PHZ injections. At day 8 of continuous exposure, reticulocytes were 6.72 ± 0.63 % in the former and 43.0 ± 1.34 % in the latter. Hypoxic control mice exhibited a rise in pEPO with two peaks of around 100 mU/ml during days 1-2 and 5-6 of exposure; pEPO was 3-4 times higher in experimental mice. A negative correlation between pEPO and hematocrit was established (Pearson r = -0.7285, r squared 0.5307, p < 0.0001). It is concluded that EPO production under hypoxic conditions is highly influenced by the circulating red cell mass, thus providing evidence for the adaptive role of the hemoglobin mass in non-genetically adapted animals.

**106. EFECTOS DE LA EXPOSICIÓN AGUDA A LA ALTURA SOBRE LA LIPÓLISIS EN TEJIDO ADIPOSITO DE COBAYOS**

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Nuestros objetivos fueron observar el efecto de la hipoxia aguda sobre la movilización y contenido de los depósitos grasos en cobayos a nivel del mar y transportados a la altura y estimar el grado de influencia del tiempo de permanencia en ella. El estudio se realizó en 40 cobayos machos nacidos y criados a nivel del mar (150 m.s.n.m.) con un peso promedio de 450 a 550 g. 32 cobayos fueron transportados a la altura (Morococha 4,540 m.s.n.m.) y fueron sacrificados a las 24 horas (CA); a las 72 horas (1A); a los 7 días (2A); a los 15 días (3A) después de su arribo a la ciudad de Morococha. Se trabajó con un grupo control (CN) a nivel del mar. Las muestras fueron plasma y tejido adiposo del epidídimo, en plasma se determinó glicerol y triglicéridos (métodos SIGMA) expresados en mg/dl; la tasa de lipólisis se midió mediante la producción de glicerol liberado método enzimático. Expresándose la concentración de glicerol por gramo de tejido húmedo por hora. Los valores medios obtenidos en animales sometidos a hipoxia aguda fueron: Glicerol: 24 horas 3.39; 72 horas 3.36; 7 días 2.67; 15 días 1.85; nivel del mar 2.01; todos ellos expresados en mg/dl; la tasa de lipólisis fue: Nivel del mar 3.48; 24 horas 4.62; 72 horas 5.09 todos expresados en nmoles de glicerol liberado/ mg de tejido/1 hora de incubación.

Conclusiones: La disminución de glicerol en plasma y el incremento de la tasa de lipólisis en tejido en la exposición aguda a la altura con respecto a nivel del mar se debería a que se está movilizando la grasa del tejido adiposo como combustible alternativo a la glucosa para ser utilizado por muchos tejidos entre ellos el hígado para proporcionar la mayor parte de ATP necesaria para la gluconeogénesis.

**108. NEURITIC PAIN AFTER HIMALAYAN EXPEDITIONS**

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In the field of mountain medicine, peripheral nerve diseases are only related to trauma or frostbite. However, according to our experience on 18 Himalayan expeditions, nearly 4% of mountaineers taking part in those expeditions suffer from a syndrome consisting of neuropathic pain and/or dysesthesias in both feet which are apparently not related to frostbite or trench foot. Pain is continuous, with lancinating exacerbations which may be very severe. It improves with cold and worsens with warmth and light touch. Patients report a "corky" sensation in their feet. This syndrome is incapacitating in a third of cases. Its etiology is probably multifactorial; the main suspected causes are metabolic alterations, nutritional deficiencies, cold and hypoxia. Pain is usually alleviated by carbamazepine. Prognosis is good, and the disorder evolves to a complete resolution in 5-6 weeks. One of such cases was studied by us but no abnormal results were found. The relationship between the disturbance and the ABC syndrome or erythralgia is discussed. The low reported incidence of this syndrome in the medical literature may be due to a lack of clinical suspicion in the field or to difficulties for further study and evaluation.

### 109. EXPEDITION SUCCESS IN THE SEVENTIES WITH A STRONG TEAM

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An expeditionary group from Manresa, a city of 60,000 inhabitants, carried out eight expeditions in unspoiled spots all around the four continents, including the first expedition of Makalu without oxygen. The team was based on a very young mountaineering group of the city and united by a close and old friendship. The success of their rope teams was based on their feeling of belonging to a group with no leader and where the summit was conquered by the whole team. We present their acclimatization techniques (in a slide of Makalu expedition), which allowed exceptional results in their period from 1969 to 1975.

### 111. POLYGLOBULIA ASSOCIATED WITH HYPERPHAGIA AND INCREASED THERMOGENESIS IN COLD-EXPOSED MICE

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One of the environmental hazards that face animals at high altitude is cold. Cold exposure activates a series of physiological events to ensure survival, notably increased thermogenesis, continuing mobilization of body fat stores that results in weight loss, and hyperphagia. Since the function of hemoglobin is the transport of oxygen, the present study was conducted to assess the response of the erythropoietic system to cold-induced increased oxygen consumption. Female mice ( $n=20$ ) of the CF#1 strain were divided into 2 groups. One group was maintained in a room at 4°C for 30 d, whereas the remaining one was kept at 23°C. Compared to controls, mice acclimated to cold increased their total food intake by 120.5% ( $P<0.0001$ ). In spite of this, body weight gain was 76.6% of that in controls ( $P=0.0132$ ). Feed efficiency was thus drastically reduced. Brown adipose tissue (BAT), which is an important site of cold-induced thermogenesis, was removed and pooled from the interscapular and subscapular sites. The brown fat was then dissected free of other tissues and weighed. BAT weight was 108.7% higher ( $P<0.0001$ ) in cold-exposed than in control mice. Total circulating red cell mass was measured at the end of the exposure period by the dilution of homologous red cells labeled *in vivo* with  $^{59}\text{Fe}$ . RCM was 47.1% higher ( $P=0.004$ ) in mice acclimated to cold than in mice that were warm-maintained. Data indicate that the erythropoietic system is highly stimulated by exposure to cold. When it is long enough, as in the present study, polycythemia ensues.

### 110. FACT OR FICTION: EVALUATING THE LACTATE PARADOX IN HUMAN HIGH ALTITUDE ACCLIMATIZATION

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It has been puzzling that (1) high altitude natives generate less lactate during maximal aerobic exercise at increasing altitudes, and (2) post-exercise blood [lactate] is increased on arrival at altitude, but decreases with acclimation, despite maintained hypoxia. We hypothesize that this lactate paradox is caused by down-regulated control contributions from oxygen delivery steps, with up-regulated control contributions from ATP demand and supply pathways at the working-muscle level. Such improved ATP coupling would lower the perturbation of numerous intermediates including lactate (Hochachka et al, NIPS, in press). Through a 3-week acclimation at the White Mountain Research Station (3,800m), we investigated post-exercise lactate clearance and phosphocreatine (PCr) recovery rates. Male subjects (12), selected to display a broad range of fitness levels, performed a series of maximal exercise tests (before, during and following acclimation), using a foot ergometer fitted to a 3 Tesla magnet and a bicycle ergometer. Blood sampling and localized  $^{31}\text{P}$  MRS were utilized to follow plasma [lactate] and gastrocnemius [PCr] for 30 minutes following volitional fatigue. We hypothesize that in post-exercise recovery a common inverse relationship between PCr vs lactate and PCr vs  $\text{H}^+$  concentrations will prevail across the wide athletic-fitness spectrum of our subjects. Supported by NSERC (to PWH), DFG (to HCG), AHFMR (to PSA).

### 112. HYPOXIA-STIMULATED ERYTHROPOIETIN SECRETION IN MICE WITH HYPERBARIA-INDUCED REDUCTION OF ERYTHROPOIESIS

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Current evidence suggests that a modulatory action on  $\text{O}_2$ -dependent EPO secretion is exerted by the erythroid/precursor cell population in the erythropoietic organs through a negative feedback system. The aim of the present investigation was to estimate hypoxia-stimulated EPO secretion in mice with hyperoxia-depressed red cell production. Female CF#1 mice aged 70 d were divided in control (C) and experimental (E) groups. The former was maintained in plastic cages in a normal environment, while the latter was placed in an environment of 60% $\text{O}_2$ /40% $\text{N}_2$  in an 85 dm<sup>3</sup> atmospheric chamber with airflow of 1 L/min.  $\text{CO}_2$  was removed from the chamber by washout and absorption with calcium hydroxide. Erythropoiesis was evaluated in 10 C and 10 E mice by iron kinetics performed 3 h after *i.v.* injection of a tracer dose of  $^{59}\text{Fe}$ . The fraction of iron going to erythroid tissue was 65.7% ( $P<0.0001$ ) lower in E than in C mice, showing the erythropoiesis-lowering effect of hyperoxia after a 72-hour exposure. Hematocrit values were similar in both groups. Oxygen-dependent EPO production was derived from pEPO (ELISA, Medac Diagnostika, FRG) changes after a 4-hour exposure to 506 mbar in a decompression chamber. Plasma EPO was 173.2% higher ( $P<0.05$ ) in E than in C mice. Data support the concept that the rate of erythropoiesis, perhaps through the number of the erythroid progenitor/precursor cell population, modulates  $\text{O}_2$ -dependent EPO secretion.

