Poster #: 1 .CARDIAC RESPONSE TO VOLITIONAL APNEA IN UNTREATED OBSTRUCTIVE SLEEP APNEA: A PROSPECTIVE OBSERVATIONAL STUDY.

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Introduction: We have previously shown that voluntary apnea during periods of chemosensitization (e.g., altitude) elicits bradyarrhythmias in healthy individuals. Obstructive sleep apnea (OSA) is also associated with chemoreflex hyperactivity and OSA patients have an increased risk of arrhythmias during sleep.Objective: We sought to evaluate whether volitional apnea may elicit bradyarrhythmia in individuals with OSA.Methods: A prospective observational cohort included 8 (5M/3F) untreated OSA patients and 4 (3M/1F) healthy controls matched for age, sex, and, BMI. The mean AHI for the OSA group was 12 ±6 and <5 in the Control group.Results: No differences were observed in baseline Heart Rate (HR) (69±12 beats per minute (bpm) in OSA vs 61±12 bpm in controls, P=0.35) or mean blood pressure (BP) (96±13 mmHg in OSA and 93±3 mmHg in controls, P= 0.65) between groups. The average apnea duration was 23±8 seconds in OSA patients and 32±7 seconds in Controls. During apnea, HR dropped -12±15 bpm in OSA and -16±9bpm in Controls; however, this was not different between groups, (P= 0.60). There were no incidences of arrhythmia in either group during or immediately following apnea. During Voluntary Apnea mean BP increased (+10 ±7mmHg in OSA and +12±5mmHg in Controls), and this increase was not different between groups (P=0.753). Conclusions: Our data suggest no differences in the incidence of bradyarrhythmias during volitional apnea among individuals with untreated OSA versus matched controls. Further participant recruitment may improve the power to detect a clinically important difference in the potentiation of bradyarrhythmia between the OSA group and the control group. Funding: This study is being Funded by NSERC

Poster #: 2 .Vagal Block Attenuates Bradycardia and Arrhythmias During Apnea at High Altitude.

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Background. Voluntary apnea at high-altitude elicits bradycardia and cardiac arrhythmias which are not seen during similar maneuvers at low-altitude. This may be related to hypoxia induced increases in chemoreceptor sensitivity and concomitantly augmented autonomic outflow. While parasympathetic cardiac activity is masked at high-altitude by augmented ventilation, apnea (via the dive reflex) provides a model to mechanistically investigate the effect of high altitude on vagal tone. To isolate the potential influences of hypoxia, chemoreflex sensitivity and/or parasympathetic drive on cardiac conduction, we investigated the heart rate and rhythm response to apnea in 9 (3 female) participants following 6-9 days of high-altitude exposure (3800m) under 1) control conditions (CON); 2), peripheral chemoreceptor blockade using low dose dopamine (DOPA); 3), following vagal block using glycopyrrolate (GLY). Methods. Participants performed a single apnea during each condition. 1 minute of baseline was analyzed

prior to apnea in each condition to obtain resting heart rate and blood pressure. The heart rate and rhythm response were assessed individually for each apnea, with the bradycardic response being evaluated as the drop in heart rate (nadir) minus the preceding baseline. Comparisons across condition were performed using a one-way ANOVA. Results. Dopamine decreased ventilation (L/min) by 58% (CON, 27 ± L/min; DOPA, 15 ± 3L/min; p=0.01), demonstrating a significant peripheral chemoreceptor block. The bradycardic response to apnea was similar between CON and DOPA conditions (-31 ± 18bpm and -33 ± 11bpm), whereas heart rate increased during GLY apneas (+10 ± 4bpm; effect of condition, p<0.001). Interestingly, the incidence of arrhythmia was similar between CON and DOPA conditions, but arrhythmias were attenuated following GLY. Conclusion. Vagal block attenuates bradycardia and arrhythmias during apnea at high-altitude; however, peripheral chemoreceptor inhibition did not alter the heart rate or rhythm response to apnea, suggesting an alternative mechanism underlying heightened vagal tone. Funded by NSERC.

Poster #: 3 .RELATIONSHIP OF NOCTURNAL OXYGEN SATURATION TO BLOOD PRESSURE AT HIGH ALTITUDE. Diana Biggs1, Andrew Burns1, Greta Carlson1, Ilaria Ferrari1, Lukas Sloan1, Linda E. Keyes1. 1University of Colorado

Objective: We evaluated the hypothesis that nocturnal hypoxia at high elevation would cause nocturnal and diurnal elevations in 24h ambulatory blood pressure (ABP).Methods: This prospective observational cohort study of adult lowlanders compared 24h ABP and nocturnal SpO2 during participants' first 24h at high altitude (2470-2700m). ABP was measured hourly 7am-10pm and every 30 minutes 10pm-7am using Welch-Allyn 6100 ABP monitors. SpO2 was measured continuously overnight using Nonin WristOx.Results: We report preliminary data on 9 participants, (mean age = 46 yo, female = 6). Mean basal nocSpO2 was 87%, 95% CI [85-89], mean minimum nocSpO2 75%, 95% CI [70-80]. The mean nocturnal SBP was 121, 95% CI [107-135], mean diurnal SBP 136, 95% CI [124-148], mean nocturnal DBP 67, 95% CI [59-75], and mean diurnal DBP 79, 95% CI [71-87]. Lower minimum nocSpO2 was weakly associated with higher mean diurnal SBP (R2=0.4), but not with mean nocturnal SBP (R2=0.1) nor the measured SBP at the time of minimum SpO2 (R2=0.2). Higher oxygen desaturation index was weakly associated with higher mean diurnal SBP (R2=0.4), but not with nocSBP (R2=0.1). Greater percent of nocturnal time < SpO2 88% was weakly correlated with higher mean nocSPB (R2=0.3), but not with diurnal SBP (R2=0.2). We found no associations between DBP and nocSpO2 parameters. In those with normal nocturnal BP dipping (n=4), the mean percent time <88% SpO2 was 34% versus 60% for non-dippers (n=4).Conclusion: Lower nocturnal SpO2 was associated with higher diurnal but not nocturnal SBP at high altitude. In contrast, DBP was not associated with nocturnal SpO2. Our preliminary results suggest that nocturnal hypoxia plays a role in the elevation of diurnal SBP observed at high altitude.Funding: Wilderness Medical Society Hultgren grant.

Poster #: 4 .RELATIONSHIP OF NOCTURNAL OXYGEN SATURATION TO SLEEP QUALITY AT HIGH ALTITUDE. Diana Biggs1, Andrew Burns1, Greta Carlson1, Ilaria Ferrari1, Lukas Sloan1, Linda E. Keyes1. 1University of Colorado

Objective: Few studies have investigated sleep quality vs. nocturnal SpO2, but rather have compared sleep fragmentation and nocturnal wakening to sleep quality. We evaluated the hypothesis that nocturnal hypoxia at high elevation would lead to poorer sleep quality.Methods: This prospective observational cohort study of adult lowlanders compared sleep quality measured by the Groningen Sleep Quality Scale (GSQ) and nocturnal SpO2 during participants' first 24h at high altitude (2470-2700m). SpO2 was measured continuously overnight using the Nonin WristOx.Results: We report preliminary data on 9 participants, (mean age = 46 yo, female = 6), none with a history of OSA. Mean basal nocSpO2 was 87%, 95% CI [85-89], mean minimum nocSpO2 75%, 95% CI [70-80] and mean percent time SpO2<88% 51%, 95% CI [27-75]. Mean GSQ was 7, 95% CI [4-10]. GSQ scores were not associated with minimum nocSpO2 (R2 = 0.0) or percent of time SpO2<88% (R2 =0.0). Lower mean nocSpO2 was associated with better perceived sleep quality (lower GSQ) (R2=0.6).Conclusion: Contrary to our hypothesis, despite participants reporting poor sleep quality the first night after arrival to high altitude, lower nocturnal SpO2 was not associated with worse sleep quality. We are unsure why higher mean nocturnal SpO2 was associated with worse sleep quality but suspect other unmeasured variables affect sleep quality.Funding: This work was supported by a Wilderness Medical Society Hultgren grant.

Poster #: 5 .INVESTIGATING SEX-RELATED DIFFERENCES IN PERIPHERAL FATIGABILITY AT HIGH ALTITUDE IN HUMANS. Christina D Bruce1, Sianna PC Tomich1, Travis D Gibbons1, Philip N Ainslie1, Chris J McNeil1. 1University of British Columbia Okanagan, Canada

Objective: Whole muscle intrinsic fatigability (i.e., peripheral fatigability) is exacerbated when male lowlanders become acutely hypoxic, which acclimatization to high altitude (HA) restores. It is currently unknown if peripheral fatigability of females is altered when oxygen availability is reduced. Therefore, we investigated the hypothesis that peripheral fatigability would be greater in females than males when acutely exposed to HA and that both groups would fatigue similarly following 14 days of residing at HA. Methods: The knee extensors of the dominant leg were fatigued via 144 electrically evoked contractions (7 pulses at 10Hz; 1.25s between trains of stimuli) in 10 females and 9 males at sea level (SL; 344m), and again after 2 and 14 days of residing at 3800m (HA1 and HA2, respectively). Initial peak force of the evoked contractions was ~25% of maximal voluntary force. To quantify fatigability, mean peak force of the last 8 contractions was expressed relative to the mean of the first 8 contractions. Results: By the end of the fatigue protocol at SL, peak force was more impaired for females (21.9%) than males (10.5%; P=0.035). At HA1 (22.8%) and HA2 (25.5%), force loss was greater for males compared to SL, whereas the fatigability of females did not change from SL (26.4 and 23.0% at HA1 and HA2, respectively). In other words, females and males experienced similar levels of fatigue while residing at altitude, but when considering changes from SL, only the fatigability of males was impaired by HA. Conclusion: Contrary to our hypothesis, female skeletal muscle fatigability was not more impaired at HA than males. These findings are relevant for determining how sex-

related differences in skeletal muscle could affect fatigability when oxygen availability is impaired. Funding: NSERC and CFI/BCKDF

Poster #: 6 .EXPEDITION 5300: CEREBRAL HOMEOSTASIS AND ORTHOSTATIC RESPONSES IN RESIDENTS OF THE HIGHEST CITY IN THE WORLD. Julien Brugniaux1, Michael Furian1, Mathilde Ulliel-Roche1, Connor A Howe2, Fanny Zerizer1, Mathieu Marillier1, Anne-Catherine Bernard1, Ivan Hancco1, Benoit Champigneulle1, Sébastien Baillieul1, Emeric Stauffer3, Philip N Ainslie2, Aurélien P Pichon4, Stéphane Doutreleau1, Samuel Vergès1. 1Université Grenoble Alpes, France, 2University of British Columbia, Kelowna, British Columbia, Canada, 3Université Claude Bernard Lyon 1, France, 4Université de Poitiers, France