**113. FITNESS PROFILE AND SAFETY IN THE MOUNTAINS**

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**Project Aim:** To promote the awareness of one's own fitness profile to follow adequate training programs for safety in the mountains. **Materials and Methods:** 177 mountains sports professionals. **Elite System:** E.M.G.s of femoral quadriceps and brachial biceps. **Microfit test (guidelines of the ACSM):**—body composition—cardiovascular fitness—flexibility of the spinal column—muscular strength. **Conclusion:** A homogenous composition (between Fit and Excellent) of the group can be noted. Having a good level of aerobic fitness means to have an endurance capacity for prolonged exercise, a quicker response time, a lower level of physical fatigue (improved oxygenation of all the organs and system). Aerobic training guarantees a control of body weight without restrictive diets (anorexia). Good anaerobic fitness means having stamina during intense and short duration exercise. Good flexibility, good joint mobility along with well distributed muscular strength ensure well balanced distribution of the weight without placing undue strain on the joints; as a consequence less energy is used. A good level of all these qualities means to have a greater margin of safety in the mountains. "Energy reserves" in order to face the possible environmental variations. In collaboration with: •Corso di Laurea in Scienze Motorie e Sportive Università di Perugia •Scuola di Specializzazione in Medicina dello Sport e Centro di Medicina dello Sport Università di Perugia •Club Alpino Italiano •Scuola di Alpinismo CAI Pordenone •Soccorso Alpino Guardia di Finanza •Truppe Alpine Esercito Italiano •Collegio Nazionale Guide Alpine Italiane •Medical Space s.r.l.

**115. DOES ACUTE BAROMETRIC PRESSURE VARIATIONS INDUCE CHANGES IN OXIDATIVE STRESS AND MUSCLE DAMAGE MARKERS IN RATS?**

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In many high-altitude physiological studies chambers are used to simulate hypoxic high-altitude environment. In these studies, the chamber must be opened frequently and rapidly for cleaning purposes, bedding replacement and replenishment of water and food. It is reasonable to speculate that the several opening times of the chamber might induce conditions of hypoxic versus normoxic blood flow and thus skeletal muscle and capillarity alterations similar to ischemia/reperfusion could be expected. Thus, the aim of this study was to examine changes in oxidative stress and muscle damage markers induced by the opening of the chamber in high-altitude simulated studies. Twenty four CD1 Charles River rats were divided in two experimental groups. Group 1 was exposed continuously to a hypobaric hypoxic simulated environment equivalent to an altitude of 5000m (55.9 kPa) for seven days. Group 2 was exposed to the same protocol but, in this case, the chamber was opened twice (at day 3 and 6) during 30 minutes. Biochemical parameters were measured in plasma (Creatine Kinase-CK, Tiobarbituric Acid Reactive Substances-TBARS) and on soleus muscle (TBARS, Reactive Carbonyl Derivatives-RCD, N-Acetyl- $\beta$ -D-glucosaminidase-NAG) at 0 and 24 hours. No significant differences were found between groups and moments in any of the biochemistry variables analyzed. In conclusion, the opening of the chamber during chronic simulated high-altitude studies with animals does not seem to induce differences among groups concerning oxidative stress and muscle damage markers.

**114. CHRONIC EXERTIONAL COMPARTMENT SYNDROME OF THE FOREARM FLEXOR MUSCLES IN SPORT-CLIMBERS—EVALUATION OF PHYSIOLOGIC STANDARD PRESSURES IN THE FOREARM FLEXOR MUSCLES DURING SPORT SPECIFIC ERGOMETRY**

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**Introduction:** Chronic exertional compartment syndromes (ccs) are a well known problem in sportsmedicine. Mostly affected is the m.tibialis anterior compartment, mainly in runners and walkers. Diagnostic and therapeutic criteria for this group are widely discussed. For ccs of the forearm flexor muscles, as suspected in an increasing number of sportclimbers, only few cases are reported. The objective of this study was to determine pressure levels inside the deep flexor compartment of the forearms during a sport specific stress. **Methods:** 10 healthy high level climbers were enrolled in a prospective study. All climbers underwent sport specific climbing ergometry, using a rotating climbing wall (step-test, total climbing time 9–15 min). Pressure measurement was performed using a slit catheter, placed in the deep flexor compartment of the forearm. Pressure registration, as well as lactic acid and heart rate measurement was done every 3 minutes and during recovery. **Results:** In all athletes physical exhaustion of the forearms defined the end point of the climbing ergometry. Compartment pressure was related to physical stress, exceeding 30 mmHg only in 3 individuals. A critical pressure of more than 40 mmHg was never observed. Lactic acid increased in relation to physical stress, reaching an average of 3.48 mmol/l. After the test in 7/10 individuals the pressure decreased within 3 minutes to normal values. The 3 athletes with higher pressure levels (>30 mmHg) required a longer time for recovery. Further criteria in terms of clinical and therapeutic consequences are proposed.

**116. MONTAÑISMO, CIEGOS Y DEFICIENCIA VISUAL**

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**Objetivo:** Actualizar el conocimiento de las dificultades médicas para la práctica del montañismo por personas consideradas ciegas o deficientes visuales por la OMS y la IBSA. El Grupo de Montaña de la ONCE, lleva 10 años practicando montañismo con ciegos y deficientes visuales, con la seguridad de los invidentes como prioridad fundamental. Ante la posibilidad de alteraciones sensoriales en altitud en deficientes visuales, se procedió con una progresión inicial con ascensiones entre 2000 y 3000m en España, con grupos cada vez más numerosos y valorando la aparición de alteraciones funcionales referentes a la agudeza, campo visual y discriminación del color. En tales condiciones no se encontraron alteraciones atribuibles a la práctica del montañismo en la población de 100 invidentes estudiados. Un grupo seleccionado de 15 invidentes participó en experiencias a mayor altitud: Alpes, Kilimanjaro, Aconcagua, Elbrus y Cotopaxi. Se realizaron estudios médicos exhaustivos antes, durante y tras las expediciones sin que apareciesen alteraciones funcionales ni otras repercusiones. Dada la heterogeneidad de las patologías causantes de ceguera y deficiencia visual y la variabilidad del resto visual funcional de cada individuo, resulta difícil extrapolar estos resultados a toda la población invidente, aunque el análisis de lo conseguido anima a seguir esta línea de trabajo. La progresión en altitud debe ser progresiva, individualizada y valorada médicamente, pues estos resultados se alcanzaron tras una correcta aclimatación. El montañismo es un excelente medio de rehabilitación personal, estímulo e integración social para estas personas. Además de este estudio médico se han diseñado medios de movilidad específicos para intentar garantizar la seguridad del deportista. La valoración estadística de los accidentes en un grupo de 200 invidentes en diferentes modalidades deportivas en montaña demuestra la eficacia de los dispositivos utilizados.

#### 117. APPETITE AND PLASMA LEPTIN LEVELS IN MICE DURING ANEMIC OR HYPOXIC FORMS OF HYPOXIA

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Leptin appears as a key mediator in the regulation of energy homeostasis and appetite. Elevated plasma leptin (pLEP) levels at high altitude that were associated with loss of appetite and weight loss were recently found in humans. Opposite results were found later in the rat, which raises doubts on the exact role of leptin in the anorectic response to hypoxia. In an attempt to clarify this point, the present study was conducted in female mice of the CF#1 strain that were made hypoxic by either continuous exposure to air maintained at 506 mbar in a simulated high altitude chamber (hypoxic hypoxia = HHx) or removal of 40% of the circulating blood volume through cardiac puncture (anemic hypoxia = AHx). pLEP was measured by immunoassay (Murine Leptin ELISA, Diagnostic System Laboratories, Texas). Food consumption and body mass were depressed during the 5-day period of exposure to hypoxia; pLEP was  $456.6 \pm 115.2$  pg/ml under normoxic conditions. HHx led to a decrease in pLEP that reached statistical significance from the second to the last day of exposure (day 5 th), recovering thereafter. AHx also induced hypophagia and body mass loss, although pLEP remained unchanged. HHx-induced decrease in pLEP could be considered a normal homeostatic adaptation to attempt to reverse HHx-induced anorexia. The reasons for the different response of leptin to HHx and AHx are not apparent at the present time.