Background. Permanent residence at high-altitude and chronic mountain sickness (CMS) may alter the cerebrovascular homeostasis and orthostatic responses. Methods. 15/13/17 healthy participants living at sea-level (LL), 3,800m (HL3800m) and 5,100m (HL5100m), respectively, and 31 additional highlanders with CMS living at 5,100m were recruited. Middle cerebral artery mean blood velocity (MCAv-transcranial Doppler ultrasound), cerebral oxygen delivery (CDO2), mean blood pressure (MAP-finger plethysmography), heart rate variability (low/high frequency – LF/HF, respectively) and baroreflex sensitivity (BRS) were assessed during 3 phases of a tilt test; while sitting, during standing-up and while standing for 3min. Cerebral autoregulation index (ARI) was estimated (ΔMCAv%baseline)/ΔMAP%baseline) in response to standing-up. Results. Altitude and CMS were associated with hypoxemia and elevated hemoglobin concentration. While sitting, MAP increased, MCAv and LFpower decreased with altitude but were not further affected by CMS and CDO2 was preserved. BRS was comparable across all altitudes, but reduced with CMS. With standing-up, altitude and CMS were associated with a lesser reduction in MAP; ARI was unaffected by either altitude or CMS. Compared to sitting in lowlanders, standing was associated with preserved MCAv, CDO2 and BRS across all altitudes. The LF/HF ratio increased in HL5100m compared to LL and HL3800m from sitting to standing. Likewise, in CMS while standing, MCAv was reduced but CDO2 remained unaffected; however, CMS showed blunted LFpower, HFpower and LF/HF ratio responses to standing compared to sitting. Conclusions. Despite altitude- and CMS-associated hypoxemia, erythrocytosis and impaired blood pressure regulation (CMS only), cerebral homeostasis while sitting, standing-up and standing was overall preserved. The origin of CMS-related neurological symptoms remains to be established.

Poster #: 7 .Loop Gain Response to Increased Cerebral Blood Flow at High-Altitude. . Andrew Burgess1, Gareth Andrews2, Katie Colby2, Samuel Lucas3, Kate Sprecher2, Joseph Donnelly4, Philip Ainslie5, Aparna Basnet6, Keith Burgess7. 1Canberra Sleep Clinic, 2Peninsula Sleep Clinic, 3University of Birmingham, 4University of Auckland, 5University of British Columbia, 6Banner University Medical Centre, 7Macquarie University

Background: Loop gain (LG) describes the stability of a negative-feedback control system; defined by magnitude of response to a disturbance, e.g. hyperpnea to an apnea in central sleep apnea (CSA). The lower the value the more stable the system. Objective: To compare LG before and during pharmacological increases in CBF at high altitude (HA). Methods:

Polysomnography (PSG) was performed on 11 volunteers after administration of I.V. Acetazolamide (ACZ-10mg/kg) + Dobutamine (DOB-2-5 μg/kg/min) to increase CBF. CBF measured by duplex doppler. CSA was measured during NREM sleep. The LG was calculated (LG=2π/(2πDR-sin2πDR) using duty ratio (DR)(hyperpnea/hyperpnea+apnea). Results: Compared to placebo-control, ACZ/DOB showed a reduction in LG (1.29±0.35 vs 1.90±0.23, p=0.0004) and a significant increase in the DR (0.79±0.21 vs 0.52±0.03, P=0.002) while ACZ/DOB increased CBF (718±120 vs 526±110ml/min, P<0.001). There was no significant change in arterial blood gases, minute ventilation (VE), or hypoxic ventilatory response (HVR), however there was a 29% reduction of hypercapnic ventilatory response (HCVR) (4.2±2.8 vs 5.9±2.7 L/min, P=0.1). Conclusion: Pharmacological elevation in CBF significantly reduced LG and severity of CSA. We speculate the effect was on HCVR "Controller Gain", rather than "Plant-Gain", because PaCO2 and VE were unchanged. An effect via reduced circulation time is unlikely, because the respiratory-cycle length was unchanged.

Poster #: 8 .MAXIMAL FAT OXIDATION AND TOTAL ENERGY EXPENDITURE ARE LOWER DURING SUBMAXIMAL STEADY-STATE CYCLING EXERCISE AT 3,800 M. Hannah Caldwell1, Jack Talbot2, Elliott Jenkins2, Connor Howe1, Jonathan Little1, Michael Stembridge2, Philip Ainslie1, Travis Gibbons1. 1Centre for Heart, Lung and Vascular Health, School of Health and Exercise Sciences, University of British Columbia Okanagan, Kelowna, BC, Canada, V1V 1V7, 2Cardiff School of Sport and Health Sciences, Cardiff Metropolitan University, Cardiff, UK

Objective: This study investigated substrate oxidation and energy expenditure during exercise at an intensity that elicits maximal fat oxidation at sea level (SL) and following 3-8 days at 3,800 m (HA). Methods: Healthy adults (SL: n=16, 9/7 females/males; HA: n=15, 7/8 females/males) completed the following protocols at SL and HA: resting metabolic rate, steady-state incremental submaximal exercise to determine maximal fat oxidation (FATmax) and peak oxygen uptake (VO2peak) tests on a semi-recumbent cycle ergometer. Thereafter, 60 minutes of steady-state cycling at FATmax was performed. Results: There was no difference between the absolute exercise intensity where FATmax was achieved between HA and SL (HA: 47 W, 95% CI: 39 to 56 vs. SL: 54 W, 95% CI: 45 to 64; P=0.081). The FATmax exercise intensity relative to maximal VO2peak wattage was also not different between altitudes (HA: 22 % VO2peak, 95% CI: 19 to 25 vs. SL: 23 % VO2peak, 95% CI: 21 to 26; P=0.529). Maximal fat oxidation achieved during the FATmax test was 26.9 % lower at HA versus SL (HA: 0.28 grams/min, 95% CI: 0.23 to 0.33 vs. SL: 0.38 grams/min, 95% CI: 0.32 to 0.45; P=0.002) which was likely attributable to the 24.4 % reduction in relative contribution of fats to total energy expenditure at rest at HA (HA: 34 % fats, 95% CI: 26 to 42 vs. SL: 45% fats, 95% CI: 36 to 53; P=0.048). Further, as there were no differences between the relative contribution of carbohydrates to total energy expenditure at rest (HA vs. SL: P=0.105) or maximal carbohydrate oxidation during submaximal steady-state exercise (HA vs. SL: P=0.058), total energy expenditure was 17.0 % lower during 60 minutes of steady-state cycling exercise at altitude-specific FATmax exercise intensity (HA: 263 kcal, 95% CI: 227 to 298 vs. SL: 316 kcal, 95% CI: 281 to 351; P=0.004). Conclusions: Reductions in the relative contribution of fats to resting energy expenditure and lower maximal fat oxidation during submaximal cycling exercise explains, in part, the attenuated total energy expenditure during 60 minutes of low intensity

cycling at high-altitude. The implications of these findings on optimizing energy requirements during prolonged submaximal exercise warrants further research.

Poster #: 9 .THE IMPACT OF ACUTE MILD CARBON MONOXIDE EXPOSURE ON FLOW-MEDIATED DILATION. Nicholas Cheung1, Scott Thrall2, Sean Van Diepen3, Craig Steinback1. 1University of Alberta, Faculty of Kinesiology, Sport and Recreation, 2University of British Columbia Okanagan, 3University of Alberta, Faculty of Medicine and Dentistry

Objective: Endogenous carbon monoxide (CO) is vasoactive, influencing endothelial dependent and independent pathways. Exogenous CO has also been shown to have vasoactive effects following prolonged exposure. We examined endothelial function, measured via flow-mediated dilation (FMD), following mild, acute carbon monoxide (CO) exposure in 19 healthy non-smoking participants (n=10 females). Methods: Participants were assessed prior to and following a room air (SHAM), or CO rebreathe exposure on two consecutive days in a randomized single-blinded crossover design. The Schmidt-Prommer rebreathe method for the measurement of Hb mass was used for the CO exposure. We hypothesized CO would increase endothelial-dependent vasodilation in vascular smooth muscle.Results: Baseline brachial artery diameter was not different between sham (3.84±0.75mm) and CO rebreathe (3.77±0.81mm, p=0.344). Baseline arterial bulk flow was also not different between SHAM (34.48± 36.90ml/min) and CO rebreathe (31.73±19.29, p=0.932) Baseline forearm vascular conductance was not significantly different between the two days (SHAM=0.50±0.32, CO=0.63±0.52, p=0.865).Carboxyhemoglobin was elevated following the CO (5.6±1.2%, Mean ± SD) compared to SHAM (1.5 ± 0.3%) rebreathe (p<0.001)No changes in absolute FMD (SHAM = 0.23±0.20mm, CO = 0.24±0.22mm, interaction p=0.690), FMD% (SHAM = 6.69±6.36, CO = 6.46±5.89, interaction p=0.840), or FMD:ssAUC (SHAM = 2.61x10–-5 ± 1.94x10-5, CO = 2.82x10-5 ± 3.55x10-5, interaction p=0.200) were observed.Conclusion: Mild elevation of Carboxyhemoglobin (COHb%) and resulting hypoxemia does not impact resting arterial diameter, flow, or endothelial function in a healthy, non-smoking population. The Schmidt-Prommer rebreathe protocol for the measurement of Hb mass does not impact vascular endothelial function.

Poster #: 10 .A COMPARISON OF METHODS OF ASSESSING PATIENT OXYGENATION DURING GENERAL ANAESTHESIA AS PART OF A LARGER RANDOMISED CONTROLLED TRIAL (PULSE Ox) . Andrew Cumpstey1, Anna Clark1, Magdalena Minnion1, Helen Moyses1, Daniel Martin2, Mark Edwards1, Martin Feelisch1, Michael Grocott1. 1University of Southampton, 2University of Plymouth

Background: Anaesthetists routinely use oxygen saturations to monitor patients' oxygenation during general anaesthesia, but the constraints of this scale (maximum of 100%) means that hyperoxaemia may remain undetected for extended periods of time during surgery. The Oxygen Reserve Index ('ORi') is a novel continuous and non-invasive measure of oxygenation status, which may allow better detection of perioperative hyperoxaemia.Objective: This study aimed to compare the ORi to other routine methods of assessing oxygenation status during general anaesthesia.Methods: Twenty-eight adult patients undergoing major (defined as needing

a central venous catheter) abdominal surgery for cancer resection received either 30%, 55% or 80% oxygen throughout anaesthesia. Patients and research staff remained blinded to the allocated intervention. Partial arterial pressures of oxygen (PaO2), peripheral oxygen saturation (SpO2) and ORi were measured and compared throughout each case.Results: The correct targets were achieved with good group separation (mean[SD] FiO2: 33.2[4.3]%/55.1[3.6]%/79.8[3.3]% for 30%/55%/80% groups respectively, $p < 0.001$). Mean SpO2 readings were not different between groups (98.0[1.3]%/98.8[1.1]%/99.3[0.4]%, $p = 0.22$). Hypoxaemia (SpO2 <90%) was rare (median(IQR): 0.11(0.03-0.44)%/0.00(0.00-0.30)%/0.00(0.00-0.01)% of total anaesthetic duration, $p = 0.03$). PaO2 increased significantly with higher FiO2 (18.1[3.9]/27.7[7.0]/46.4[9.1]kPa, $p < 0.001$) but required arterial sampling, distant processing and only allowed intermittent monitoring. ORi also increased significantly with higher FiO2 (0.13[0.18]/0.51[0.32]/0.72[0.25], $p < 0.001$), and this point-of-care test could be measured continuously in a non-invasive fashion.Conclusion: ORi allows a convenient, simple and non-invasive way of continuously monitoring for hyperoxaemia in anaesthetized patients and could have clinical application in helping anaesthetists avoid hyperoxaemia during general anaesthesia.Funding: Doctoral Fellowship (Southampton NIHR Biomedical Research Centre). Equipment loaned by Masimo for this study.