#### 119. HYPOXIA-INDUCED ERYTHROPOIETIN SECRETION: PREDOMINANT ANDROGENIC COMPONENT IN THE EFFECT OF NANDROLONE

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Testosterone is a potent inducer of EPO-hypersecretory state (EPO-HS). The steroid exerts both androgenic and anabolic effects. The present study was done to investigate which of these activities is more important to induce EPO-HS, by estimating the effect of increasing doses of nandrolone (19- nortestosterone, N, Decadurabolin, Organon), a potent anabolic steroid, on hypoxia-induced EPO secretion in orchidectomized-hypertransfused mice. 70 CF#1 mice were orchidectomized when aged 30d. One month later, groups of 10 animals were injected three times a week for 3 weeks with N at doses of 0, 50, 100, 200, 400, 800 or 1600  $\mu\text{g}/\text{d}$ . A group of entire male mice were used as normal control. All mice were hypertransfused 4 d after the end of the injection period. They were exposed 50 506 mbar for 6 h, 1 d later. Plasma EPO titer (ELISA Medac Diagnostika, Germany) was determined. Kidney, seminal vesicle and levator ani muscle weights were registered as index of renotropic, androgenic or anabolic effects, respectively. EPO production in response to hypoxia increased with increased doses of N. Significant positive correlation was observed between EPO production and kidney and seminal vesicle weights; correlation was not significant with levator ani muscle weight. Nandrolone thus induced an EPO-HS, which was dose related and apparently associated with the renotropic and androgenic effects of the steroid.

#### 118. SERUM LEPTIN LEVELS IN MALES LIVING IN THE PERUVIAN ANDES

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Lower plasma leptin levels in Aymara natives in comparison with Caucasoid subjects suggest ethnic differences. We hypothesized that the altitude modifies serum leptin levels. So, we compared serum leptin levels of dwellers from sea level and from two places in the Peruvian Andes. Ten dwellers from Lima (150 m), twenty-seven from Huancayo (3250 m), and eighteen from Morococha (4550 m). The mean age was  $24.49 \pm 4.1$ . The body mass index (BMI) of the population was  $22.62 \pm 0.87$ ;  $22.25 \pm 1.69$ ;  $22.63 \pm 1.60$ ; at Lima, Huancayo and Morococha, respectively. The mean leptin at sea level was  $1.8 \pm 0.7$  g/L ( [CI] of 95% 1.3–2.3);  $1.4 \pm 1.0$  g/L (CI 1.0–1.8) at 3250 m; and  $1.1 \pm 0.9$  g/L (CI 0.7–1.6) at 4550 m. The comparison of leptin values in the three populations was not significant neither there was correlation between leptin and BMI. Our data, although were not statistically significant, show a moderate inverse variation of leptin concentration with altitude.

#### 120. HYPOXIC STATES: CLASSIFICATION

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In 1905 P. Albitsky offered to distinguish different types of oxygen starvation on the basis of oxygen delivery as well as oxidizing processes in tissue (cytotoxic type). J. Peters's and D. Van Slykes's included this tissue type in the concept of "anoxia" (1922). Classification of hypoxias that included the cytotoxic type were accepted at the conference in Kiev, Ukraine in 1949. G. Derviz offered to subdivide this type of hypoxia into the separate group of disoxidative states at this conference. Today we offer the "Elbrus" classification. HYPOXIC STATES are the states of organism that appear in case of its insufficient maintenance by oxygen or insufficient oxygen in tissues.

1. HYPOXIAS—are the states of tensions in oxygen transport organism functions directed at the liquidation of oxygen deficiency. Types of hypoxias are: 1) hypoxic-baric, 2) types that depend on the damage of oxygen delivery (respiratory, circulatory, hemic, barrier), 3) dis-regulated, 4) hypermetabolic, 5) mixed
2. DISOXIDATIONS—are the states when the oxygen delivery is sufficient but this oxygen does not satisfy organism energy needs of damages in cellular mechanisms of oxygen utilization. This classification is supplemented by the different degrees hypoxia (latent, compensated, subcompensated, discompensated, terminal), as well as by forms of hypoxia (lightning, acute, subacute, chronic; adaptiveness of the high mountains natives is the subject of the special attention).

### 121. MATHEMATICAL METHODS FOR INVESTIGATING THE RELIABILITY OF ORGANISMS FUNCTIONING UNDER THE EXTREME CONDITIONS OF HIGH MOUNTAINS

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The health of a person and his capacity for work under conditions of high mountains in many respects is determined by the reliability of the function of physiological systems. Mathematical methods of both the reliability theory and mathematical simulation of basic functional systems are proposed to be used for investigating the reliability. It is shown that the most suitable reliability model for living systems is a chain model—a successive connection of links representing separate functional systems of organism—respiration, blood circulation, thermoregulation, eyesight, motion. Besides, the weakest links determining the reliability of functioning of the whole organism under the extreme conditions of high mountains even for a healthy person are—respiration, blood circulation, thermoregulation and psychophysiological systems. Quantitative characteristics of the reliability of these systems are determined through the main indicators. The influence of non-sufficient contents of oxygen in respiration mixture, low atmospheric pressure, low temperatures of the environment are simulated by computer models of organism. An analyses of modeling data shows that moderate physical loading improves indicators of organisms adaptivity to external conditions of high mountains and promotes the increasing of persons capacity for work and the reliability of his functioning.

### 123. PECULIARITIES OF ADAPTIVE REACTIONS TO MOUNTAIN HYPOXIA IN AGE ASPECT

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Mountaineers of different age groups were studied. The special attention was paid to the examination and analysis of clinical and physiological data of participants of open championship between mountain climbing veterans of Ukraine (J.U.IAA, N3, 2000). Winners of this championship were 78-year old representative of Russia—M.M. Bobrov, who climbed on Elbrus mountain (5621 m) and 75-year old V.D.Monogarov, who climbed on Elbrus four times in summer 2001 during his preparation for climbing on Everest. We studied cardiorespiratory system that characterize velocity and effectiveness of oxygen transport on all stages of its delivery. It was shown that veterans of mountaineer who train themselves annually in mountains have higher safety for such factors as hypoxic environments or cold, their stressful reactions are expressed less, they have wider ranges of respiration and circulation reaction, their systems of gas exchange and blood circulation are more economic and may be restored more quickly. Therefore, the ability of organism for adaptation decreases with the age, however, it does not lost absolutely. The adaptation for hypoxic environment with taking into account changes of organism reactivity with age increases organism capacity for work and stability, protects it from early aging and promotes longevity.

### 122. ESTIMATION OF FUNCTIONAL STATE FOR ALPINISTS

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Selection and preparation of mountaineers and people of other special groups to work in mountains in conditions of the reduced partial oxygen pressure (hypoxobaria) is going in few following stages. 1) Stage of clinical and physical checkup in dispensary. 2) Special investigation during the elevation in altitude chamber and during the loading tests. 3) Tracking of adaptation process to the high mountain conditions. 4) Using of mathematical models of hypoxic states. Estimations of function efficacy for the oxygen transport system on all phases were done: mental, physical, aerobic, anaerobic efficiency, adaptive and adapted states, stress conditions, cool resistance and others. The special system of the estimation of human states was elaborated, the states were estimated in points. At the beginning the estimations of all organism systems are done, further we did the final summation of all points taking into account the contribution value (%) of each parameter. Such approach allowed us to predict the reliability of organism functioning in extreme conditions and to prepare more than ten successful expeditions to high mountains (round 8 thousand meters) in The Himalayas.

### 124. DIARRHEA AND MOUNTAINEERING

Rafael Battestini. Institut d'Estudis de Medicina de Muntanya, Barcelona, España

During a mountaineering expedition diarrhea, defined as more than three fecal fluid discharges and abdominal pain, can be a serious incident. Physiopathology: Enterocyte is inflamed, peristaltism is increased, balance absorption/secretion becomes negative Etiology: Disbacteriosis (traveller's diarrhea); infection (poor hygiene); hypoxia-ischaemia (enterocyte and muscular cells inflammation); enterocyte irritability (mica particles in water) Clinically the patient presents: Fluid fecal discharges, abdominal pain, nutrient malabsorption, adynamia, sometimes fever. At high altitude diarrhea is not a self-limited pathology. There is a pathological feed back: Hypoxia increases enterocyte inflammation, diarrhea decreases high altitude acclimatization. Prophylaxis: Water filter, for bacteriae and mica particles, ebullition of all cooking water, aseptic cooking processes, ferments, like sacaromyces, against disbacteriosis Therapy: Hydro-electrolytic solutions, adsorbents (like vegetal coal or attapulgitte), loperamide, antibiotics and antipaludic drugs, if fever, oxygen supply, at high altitude.