Poster #: 11 .INTRAOPERATIVE OXYGEN CONCENTRATIONS INCREASE PERIOPERATIVE OXIDATIVE STRESS IN A DOSE-DEPENDENT MANNER – A RANDOMISED CONTROLLED TRIAL (PULSE Ox) . Andrew Cumpstey1, Anna Clark1, Magdalena Minnion1, Renato Nogueira2, Helen Moyses1, Daniel Martin3, Jose Tanus-Santos2, Mark Edwards1, Michael Grocott1, Martin Feelisch1. 1University of Southampton, 2University of São Paulo, 3University of Plymouth

Background: The World Health Organization (WHO) recommends all anaesthetised patients receive 80% oxygen during surgery to reduce the risk of surgical site infection (SSI). Results from the PROXI trial (no difference in SSI rates between 30% and 80% oxygen but possibly worse postoperative outcomes with 80% oxygen) would caution against this but were considered 'mechanistically implausible' (WHO).Objective: To investigate whether administering higher inspired oxygen concentrations during anaesthesia might increase systemic oxidative stress (and therefore predispose to adverse outcomes).Methods: Twenty-eight adult patients undergoing major (central venous catheter required) abdominal surgery were randomly allocated to receive 30%, 55% or 80% oxygen throughout anaesthesia. Paired arterial and central venous blood gases (to measure oxygen extraction) and samples were collected 2-hourly. Total nitroso species (RxNO) and Nitric Oxide (NO) scavenging were quantified using gas phase chemiluminescence. Total free thiols (TFTs) and ferric reducing ability of plasma (FRAP) were measured colorimetrically.Results: Higher oxygen was associated with higher RxNO concentrations (Mean[SD] 52.6[19.1]/100.2[36.1]/91.2[34.4] nM for 30/55/80% respectively, $p = 0.05$) & reduced NO scavenging (4.4[0.7]/3.5[0.4]/3.6[0.6]uM, $p = 0.02$) at the end of surgery. Normalized TFTs increased throughout surgery but with no difference between groups (4.5[0.3]/4.1[0.3]/4.2[0.4], $p = 0.26$). FRAP concentrations did not change overall (866.5[52.0]/908.1[37.1]/810.6[57.4], $p = 0.42$) but decreased markedly in some patients. Why inter-individual perioperative oxygen sensitivity differs merits further investigation. Tissue oxygen extraction reduced significantly with 80% oxygen (0.28[0.10]/0.23[0.08]/0.20[0.06], $p < 0.001$), supporting previous data in critically ill patients.Conclusion: Higher intraoperative

oxygen concentrations significantly increase markers of oxidative stress, lower systemic antioxidant capacity and decrease oxygen extraction during surgery in a dose-dependent fashion.Funding: Doctoral Fellowship (Southampton NIHR Biomedical Research Centre)

Poster #: 12 .MAPPING RESTING CEREBRAL BLOOD FLOW DISTRIBUTION USING MAGNETIC RESONANCE IMAGING DURING A STEP CHANGE IN OXYGEN TENSION . James Duffin1, Ece Su Sayin1, Olivia Sobczyk1, Julien Poublanc2, Harrison Levine1, David Mikulis2, Joseph Fisher 1. 1University of Toronto, Canada, , 2University Health Network, Toronto, Canada.

Mapping RESTING cerebral blood flow DISTRIBUTION using magnetic resonance imaging DURING a step change in oxygen tension James Duffin, Ece Su Sayin, Olivia Sobczyk, Julien Poublanc, Harrison T. Levine, David J. Mikulis, Joseph A. Fisher University of Toronto, Canada, j.duffin@utoronto.caObjective: We examined the premise that a step change in lung oxygen tension generates a step change in arterial deoxyhemoglobin concentration, which, acting as a susceptibility contrast agent during magnetic resonance imaging (MRI), enables the calculation of resting cerebral perfusion measures.Methods: In 24 volunteers we precisely controlled inspired oxygen tensions to deoxygenate their arterial blood to target PO2 of 40 mmHg for 2 consecutive 60 s intervals. Each interval concluded with a rapid step reoxygenation accomplished during a single inspiration. The step reoxygenation produced a step decrease in deoxyhemoglobin and its susceptibility effect as it passed though the cerebral vasculature and was detected as an increase in the blood oxygen level dependent (BOLD) signal with MRI. These BOLD signal changes were assumed to result from a step input function and analysed to calculate voxel wise hemodynamic measures. Anatomical maps of these measures for the 24 volunteers were combined to calculate average measures maps. In addition, example maps from a healthy control and a patient were compared with maps calculated with a conventional deconvolution-based method that requires an arterial input function. Results: All the maps from the step analysis showed similar regional differences to those seen in published maps using deconvolution-based methods requiring the identification of an arterial input function. The patient example maps showed regional areas corresponding to the patient's known pathology. Conclusion: A step change in oxygen tension can be used with magnetic resonance as a non-invasive means of imaging and calculating resting cerebral perfusion measures.