### 125. MILD ALTITUDE EXERCISE ENHANCES HUMAN ANTIOXIDANT ACTIVITY TO DECREASE OXIDATIVE STRESS

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Increased oxidative stress has been associated with work at high altitude; however, it is not known whether oxidative stress is a significant problem at moderate altitudes. The oxidative stress indicators, reactive oxygen species scavenging activity (RH<sub>2</sub>O<sub>2</sub> and RHOCl), total antioxidant status (TAS), oxidized protein products (methylguanidine and dityrosine), and lipid peroxides (PCOOH) and biochemical parameters, like hematocrit (Hct), were measured in blood samples from thirty Taiwan mountain climbers (18 females and 12 males, age from 27 to 56 years old) engaged in moderate altitude (approximately 2,200 m). The blood samples before and after 3 day's mild altitude exercise (for 2-4 hour walking) were drawn from the antecubital vein and assayed the biochemical and oxidative stress. Our results showed that after 3 day's exposure to mild altitude, the oxidative stress, including the levels of RH<sub>2</sub>O<sub>2</sub> and RHOCl, methylguanidine and dityrosine, and PCOOH were significantly reduced, while TAS and Hct were markedly enhanced. In addition to the reduction of oxidative stress, interestingly, the plasma lipids including total cholesterol and triglyceride, and complement 3 and complement 4 were also reduced. We conclude that mild altitude exercise by hypoxic stimulation increases the endogenous total antioxidant status and, therefore, decreases reactive oxygen species induced oxidative stress.

### 127. CRYOANESTHESIA AND ENDOGENOUS TESTOSTERONE HAVE LONG-TERM DELETERIOUS SYNERGIC EFFECTS ON HYPOXIC VENTILATORY RESPONSE IN YOUNG RATS

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Cryoanesthesia is commonly used for neonatal hormonal manipulations and has long-term deleterious effects on several brain's areas on rats. This study hypothesizes that cold exposure not only causes long-term consequences in brain stem structures (harboring cardio-respiratory cell groups), but that these effects are dependent on the hormonal state of the male pups. One day old rats were immersed 15 minutes in ice prior to gonadectomy. Three weeks later, minute ventilation and hypoxic ventilatory response (10% O<sub>2</sub>) were assessed by whole body plethysmography. Results show that hypoxic respiratory pattern is synergistically modified by cryoanesthesia and testosterone. In comparison with control animals, cold exposed-sham operated and cold exposed-castrated-testosterone injected (1mg, sc) animals had a deficient hypoxic ventilatory response characterized by a dramatically reduced response of tidal volume and more elevated respiratory frequency under hypoxia. Cold exposed-castrated rats display the inverse responses. These findings demonstrate that cryoanesthesia has long-term consequences on respiratory control, and that these effects are dependent on the hormonal condition of newborn male rats.

### 126. VARIATIONS IN HEARING LEVEL IN ALPINISTS TO HIGH ALTITUDE

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Eight women were analysed in the context of expedition to an 8000 metre peak in the Himalayas. The control audiometry was realized in Barcelona and the rest of the measuring done with an officially approved portable audiometer model Grason Stadler GSI-17. The data obtained in relation to the control audiometry were the following: to 1850 m, increase of audition in some frequency for the 100% of alpinists and worse results in other frequencies for 75%; to 3450 m, increase in some frequency for the 66.6%; to 4300 m, worse hearing in some frequency for 83.3% and no improvement for anybody. At the Advanced Base Camp (5550 metres): worse results in the whole frequency spectrum for the 87.5% and no improvement for anybody. Four days later, improvement in low frequencies for the 100%. Later measures showed hearing losses experienced by the alpinists descending from the altitude camps. Back in Kathmandu, improvement in intermediate frequencies and worsening in low frequencies for the 100%, but the audiometries were under the reference. Our results suggest that high altitude causes variations in hearing level.

### 128. MANAGEMENT OF RUPTURES OF FINGER FLEXOR TENDON PULLEYS IN SPORTCLIMBERS

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The closed traumatic rupture of a flexor tendon pulley of sportclimbers appeared as a new complex finger trauma in the mid 1980's. As the diagnostic and therapeutic procedures were variable in the beginning, nowadays a non surgical approach, at least for the single rupture, becomes standard. With fifty documented cases of pulley ruptures we are showing the diagnostic and therapeutic criteria. In our group, we had 90% singular and 10% multiple pulley ruptures. Leading is the ring finger, second the middle finger. After clinical suspicion and exclusion of fracture or injury to the capsula/ligament-system, the diagnosis can be proven with ultrasound examination. If this fails to give exact diagnosis an MRI should be performed. For a single rupture, we recommend conservative procedure, with initial immobilisation and early functional treatment. For the multiple pulley rupture surgical reconstruction is necessary. We favorite the "loop and a half" technique of Widstrom 1989, alternative the repair according to Weilby 1978. Postoperative we rely on initial immobilization and early functional treatment under external pulley protection.

### 129. RELATIONSHIP BETWEEN HYPOXIC TOLERANCE AND CARDIOPULMONARY FUNCTIONS IN TRAINED MOUNTAIN-CLIMBERS

Wen-Chih Lee (presenting author), SHU; Shiun-Ping Lin, CHIP; Chung-Jung Chen, HWC; Ming-Pen Liang, CAA; Jin-Jong Chen, YMU

The purpose of this study was to examine the relationship among cardiopulmonary function (CP), hypoxic tolerance (HT), and high mountain-climbing performance (HP). Fourteen male subjects participated in the PAMIRS EXPEDITION RECRUIT ACTIVITY sponsored by LaNew Company. Heart rate during the activity was recorded in Mountain Snow (altitude approximately 3500 m) in Taiwan. All subjects were divided into three groups excellent (E); good (G) & disqualified (D) according to their average % HRmax as a performance indicator. HT was evaluated by recording the SaO<sub>2</sub> after a five minutes acute hypoxic exposure (FIO<sub>2</sub> = 8%). Maximal oxygen consumption (VO<sub>2</sub>max), oxygen pulse, and maximal ventilation were measured at sea level. E group subjects exhibited lowest % HRmax displayed greatest VO<sub>2</sub>max, maximal ventilation and oxygen pulse. E group subjects also demonstrated a greater SaO<sub>2</sub> than G and D groups. These results suggest that both CP and HT attribute HP independently.

### 131. ESTIMATION OF COLD STEADINESS FOR MOUNTAINEERS

P. Beloshitsky, J. Kravchenko, A. Krasjuk. Elbrus medical and biological station of NAS of Ukraine.

Hypoxic environment promotes the lowering of organism heat generation, the acceleration of body temperature (BT) lowering and, therefore, there is a problem of mountaineer steadiness in the cold. One of the main paths of heat loss is through the skin vessels, in which vasodilation may increase the heat emission up to 90 % and vasoconstriction may reduce it up to 70 %. Taking this fact into account we measured the skin temperature lowering for all fingers of the hand immersed in water of T +7°C (room T +22°C) and subsequent T restoration during 10 minutes (doing this at the sea level and at the different heights—up to 5600 m). For measurement of the total organism reaction for the local cooling, we recorded T of finger skin on a hand which was not cooled. Simultaneously we registered the heat loss (in W/ m<sup>2</sup>), SaO<sub>2</sub> (%) as well as erythrocyte resistance to cold (T -4°C, 1 hour). These measurements gave us a possibility to predict the appearance of cold-reactive antibodies and damage of microcirculation. We developed a computer program for T recording and analysis of T changes. This program allows to estimate the level of resistance for cold, to give recommendations concerning the total and local training (on the basis of analysis of rates for T decrease and restoration, etc.). Such approach gave us a possibility to select 10 persons from Krasnodar University and to prepare them during 2 years for the successful and without chilblains climbing to Everest in 2000.

### 130. HYPERCOAGULABILITY DURING A LONG HAUL FLIGHT? PROJECT ECS 2001

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Deep venous thrombosis (DVT) and pulmonary embolism are severe complications of long-haul flights. At present hemostasis was not investigated during and after a real long haul flight. The goal of the project ECS-2001 was to determine the influence of a long-haul flight on the coagulation system. Blood was collected from 20 volunteers, 10 with low risk and 10 with moderate risk for DVT before, during a 9h flight (Vienna-Washington), on the flight back, and one and three days after return. Following parameters were measured: PT, aPTT, maximal clot firmness (MCT) and  $\tilde{\sim}$ -ankle (roTEG), thrombin-antithrombinIII-(TAT) complexes, D-dimer, plasmin- $\tilde{\sim}$ 2-antiplasmin (PAP), t-PA, PAI-1, factors VII and VIII, protein C and S. Statistics: Manova for repeated measures. Level of significance P < 0.05. PT did not change, but aPTT was significantly reduced after the flight. MCF and  $\tilde{\sim}$ -ankle were increased during and after the flights. TAT, D-dimer and PAP remained unchanged. T-PA was decreased after the flights and PAI-1 was increased, the t-PA-PAI-1 ratio dropped. Coagulation factors VII and VIII were elevated during and after the flights. No change was found for protein C and S. We conclude that the long-haul flight induced a hypercoagulable state independent of the risk profile for DVT as evidenced by thrombelastographic measurements and analysis of FVII and VIII. In addition the fibrinolytic potential was suppressed. In the presence of additional risk factors these hemostatic changes may trigger DVT in passengers.