Poster #: 13 .CHARACTERIZING THE CARDIOVASCULAR COMPENSATORY RESPONSES TO ORTHOSTATIC STRESS AT SEA-LEVEL AND HIGH-ALTITUDE. Jennifer S Duffy1, Travis D Gibbons1, Liisa Wainman1, Elliott Jenkins2, Jennavieve R Crockett3, Philip N Ainslie1, Christopher R West1, Alexandra M Williams1. 1Centre for Heart, Lung and Vascular Health, University of British Columbia, Kelowna, BC, Canada, 2Cardiff Centre for Exercise & Health, Cardiff Metropolitan University, Cardiff, United Kingdom., 3Kelowna Secondary School, Kelowna, BC, Canada

OBJECTIVE: To determine the relative contributions of cardiac output (Q) and total peripheral resistance (TPR) in maintaining blood pressure during orthostatic stress at sea-level and high-altitude. We further interrogated how changes in leg arterial vascular conductance and leg venous compliance might contribute to these responses. METHODS: Seventeen young healthy

humans (27 ±4 years, 9F) completed a head-up-tilt (HUT) comprising four 5-minute stages of 0°, 20°, 40°, and 60° at sea-level (Kelowna, 355m) and high-altitude (days 3-5 at Barcroft Field Station, 3800m). At 2-5 minutes into each stage, superficial femoral artery blood flow was measured via duplex ultrasound and mean arterial blood pressure (MAP), stroke volume (SV) and heart rate (HR) were assessed via automated sphygmomanometry, echocardiography and electrocardiogram, respectively. Venous compliance was estimated via great saphenous vein pressure (direct catheterization) and calf volume (air plethysmography). RESULTS: Symptoms of orthostatic intolerance prematurely terminated the study in 2 and 4 individuals at sea-level and high-altitude, respectively. MAP was 9 ±7 mmHg higher at high-altitude ($p<0.0001$), driven by a tachycardia-mediated (+11 ±9 bpm, $p=0.0002$) increase in Q (0.5 ±0.2 L/min, $p=0.0025$). SV was unchanged at high-altitude ($p=0.2478$) despite a 9 ±7% reduction in blood volume ($p=0.0002$) and no change in arterial conductance, venous capacitance or compliance (all $p>0.1425$). Irrespective of altitude, upon HUT to 60° (or last completed stage) MAP increased by 4 ±5 mmHg ($p=0.0101$); mediated via increased TPR (3.0 ±2.9 mmHg/L·min-1, $p=0.0013$) that compensated for decreases in SV (-29.1 ±9.3 mL, $p<0.0001$) and Q (-0.5 ±0.5 L/min, $p=0.0025$). Arterial conductance and venous compliance decreased linearly with HUT, independent of altitude (both $p\leq0.0006$). CONCLUSION: MAP is maintained or enhanced with tilt at both altitudes owing primarily to increases in TPR, reflected by decreases in venous compliance and arterial conductance.

Poster #: 14 .ACTIVE ASCENT ACCELERATES THE TIME COURSE OF ACUTE MOUNTAIN SICKNESS (AMS) IN AMS-SUSCEPTIBLE INDIVIDUALS AT 3600M

. Peter Figueiredo1, Steven Landspurg1, Jon Femling2, Jason Williams2, Mark Buller1, J Philip Karl1, Janet Staab1, Reed Hoyt1, Aaron Reilly2, Trevor Mayschak2, Emma Atkinson1, Tim Mesite1, Beth Beidleman1. 1US Army Research Institute of Environmental Medicine, 2University of New Mexico

Objective: Acute mountain sickness (AMS) typically peaks following the first night at high altitude (HA) and resolves over the next 2-3 days but the impact of active ascent on the time course of AMS is debated. Methods: To determine the impact of ascent conditions on the incidence, severity, and time course of AMS, 78 healthy Soldiers (mean±SD; age=26±5yr) were tested at baseline residence, transported to Taos, NM (2845m), then hiked (n=39) or were driven (n=39) to HA (3600m), and stayed for 4 days. AMS Cerebral Factor Score (AMS-C) was assessed using the Environmental Symptoms Questionnaire at HA twice on day 1 (HA1), five times on days 2 and 3 (HA2 and HA3) and once on day 4 (HA4). If AMS-C was ≥0.7 on any assessment, individuals were categorized as AMS-susceptible (AMS+; n=33); others were non-susceptible (AMS-; n=45). The peak AMS incidence and severity were recorded daily and used for analyses. Results: The AMS- group demonstrated no difference in AMS incidence or severity between active and passive ascent at 3600m. The AMS+ group, however, demonstrated a higher AMS incidence in the active vs. passive group on HA1 (93 vs. 56%, $p=0.001$), similar incidence on HA2 (60 vs. 78%, $p=0.10$), lower incidence on HA3 (33 vs. 67%, $p=0.003$), and similar incidence on HA4 (13 vs. 28%, $p=0.12$). The AMS+ group also demonstrated a higher AMS severity score in the active vs. passive group on HA1 (1.35±0.97 vs. 0.90±0.70, $p=0.02$), similar score on HA2 (1.00±0.97 vs. 1.34±0.70, $p=0.08$), and lower score on HA3 (0.56±0.55 vs. 1.02±0.75, $p=0.005$) and HA4 (0.32±0.41 vs. 0.60±0.72, $p=0.05$). Conclusion: Active compared to passive ascent accelerated the AMS time course in AMS+ individuals with more

individuals sick on HA1 and less individuals sick on HA3 and HA4. Authors' views not official U.S. Army or DoD policy. Funding: USAMRDC