### 132. EXPERIENCE IN FROSTBITE TREATMENT IN EXPEDITIONS IN THE SIXTIES

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In several expeditions in the Himalayas—from 1960 to 1975—, we cared for frostbite of different degrees in hands and feet, over 7000 meters. The treatment of the 7 cases of deep frostbite was always medical (no surgical treatments on site) intended for prevention of infection, followed by local treatments with small healing. All injuries were completely rehabilitated and just one subject needed partial amputation of one hand's fingers. Local pain disappeared and total functionalism was achieved after treatment no longer than three months.

### 133. AN EXPERIMENTAL MODEL OF HYPOTHERMIA IN RATS. EFFECTS ON THE LIVER BLOOD FLOW

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Accidental hypothermia leads to different physiological reactions depending on the level of hypothermia, such as cardiac output, decreasing of metabolic rate, ischemia or death. We studied the effect of deep hypothermia induction (20°C) and rewarming on hepatic regional flow and blood oxygenation in animals exposed to different rates of cooling and rewarming. Two groups of rats were cooled and rewarmed at 0.35 and 0.25 °C/min (high cooling/rewarming rate, HR and moderate rate, MR), by circulating cold or warm water through a coil of polyethylene tube placed in the abdominal cavity. A normothermic group, NT, was used as a control. All animals were maintained with respiratory aid, core temperature and portal vein flow variations were continuously monitored. Our results showed that HR animals had a mortality rate higher than 40%, and death occurred during the first 30 minutes of rewarming, although all MR animals survived. The portal blood flow decreased about 80% during the hypothermia period but a completely recovered flow after rewarming was observed. Values of pO<sub>2</sub>, pCO<sub>2</sub> and oxygen saturation were in the normal ranges, but a slight pH diminution was observed at the end of rewarming. The transaminases levels (AST, ALT) did not change during hypothermia, but an augmentation was observed after rewarming was completed.

### 135. "AIUT ALPIN DOLOMITES" MOUNTAIN HELICOPTER RESCUE OF C.N.S.A.S., (CORPO NAZIONALE SOCCORSO ALPINO E SPELEOLOGICO), VOLUNTARY ALPINE RESCUE SERVICE OF ITALY

Giovanni Cipolotti, Michele Nardin, Medical Commission of CNSAS Raffael Kostner, CNSAS Alto Adige, Aiut Alpin Dolomites. ([www.val-gardeena.com/aiut-alpin](http://www.val-gardeena.com/aiut-alpin))

Aiut Alpin Dolomites is a non-profit organization founded in 1990 with the union of rescue squads of CNSAS of Dolomitic region, to improve quality and quickness of mountain rescue missions; from 1998, the helicopter medical service of Aiut Alpin Dolomites is integrated with Ato Adige network of health rescue service. The staff of the organisation is composed by volunteers of mountain rescue groups in 14 teams, mountain guides, helicopter pilots, emergency physician specialized in anaesthesia/reanimation, and a lot of financial supporter; the crew is composed by a pilot, a mountain guide, a rescue volunteer of CNSAS and an emergency physician. The helicopter medical service is organized with an operative base positioned in Alpe di Siusi (1980 m.s.l.), and a technical base positioned in Val Gardena, near Ortisei, in which there are the hangar, a dispatch center and quarters for the crew. The total number of missions effected by Aiut Alpin Dolomites from 1991 to 2001, during the periods of december-march and june-october, is 5358, with an average of about 500 missions/year; more than 60% of patients have traumatic injuries. About 40% of rescue missions were effected using stationary flight, winch or fix rope applied on the helicopter center hook. The NACA index of patients is: "NACA 1-2" 33%, "NACA 3" 43%, "NACA 4-6" 15%, "NACA 7" 9%, and mean time from alarm and patient arrival to the hospital is 38 minutes; in-hospital mortality within 48 hours is < 0.5 %.

### 134. CHARACTERISTICS OF EMERGENCY IN MOUNTAIN ACCIDENTS. RESCUE IN THE CENTRAL APENNINES OF ITALY

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In the last fourteen years mountain rescue teams of Abruzzo rescued over 1,100 persons in the central part of Appennines, doing 235 on 815 rescues by helicopter. Exact statistic data is available from CNSAS (Corpo Nazionale Soccorso Alpino e Speleologico), which is responsible for most part of mountain rescues in Italy. All rescued persons were rated according to a medical (NACA Medical 0 to 7) and a topographical index (NACA Topo A to H). Moreover, every rescued person was rated according to APVU system (Alert, Pain, Verbal, Unresponsive). Of the 1147 rescued persons 86% were rescued from easy accessible place (Topo A-E), 11% from difficult accessible place (Topo F) and only 3% from extremely difficult accessible sites of accident (Topo G-H). Regarding those rescued, 55% were not injured, 34% showed mild injuries and 3% severe injuries. 0.3% suffered of a life-threatening injury and 8% were dead-body evacuations. People alert were 85%, 4% responded at verbal stimulation, 1% at painful stimulation and 9% were unresponsive.

We conclude that it is possible to learn from years of rescues and to organise our mountain rescue service according the results of this study.

### 136. CARDIOPULMONARY RESUSCITATION IN CANYONS

F. Thomas, P. Guin, M. Barcelo, F. Coll SAMU 66, CHG Perpignan, France

The emergency medical service (Samu 66) is summoned on the 3.06.01 to a canyon where cardiopulmonary resuscitation is being performed by friends of the victim. A team composed of an emergency doctor and a mountain rescue specialist is taken on spot by helicopter and need to adapt themselves and their equipment to this situation. We conclude that canyon rescue requires specific materials and equipment but also heavy resuscitation equipment that can be winched from helicopter.

**137. PATHOGENESIS OF CANYON ACCIDENTS**

P. Guin, F. Thomas, M. Barcelo, F. Coll SAMU 66, CHG Perpignan, France

The emergency service Samu 66 realised 49 medical rescues in canyons between 1993 and 2001. Only persons practicing canyoning were included in this study. It is a retrospective study over 9 years and includes 47 patients. 85% were rescued for trauma, 6.5% for medical reasons. Two patients had cardiac arrest on arrival of the rescue team. The traumatic injuries were as follows : 42.5% spine injuries of which 53% had fractures, 22.5% leg injuries of which 66% were fractures, 20% shoulder injuries of which 87.5% were joint dislocations, 17.5% head trauma of which 86% had a loss of consciousness.

The conclusion is that canyon injuries are usually characteristic and serious. The causes can be explained by the nature of canyoning and the morphology of canyons.

**138. PHYSIOLOGICAL PARAMETERS EVOLUTION IN AN EXTREME SITUATION: CAVE DIVING EXPEDITION LA FOU DE BOR**

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"Fou de Bor" is a cavity located in Pyrenees 3.406 meters long, 295 of them underwater. Water temperature around 7° C. Its location, 1.160 meters above sea, conditions the dive type and decompression. Accidents, specially dysbaric, in this context, needs highly specialized response Objectives. Quantitative: evaluate diver's physiological changes. Qualitative: development of emergency medical procedures in cave diving.

Methodology.1.Population: two teams working alternate days to avoid residual nitrogen. 2. Study definition: observational and transverse. 3.Incorporation criteria: firemen with high technical skills and vast experience in cave diving. Participation witting. 4. Instrumentation: Daily controls: BP, HR, SpO<sub>2</sub> & temperatures. Continuous analyses: HR records through pulsioximeter in pre-immersion, dive and post-dive. Dive parameters record through personal computers. Last decompression stops with pure O<sub>2</sub> (max. 1.6 bars) .

Results. Maximum values of BP correspond to the moment of maximum fatigue: post-dive, and are related to lowest values of sublingual temperature. In HR temporary series were not observed neither trend nor cyclical components. It could be observed that dive effect provokes HR increase and corresponds to each three phases of dive activity. It was observed some moderate hypothermia signs, exhaustion, cramps, cervical pain, cutaneous hypersensitivity, tachypnea and tachycardia. Conclusions: Right emergency medical organization. Confirmed changes in HR. Continuous BP & T recording needed.

**139. IMPACT OF HYPERVENTILATION, HIGH ALTITUDE, AND ACUTE MOUNTAIN SICKNESS (AMS) ON BLOOD FLOW VELOCITY IN THE MIDDLE CEREBRAL ARTERY (MCAv)**

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Background. There is a controversy as to whether cerebral blood flow changes in subjects with AMS. Methods. MCAv was measured with a transcranial Doppler during normo- and hyperventilation in 41 volunteers at baseline (353m) and after a 22h ascent to 4,559m. AMS was evaluated using the Lake Louise score. Comparisons were made during normoventilation using an unpaired t-test. Results. At both baseline and high altitude, MCAv during hyperventilation (defined as a drop of 30 % in ETCO<sub>2</sub>) was consistently and significantly decreased compared with normoventilation (P<0.0001). 23 subjects (56%) had no or mild AMS (score<6). In those, SpO<sub>2</sub> decreased from 98±1% at baseline to 79±8% at altitude (P<0.0001); MCAv remained unchanged (58±11 vs 57±12cm/s). 18 subjects had moderate to severe AMS (score =6). In those, SpO<sub>2</sub> decreased from 98±1% at baseline to 71±9% at altitude (P<0.0001); MCAv remained unchanged (61±13 vs 65±17cm/s). The differences in MCAv between subjects with scores <6 or =6 was not significant. Nine severely ill subjects (score 10±3) were treated with dexamethasone, acetazolamide, and O<sub>2</sub>. In those, the score decreased to 3±2 (P<0.0001); MCAv before and after treatment was unchanged (67±18 cm/s vs 64±11cm/s). Conclusions. At both low and high altitude, MCAv measured by transcranial Doppler decreases during hyperventilation compared to normoventilation. Altitude per se and the severity of AMS have no impact on MCAv.

**140. CEREBRAL AUTOREGULATION IN SHERPAS AT DIFFERENT ALTITUDES**

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To investigate the effect of different altitude levels on cerebral autoregulation (CA) in high altitude natives, CA was determined in Sherpas in Nepal at 4,200 m (group-A), 3,400 m (group-B), 2,600 m (group-C), 1,300 m (Kathmandu, group-D) and in a Caucasian control group at sea level (group-E). Each group contained 10 subjects. In each subject 5-12 paired measurements of mean arterial blood pressure (MABP) and middle cerebral artery flow velocity were performed using Transcranial Doppler, during slow infusion of phenylephrine in order to increase MABP by at least 30 mmHg. Regression lines were obtained from the paired measurements and an Autoregulation Index (AI) was calculated. AI of 1 equates to complete autoregulation.

AI of 0 equates to pressure dependent cerebral blood flow. AI in group-A: 0.22±0.29 (mean ± SD); group-B: 0.51±0.15; group-C: 0.62±0.15; group-D: 0.60±0.26; group-E: 0.82±0.18. Autoregulation at 4,200 m is most disturbed and AI in group-A is significantly different from group-C, -D and -E (all groups: p<0.0002; ANOVA, Bonferroni). Autoregulation in Sherpas at 3,400 m, at 2,600 m and at 1,300 m is similar, and shows more modest disturbance. Autoregulation at sea level is intact, and AI in group-E is significantly different from group-A and -B (both groups: p<0.002).

#### 141. LEFT VENTRICULAR DYSFUNCTION IN CORONARY HEART DISEASE AT HIGH ALTITUDE

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Official guidelines do not address exposure to high altitude (HA) of patients (pts) with asymptomatic left ventricular dysfunction (LVD). Good tolerance to exercise at 2500 m was observed in coronary (CAD) pts with LVD without residual ischemia, but direct measures of LV function at altitude are not reported in such pts. Fifteen pts (14M, 1F) aged 45–70 (mean 58.8 yrs) with CAD, LVD (left ventricular ejection fraction, LVEF 32.7%), all NYHA class I, without residual ischemia on maximal symptom-limited bicycle stress test or echo-dobutamine stress test, all used to mountaineering or hiking before CAD, were studied after a cardiac rehabilitation program. They first underwent bidimensional echocardiography with color-Doppler at low altitude (320m, LA) and a second examination within one month, at HA (2874m) reached by cable car and a 30 min walk. All pts were asymptomatic at HA; no pts complained of symptoms nor had signs of acute mountain sickness or heart failure. Mean LVEF did not change from LA to HA: 32.7% vs 33.8% respectively, but individual changes ranged from a –9% decrease to a +7% increase; 4 pts had a 5% decrease, 5 pts had a 5% increase. Pts presenting with HA deterioration in LV function showed lower E/A and prolonged deceleration time of early filling at LA Doppler mitral flow velocity profile. LVD does not seem an absolute contraindication to HA (< 3000 m), but appropriate functional evaluation of these pts needs to be established.

#### 143. EXCESSIVE POLYCYTHEMIA OCCURS IN YOUNG HIGH-ALTITUDE (3600 M) RESIDENTS IN THE ABSENCE OF LUNG DISEASE

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Objective: Chronic Mountain Sickness occurs in ~8% of the La Paz population. We asked whether its primary diagnostic sign, excessive polycythemia (EP), occurred in younger-aged persons without lung disease. Methods: In the 6200 persons referred to IBBA over the past 5 yrs, male hemoglobin (hgb) averages 17.5

| Variable (x ± sem)       | Control    | Younger EP  | Older EP     |
|--------------------------|------------|-------------|--------------|
| Hgb, gm/dL               | 16.8 ± 0.1 | 19.6 ± 0.3* | 21.6 ± 0.5** |
| PaO <sub>2</sub> , mmHg  | 60.8 ± 0.3 | 53.8 ± 1.0* | 49.8 ± 0.8** |
| PaCO <sub>2</sub> , mmHg | 30.4 ± 0.4 | 31.7 ± 1.1  | 35.1 ± 0.6** |
| SaO <sub>2</sub> , %     | 91.1 ± 0.3 | 87.2 ± 1.1* | 83.0 ± 0.9** |
| ΔVe hypoxia, l/min       | 3.8 ± 0.6  | 1.1 ± 0.2*  | .03 ± 0.2**  |
| FVC, % predicted         | 111 ± 2.5  | 108 ± 2.6   | 102 ± 3.2**  |
| FEV1/FVC, %              | 89 ± 1.4   | 88 ± 1.1    | 77 ± 1.4**   |
| DLCO, ml/min/mmHg        | 38 ± 2.5   | 29 ± 1.9*   | 24 ± 1.2*    |

\* p < .05 vs C; \*\* p < .05 vs YEP. From this population, we selected 26 younger- and 31 older-aged persons with EP (YEP, age = 20+1 yr; OEP, age = 36+1 yr) and 30 younger controls (C, age = 22+1 yr). Results: Height was similar but OEP weighed more (68.8+1.1 kg) than C or YEP (60.7+1.4, 63.7+1.4 kg, both p < .05 vs C). YEP and OEP had lower PaO<sub>2</sub> and SaO<sub>2</sub> than C, but PaCO<sub>2</sub> was higher only in OEP. Higher hgb was associated with lower PaO<sub>2</sub> (R<sup>2</sup> = 0.55) and higher PaCO<sub>2</sub> (R<sup>2</sup> = 0.36) in all subjects. The increase in ventilation following 3 breaths of 10% O<sub>2</sub> in N<sub>2</sub> was reduced in YEP and OEP vs C. Forced vital capacity (FVC) and the FEV1/FVC ratio were similar in YEP and C but reduced in OEP. Diffusing capacity for CO was lower in YEP and OEP vs C but similar when controlled for hgb. Conclusion: EP occurs in younger-aged men in the absence of apparent lung disease but in the presence of a blunted ventilatory response to hypoxia and a suggestion of hypoventilation. (Supported by the French Cooperation and Universidad Mayor de San Andrés, La Paz, BO).

#### 142. CARVEDILOL ATTENUATES RIGHT VENTRICULAR HYPERTROPHY IN CHRONICALLY HYPOXIC RATS

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Acclimatization to hypoxia is characterized by increased sympathetic activity and by pulmonary hypertension (PH) leading to right ventricular hypertrophy (RVH). One of the mechanisms involved in the development of ventricular hypertrophy is sympathetic nervous system activation through α<sub>1</sub> and β adrenoceptor stimulation.

The objective of this study was to test the hypothesis that a treatment by carvedilol, which blocks the sympathetic nervous system, would result in a reduced right ventricular hypertrophy. Wistar rats were divided into four groups, normoxic (PB 760 Torr) and hypoxic (PB 380 Torr) non-treated (NX, HX) and normoxic and hypoxic treated (NT, HT) by carvedilol (IP; 10 mg/kg/day). After 3 weeks of exposure, right ventricular pressure and heart rate were measured. The heart was removed and the right and left ventricles separated to study the adrenoceptor density by radioactive binding. The right ventricular pressure was 38% lower (p < .001) and Fulton's ratio (RV/LV) 31% lower (p < .001) in HT compared to HX.

In the hypoxic untreated rats, myocardial β-adrenoceptor density decreased while carvedilol prevented this downregulation. In conclusion, carvedilol attenuates right ventricular hypertrophy through a decrease in PH. These results suggest that sympathetic nervous system plays an important role on right ventricular hypertrophy and/or hypoxia-induced pulmonary hypertension. The specific role of α<sub>1</sub> and β-adrenoceptor on RVH and PH remains to be determined.