Poster #: 15 .EFFECTS OF NALTREXONE ON SLEEP QUALITY AND PERIODIC BREATHING AT HIGH ALTITUDE. Katharine Foster1, James Anholm2, Gary Foster3, Prajan Subedi2. 1Emergency Medicine, Loma Linda University School of Medicine, Loma Linda, CA 92354, 2Pulmonary & Critical Care, VA Loma Linda Healthcare System & Department of Medicine, Loma Linda University School of Medicine Loma Linda, CA 92357, 3Cardiology, St. Charles Health System, Bend, OR 97701

Objective: This study examined the role of the Mu-opioid receptor (MOR) on breathing and sleep at high altitude (HA). We hypothesized that MOR blockade with naltrexone would result in higher nocturnal oxygen saturations, fewer apneas and improved sleep at high altitude.Methods: This double blind, placebo-controlled, crossover study included 9 healthy subjects aged, 27.9 ± 4.6 years. Two overnight trips spaced at least two weeks apart occurred from Loma Linda, CA (355m) to Barcroft Laboratory, CA (3810m) for each arm. Subjects took either 50 mg naltrexone or matching placebo at bedtime. Sleep metrics were recorded using WatchPATTM device (Itamar Medical Ltd.). Subjective data was measured with the Groningen Sleep Quality Scale, Stanford Sleepiness Scale and Lake Louise Score (LLS) for acute mountain sickness (AMS).Results: Mean overnight SpO2 was lower after taking naltrexone, 81 ± 6% vs. 83 ± 4% (mean difference 1.9 ± 2.1%), 95%CI=0.1–3.6, p=0.04). Minimum overnight SpO2 was lower on naltrexone 70 ± 6% vs. 74 ± 4% (dif. 4.6% ± 4.3%) CI=1.0–8.2, p=0.02). Total sleep time and total apnea-hypopnea index(AHI) were not different. Subjective sleep quality was significantly worse on naltrexone measured via Groningen ($p<0.03$) and Stanford Sleepiness Scale ($p<0.03$). AMS measure via the LLS was significantly worse while taking naltrexone ($p<0.03$).Conclusion: In contrast to our hypothesis, this study demonstrated a significant decrease in oxygen saturation and sleep quality with no change in sleep time or AHI. AMS scores were significantly worse after taking naltrexone. To our knowledge this is the first study to test physiologic effects of MOR blockade in humans at altitude. Further characterization of the MOR's vasoactive and sympathetic modulation and its effects on regulation of cerebral blood flow are needed to further interpret these results.

Poster #: 16 .Effects of Pentoxifylline on Sleep and Periodic Breathing at High Altitude. Katharine Foster1, Craig Steinback2, Travis Gibbons3, Connor Howe3, Andrew Steele3, Joshua Tremblay4, Philip Ainslie3, James Anholm5, Prajan Subedi5. 1Emergency Medicine, Loma Linda University School of Medicine, Loma Linda, CA 92354, fostkath@gmail.com, 2University of Alberta, Edmonton, Alberta, Canada, 3University British Columbia Okanagan, Kelowna, BC, Canada, 4School of Sport and Health Sciences, Cardiff Metropolitan University, Cardiff, UK, 5Pulmonary & Critical Care, VA Loma Linda Healthcare System & Department of Medicine, Loma Linda University School of Medicine Loma Linda, CA 92357

Objective: This study examined the effect of pentoxifylline on sleep at altitude with the hypothesis that pentoxifylline would improve arterial oxygen saturation during sleep and reduce the amount of periodic breathing during sleep when compared to placebo.Methods: Of 16

participants, 13 had usable sleep data (6M/7F, age = 26 ± 4 years) in this double blinded, randomized, placebo-controlled crossover trial. After residing at 3810m altitude for approximately one- and one-half weeks, participants received either pentoxifylline ER 400mg or matching placebo at bedtime followed by the alternate pill two nights later. The order of medication vs. placebo was randomized. Sleep data was recorded with WatchPAT® (Itamar Medical Ltd.) device.Results: Total sleep time was decreased on pentoxifylline compared to placebo (366 ± 90 min vs. 420 ± 71 min, p=0.02). Time spent sleeping in the supine position, but not in the prone position, was also reduced with pentoxifylline (228 ± 112 min vs. 178 ± 125 min, p=0.01). Cumulative time spent with SpO2 < 88% was lower on pentoxifylline (258 ± 80 min vs. 338 ± 108, p=0.03). The Respiratory Disturbance Index (RDI) and Apnea-Hypopnea Index (AHI) were reduced in the prone position with pentoxifylline compared to placebo: RDI (63.4 ± 34.4 vs. 82.2± 31.1, p=0.01), AHI (63.1 ± 34.8 vs. 81.6 ± 31.0, p=0.01). There were no significant differences in overnight mean arterial oxygen saturation or total number of oxygen desaturations.Conclusion: These results indicate that pentoxifylline reduced overall sleep time and periodic breathing in the prone position with no change in overall nocturnal oxygen saturation. Further study with more prolonged use of pentoxifylline at higher altitude will be needed to extend these findings.