#### 144. DOMPERIDONE: A POSSIBLE STRATEGY FOR CMS THERAPY

LEÓN-VELARDE Fabiola, GAMBOA Jorge, GAMBOA Alfredo, RIVERA-CHIRA María, MACARLUPU José Luis and MONGE C Carlos

Alveolar hypoventilation and a blunted ventilatory response have been associated with polycythemia, the main sign of Chronic Mountain Sickness (CMS). To investigate if a reduction in the activity of inhibitory dopaminergic mechanisms (IDM) could improve the blunted ventilatory response, high altitude (HA) natives (n=5, and n=5 CMS) living at 4,300m were evaluated with domperidone treatment (DOM; single oral dose of 40 mg). Additionally, 18 hypoxic rats (5 weeks, PB = 433 Torr) were studied with and without DOM treatment (1 mg/kg). In man, the slope of the relationship isocapnic ventilation (VE, l/min/%) with 100-SaO<sub>2</sub> increased significantly after DOM treatment in sea level, HA and CMS subjects (average: 53%). In rats, acute and chronic D2-R blockade increased the poikilocapnic ventilatory response to hypoxia (VE ml/min/kg at 0.1 FIO<sub>2</sub> – VE at 0.21 FIO<sub>2</sub>) significantly, from 50±36 SEM to 69±48; and from 39±37 to 66±81. DOM treated rats decreased their hemoglobin concentration (Hb, g/dl) from 21±0.29 to 18±0.19 (p < .01). In conclusion, the reduction of the IDM increased the sensitivity to hypoxia in both rat and man, and decreased Hb concentration in rats. A possible strategy for CMS therapy with domperidone could limit the dopaminergic neuromodulation of carotid body chemosensitivity and reduce polycythemia.

**145. ANGIOTENSIN-CONVERTING ENZYME GENE I/D POLYMORPHISM AND HIGH-ALTITUDE PULMONARY HYPERTENSION IN HIGH-ALTITUDE RESIDENTS**

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**BACKGROUND:** Recently it has been implicated angiotensin converting enzyme (ACE) in the development of high altitude pulmonary hypertension (HAPH). The ACE I/D gene polymorphism is known to determine the level of plasma and tissue ACE. **AIM:** The aim of our study was to investigate an association between ACE I/D gene polymorphism and developing of HAPH in Kyrgyz highlanders. **METHODS:** We determined the ACE genotype and its enzyme activity in serum in 167 Kyrgyz highlanders (63 healthy subjects and 104 subjects with HAPH). The pulmonary artery haemodynamic was measured by right heart catheterization. The patients were diagnosed with HAPH when had: 1) living in high altitude, 2) mean (MPAP) higher than 25 mm Hg, 3) pulmonary vascular resistance (PVR) greater than 200 Dyn/sec/m<sup>2</sup> or 4) more than 2-fold increase in MPAP or PVR when breathing 10% O<sub>2</sub> for 30 min., 5) absence the other causes of the increase pulmonary arterial pressure. Genomic DNA was extracted from blood samples and ACE I/D genotype was determined by PCR. **RESULTS:** Subjects with HAPH had a 2-fold higher frequency of I/I homozygotic genotype compared to normal subjects (36% vs 16%, p<0.05). The frequency of the I allele in subjects with HAPH was about 1.5-fold higher than that in normal subjects (0.60 vs 0.40, respectively, p<0.05). The I allele was also associated with lower expression of ACE in plasma. **CONCLUSIONS:** We suggest that II genotype apparently is associated with the development of HAPH. The I allele of ACE genotype could be a useful genetic marker for susceptibility to HAPH in the populations of the high-altitude residents.

**147. SIMULATION OF A LONG-DISTANCE FLIGHT IN PATIENTS WITH CYSTIC FIBROSIS**

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Due to the increasing age and mobility of patients with cystic fibrosis, the number patients performing long-distance flights increases. There are limited data about the cardio-pulmonary risk of an exposition for several hours to an altitude of approximately 2600 m in these patients, equivalent to the pressurized cabin of an aircraft at cruising altitude. We examined patients with cystic fibrosis at an altitude of 2660m over a period of 8 hours, performing lung function tests, capillary blood gas analysis and echocardiography at rest. To evaluate the effect of moderate exercise at altitude, we draw additional blood gas samples during cycling at 60 watt. **Results:** We included 34 patients in the study, average age 30.1 years (19-47), 14 women. 32 % of our patients had a PaO<sub>2</sub> of 50 mmHg or lower at rest after 8 h. However, none of them had to be treated with oxygen or

| variable (mean values)   | 500 m | 2660m, at arrival | 2660m, after 8h | moderate exercise 2660m |
|--------------------------|-------|-------------------|-----------------|-------------------------|
| FEV1 % Soll              | 66.3  | 71.1              | 70.4            |                         |
| R tot (kpa*s/l)          | 0.4   | 0.35              | 0.37            |                         |
| ITGV %                   | 118.4 | 133.5             | 136.8           |                         |
| VC max (l)               | 3.97  | 3.96              | 3.95            |                         |
| PEF % Soll               | 71    | 84.9              | 82.2            |                         |
| MEF25 % Soll             | 25.96 | 32.52             | 30.33           |                         |
| PaO <sub>2</sub> (mmHg)  | 75.9  | 52.8              | 52.8            | 47.8                    |
| PaCO <sub>2</sub> (mmHg) | 38.3  | 35.2              | 37.8            | 34.2                    |

and high altitude PaO<sub>2</sub> was 0.69 (p<0.01). In multivariate analysis, MEF25 (percent predicted) was the best predictor of PaO<sub>2</sub> at altitude. **Conclusion:** Even with moderate exercise, patients with cystic fibrosis are able to tolerate PaO<sub>2</sub>-values below 50 mmHg over a period of up to 8 hours. Therefore, some of the international guidelines concerning fitness to fly in these patients may be too rigorous.

**146. CYSTIC FIBROSIS AT EXTREME ALTITUDE**

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There is an increasing number of people with a variety of chronic illnesses traveling to high altitudes. In this report we present a 40 year old individual with cystic fibrosis who travels to extreme altitude (above 5500 m, 18,000ft) while trekking in Nepal. Information about people with cystic fibrosis traveling to altitudes above 2000 m is limited, but most studies report significant oxygen desaturation during exercise at altitudes above 1500 m. We report that this individual trekked to an elevation of 5554 m (Kala Patar) and maintained oxygen saturations within normal range for healthy individuals at similar altitudes.

Baseline pulmonary function data, genotype, medical and exercise history are presented. We conclude that select individuals with cystic fibrosis who are optimally treated and have excellent baseline pulmonary function tests may be able to travel above moderate altitudes.

**148. SAFETY AND EFFECTIVENESS OF PULMONARY REHABILITATION AT MODERATE ALTITUDE IN COPD PATIENTS**

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This study evaluated the impact of a pulmonary rehabilitation program at an average altitude of 1250m in patients with moderate COPD. **METHODS:** Fourteen patients aged 59.42±2.7 years with moderate COPD (FEV-1/FVC=56.5±2.4%, FEV-1=59.14±3.4%pred) that attended our clinic for a 29 day rehabilitation program participated. This is based on an exercise program performed at the anaerobic threshold. All patients performed a maximal cycle ergometer exercise test at entry. A 6 minute walking test (6-MWT) in which SaO<sub>2</sub> was measured each minute and dyspnea was measured at rest and at the sixth minute, was performed at entry and at the end of the stay. **RESULTS:** No patient had a significant problem that caused a stop of the program and a return to low altitude. Distance in the 6-MWT was significantly improved: 480.07±21 vs 530.5±22 m (p<0.001). Dyspnea showed a non-significant trend to diminish: 5.3±0.7 vs 4.59±0.7. SaO<sub>2</sub> did not change significantly: rest 95.15±0.55 vs 96±0.42 %, sixth minute 89.8±1.4 vs 90.7±1.5 %. In conclusion, patients with moderate COPD can stay at an altitude of 1250 meters safely. They can even improve their exercise tolerance with an appropriate exercise program.

#### 149. OBSERVATIONAL FIELD STUDY OF 15 TYPE I DIABETIC MOUNTAINEERS AT HIGH ALTITUDE (ACONCAGUA: 6962m)

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**Objectives:** To observe the management of the disease by diabetic climbers, to reach the summit without complications (serious AMS and ketoacidosis) and to establish a study method to determine variations in insulin requirements at high altitude. **Subjects, material and methods:** 15 (11 male, 4 female) type I diabetic mountaineers (8 summit team, 7 base camp team, 4200 m). Age: 30,4 years (25–45). Time of diabetes: 12,3 years (6–26). Treatment was free regarding injection method (pump/multi-injection) and dose. Every subject recorded blood glucose, carbohydrate intake, exercise, altitude and other events. **Results:** 7 of 8 subjects reached the summit with no serious complications. Because of incomplete records the relation between insulin units and carbohydrate in different situations could not be determined.

**Conclusions:** An optimal management of diabetes and acclimatization were the key for success. All the team was good at self-monitoring in any conditions, had skills to calculate insulin and carbohydrates and the ability to handle early hyper and hypoglycemia. More studies are required to determine a possible variation in insulin requirements at high altitude. Diabetic climbers should not avoid going to altitude, if they are aware of increased risks, of the importance of frequent self-monitoring and acclimatize slowly to avoid AMS.

#### 151. HEMATOLOGICAL RESPONSE IN CHILEAN WORKERS IN INTERMITTENT HYPOXIA (IH)

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A prospective evaluation is performed on hematocrit (Ht), hemoglobin (Hb) and erythropoietin (Epo) at sea level (SL, 2<sup>nd</sup>-6<sup>th</sup> day) and at altitude (HA, 6<sup>th</sup> day), in 18 workers without previous altitude exposure, working 7-day at 4200m by 7-day rest at SL.

| Month       | 0               |          | 12th     |         | 19th     |          | 31th     |         |
|-------------|-----------------|----------|----------|---------|----------|----------|----------|---------|
|             | SL Pre-Exposure | HA       | SL       | HA      | SL       | HA       | SL       | HA      |
| N           | 29              | 23       | 18       | 10      | 13       | 12       | 21       | 16      |
| Ht          | 43.16           | 48.1     | 47.48*   | 50.3    | 47.6*    | 52.7     | 44.92    | 48.03   |
| Hb          | 14.6            | 16.48    | 16.3*    | 17.3    | 16.5*    | 18       | 15.12    | 16.25   |
| EPO (pg/ml) | 6.8–2.4         | 12.5–4.8 | 4.8–1.9* | 9.0–5.2 | 3.5–1.5* | 10.5–5.0 | 2.0–2.0* | 5.6–4.7 |

\*p<0.05 vs pre-exposure

There is evidence of significant increase in Ht, Hb and EPO at every altitude exposure, indicating acute hypoxic effect even after 31 months of IH. During the first 19 months, Ht and Hb increase considerably at SL; their drop after 31 months would indicate acclimatization. The EPO progressive drop up to the 31<sup>st</sup> month would indicate that the acclimatization process is still in evolution. Supported by grant FONDEF/D9711068-Chile, Arturo Prat University

#### 150. PULMONARY ARTERY PRESSURE (PAP) IN CHILEAN MINERS IN INTERMITTENT HYPOXIA (IH)

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The PAP was measured in 22 workers aged  $25 \pm 3$  years, with cardiac ecodoppler (HP-25 MHz) at sea level, normoxia (N) and simulated hypoxia (FiO<sub>2</sub> 11.4%), at pre-exposure and then at 12, 19 and 32 months of IH, working at a 7-day at 4200m by 7-day rest at sea level shift.

| Month                   | 0               |           | 12         |           | 19        |          | 31        |           |
|-------------------------|-----------------|-----------|------------|-----------|-----------|----------|-----------|-----------|
|                         | SL pre-Exposure | Hypoxia   | N          | Hypoxia   | N         | Hypoxia  | N         | Hypoxia   |
| n                       | 31              |           | 20         |           | 10        |          | 22        |           |
| Sat O <sub>2</sub> (%)  | 97,5–1,5*       | 79,4–5,6  | 97,1–1,5*  | 82,8–5,8# | 98,0–1,0* | 81,1–3,3 | 98,8–0,6* | 82,9–4,5# |
| HR (min <sup>-1</sup> ) | 70,3–12,5*      | 84,3–13,1 | 64,6–9,9*# | 74,9–11,0 | 66,1–9,8* | 72,0–7,1 | 68,7–8,6* | 75,2–8,7# |
| PAP mmHg                | 19,0–5,4*       | 31,0–8,1  | 18,9–4,5*  | 33,7–6,3  | 20,2–5,6* | 33,3–5,7 | 17,7–6,4* | 23,6–8,2  |

\* p<0.05 Normoxia vs Hypoxia

# p<0.05 vs pre-exposure

In normoxia, the PAP remained normal after 32 months of IH. There was a significant PAP increase in every simulated acute exposure, with a decreased vascular pulmonary response to hypoxia at the 31<sup>st</sup> month. No cases of vascular hyperreactivity were observed.

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#### 152. AMBULATORY BLOOD PRESSURE MONITORING (ABPM) IN INTERMITTENT HYPOXIA (IH)

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A 24-hour ABPM was performed on 18 workers,  $25 \pm 3$  years, every 15 minutes/day and every 30 minutes/night at 0, 12, 19 and 31 months of IH, at sea level (SL) and at high altitude 3800–4200 m (HA). As abnormality criteria, systolic arterial pressure (SAP) and diastolic arterial pressure (DAP) of  $\geq 135/85$  for daytime and of  $\geq 120/75$  for sleeping time were considered. In every control, the 24-hour Mean Systemic Arterial Pressure results were higher at HA than at SL, with a gradual decrease in both readings starting 19<sup>th</sup> month. The abnormal cases increased as of the 12<sup>th</sup> month both at SL (SAP 26% and DAP 25%), and at HA (PAS 32% and DAP 44%), decreasing at the 31<sup>st</sup> month at SL (SAP 5% and DAP 6%) and at HA (SAP 12% and DAP 17%), figures similar to month 0.

**Conclusion:** After 32 months of IH there is a significant reduction of pressure response and in abnormal cases. There is no deleterious effect on arterial pressure.

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**153. WHITE MOUNTAIN RESEARCH STUDY—2001. LONG-TERM HYPOXIC-HYPOBARIC EXPOSURE (~3,800 M) AS A TERRESTRIAL ANALOG FOR FUTURE PLANETARY MISSIONS: HAEMATOLOGICAL ADAPTATIONS AND CHANGES IN CAPILLARY DENSITY**

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The hypoxic-hypobaric environment reduces the overall physical performance of humans. Already today, under real micro-g conditions astronauts/cosmonauts are frequently exposed to an artificial hypobaric-hypoxic environment during extravehicular activities (EVA). Furthermore, it can be assumed that in future during long-term space flights and/or for base camps on planets like Mars the environmental conditions in the spacecrafts and habitats at the landing site will be hypobaric-hypoxic ones due to financial and logistic reasons. Therefore it is necessary to analyze the acute, intermittent and long-term effects of hypobaric-hypoxic exposure on the human body. In the course of the White Mountain Research Study 2001 we investigated the human long-term adaptation to an altitude of approximately 3,800 m above sea-level (Barcroft Facility, California, USA). It was the aim to study the changes regarding body composition (lean body mass, fat mass, total body water), circulation, blood physiology, muscle metabolism, capillary density and psycho-physiology. We will present here preliminary data regarding the haematological adaptations and the changes of capillary density in muscle fibers (vastus lateralis) due to the long-term high altitude stay. 11 male subjects (age 26.6 ± 2.1 years, body height 1.79 ± 0.05 m, body mass 74.4 ± 10.7 kg, BMI 23.5 ± 3.5) were studied. Five blood samples (before, during, and after) and 2 muscle biopsies were taken (before and after) the five week study. Statistical analysis: MANOVA; SPSS 10.0 für WINDOWS. Packed cell volume [PCV], hemoglobin concentrations @HB; transferrin-receptors [Tfr-R], and erythropoietin [EPO] concentrations increased significantly during the exposure (p<0.01). Ferritin [FER] significantly decreased (p<0.01) and the circulating vascular endothelial growth factor [VEGF] concentrations remained unchanged, although the capillary density increased significantly by approximately 24% (p<0.01). The preliminary data show that 5 week exposure to high altitude (3,800 m) causes a transient increase in [EPO] and the concomitantly [FER] decrease, and [PCV], @HB; and [Tfr-R] increase indicate a sustained stimulation of erythropoiesis combined with a stimulated angiogenesis as shown by the increase in capillary density. It is concluded that during long-term space flights a hypobaric-hypoxic environment inside space crafts or habitats could be used to trigger erythropoiesis and angiogenesis. Sponsored by Deutsches Zentrum für Luft- und Raumfahrt, Germany (Gunga DLR-Project # 50-WB 0022).

**154. SHORT INTERMITTENT EXPOSURE INDUCES ACCLIMATION TO HIGH ALTITUDE, ERYTHROPOIESIS AND INCREASES AEROBIC CAPACITY**

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Different experimental designs and protocols of short-term intermittent exposure to hypoxia in a hypobaric chamber, simulating an altitude of 4,000 up to 5,500 m were able to elicit EPO secretion and hematological adaptive responses. These procedures have also shown their ability to induce acclimation to altitude and also an improvement of aerobic endurance in healthy subjects. Increased erythropoiesis causing a rise in red cell mass and a subsequent increase in blood oxygen transport capacity are the main observed mechanisms for improving performance capacity. The polycitemia was not accompanied by a significant increase in blood viscosity. Short-term intermittent exposure to hypobaric hypoxia increases ventilatory response and SaO<sub>2</sub> during exercise at simulated altitude prior to significant haematological changes. This is interpreted as early acclimatization to altitude. Heart rate during submaximal exercise at simulated altitude shows to be a very sensitive parameter to reveal adaptation to acute hypobaric hypoxia. Monitoring ventilatory response, heart rate and SaO<sub>2</sub> during exercise in hypobaric hypoxia may be a valuable instrument to detect the first signs of acclimatization. Our data indicate that intermittent hypoxia works well, even with limited exposure schedules, time availability of the subjects and their facility may ultimately determine the choice of exposure protocol. We investigate now the oxidative stress induced by intermittent exposure to hypobaric hypoxia