Poster #: 17 .ACUTE MOUNTAIN SICKNESS IS ASSOCIATED WITH REDUCED REACTION TIME FOLLOWING BOTH ACTIVE AND PASSIVE ASCENT TO 3600M. Karl Friedl1, Steven Landspurg1, Peter Figueiredo1, Janet Staab1, Mark Buller1, J Philip Karl1, Reed Hoyt1, Jon Femling2, Jason Williams2, Aaron Reilly2, Trevor Mayschak2, Emma Atkinson1, Tim Mesite1, Beth Beidleman1. 1US Army Research Institute of Environmental Medicine, 2University of New Mexico

Objective: Cognitive performance is known to decrease following acute exposure to high altitude (HA) (>3500m) but it is unknown whether acute mountain sickness (AMS) and active ascent affects the cognitive decline. Methods: To determine whether reaction time is differentially impacted at HA by the presence of AMS and ascent conditions, 78 healthy Soldiers (mean±SD; age=26±5yr) were tested at baseline residence (BLR), transported to Taos, NM (2845m), then hiked (n=39) or were driven (n=39) to a HA facility at 3600m and stayed for four days. AMS-Cerebral Factor Score (AMS-C) was assessed using the Environmental Symptoms Questionnaire at HA twice on day one (HA1), and five times on days two (HA2) and three (HA3). If AMS-C was ≥0.7 at any assessment, individuals were categorized as AMS-susceptible (AMS+; n=33); others were non-susceptible (AMS-; n=45). Simple reaction time (SRT), fatigued reaction time (FRT) and go-no-go choice reaction time (GNG) were measured using the Automated Neuropsychological Assessment Metrics (ANAM) in the mornings on BLR, HA2, and HA3. Results: Ascent conditions did not differentially impact reaction times. The percent change (%) in SRT from BLR was more negative in AMS+ vs. AMS- groups on HA2 (-10.8±17.3 vs. -3.8±13.8, p=) but not HA3 (-4.7±13.1; 0.0±12.0, p=). Similarly, the percent change (%) in FRT from BLR was more negative in the AMS+ group on HA2 (-13.2±19.5 vs. -5.6±20.9) but not HA3 (-2.6±14.7; -4.3±18.4). There were no changes in GNG from SL to HA1 or HA2. AMS-C was also negatively correlated with SRT and FRT, respectively, at both HA2 (r=-0.32, p=0.004; r=-0.29, p=0.01) and HA3(r=-0.38, p=0.001; r=-0.23, p=0.04) but GNG was only negatively correlated at HA2 (r=-0.35, p=0.004). Conclusion: Symptoms of AMS were

associated with greater decrements in reaction time, regardless of ascent conditions. Authors' views not official U.S. Army or DoD policy. Funding: USAMRDC

Poster #: 18 .PARTIAL PRESSURE OF ARTERIAL OXYGEN IN HEALTHY AT ALTITUDE. A META-ANALYSIS USING INDIVIDUAL PATIENT DATA . Aglaia Forrer1, Thomas Gaisl1, Ahmet Sevik1, Michelle Meyer1, Luzi Senteler1, Mona Lichtblau1, Konrad E Bloch1, Silvia Ulrich1, Michael Furian1, 2. 1Department of Respiratory Medicine, University Hospital of Zurich, Zurich, Switzerland, 2Research Department, Swiss University of Traditional Chinese Medicine, Bad Zurzach, Switzerland

Importance With increasing altitude, the partial pressure of inspired oxygen falls and consequently the arterial partial pressure of oxygen (PaO2) decreases. Even though this phenomenon is well known to occur in healthy people, the extent of the reduction as a function of altitude remains unknown.Objective The aim of this study was to present an effect size for the decrease in PaO2 that comes with each kilometre vertical gain and to identify factors influencing PaO2 at altitude. The study is registered at www.crd.york.ac.uk/prospero:CRD42021283236.Data Sources and Study Selection A systematic search of PubMed and Embase was performed from database inception to March 04, 2022. Peer-reviewed, prospective studies in healthy adults providing arterial blood gas analysis at low altitude (<1500m) and within the first 3 days at the target altitude (≥1500m) were analysed. Language was restricted to English, French and German.Data Extraction and Synthesis Main and secondary outcomes as well as study characteristics were extracted from the included studies and if possible the individual patient data was obtained. Estimates were pooled using a random-effects DerSimonian–Laird model for the meta-analysis.Main Outcomes and Measures Mean estimates and 95% confidence intervals of the association between PaO2 and altitude in healthy adults.Results 53 studies (777 individuals, 34.4% female) reporting 171 group ascents including an altitude range from 1524m to 8730m were included in the qualitative and 13 studies (305 individuals, 45.1% female) reporting 29 ascents were included in the quantitative analysis. The estimated effect size PaO2 was -1.60kPa [-1.73 to -1.47kPa] for each 1000m of altitude gain.Conclusions and Relevance This systematic review and meta-analysis provides estimates of altitude-related reductions in PaO2 in healthy individuals above 1500m. This effect estimate of 1.60kPa/1000m vertical gain for healthy people will contribute to a better understanding of hypobaric hypoxia and provide a basis for investigation in chronically ill people.

Poster #: 19 .SELF-MONITORING TO DETECT EARLY SIGNS OF ALTITUDE ILLNESS IN COPD. A DIAGNOSTIC ACCURACY STUDY. Michael Furian1, Aurelia Reiser1, Maamed Mademilov2, Konstantinos Bitos1, Simone Buenzli1, Ainura Abdraeva2, Benoit Champigneulle3, Arcangelo Carta1, Meret Bauer1, Tanja Ulrich1, Philipp Scheiwiller1, Julian Mueller1, Ahmet Sevik1, Stefanie Ulrich1, Laura Mayer1, Mirjam Grimm1, Simon R Schneider1, Ulan Sheraliev2, Aichurok Alymbekova2, Nurdin Shakiev2, Aijan Taalaibekova2, Aigul K Ozonova2, Kamilla Magdieva2, Gulzada Mirzalieva2, Azamat Akylbekov2, Saltanat Shabykeeva2, Talant M Sooronbaev2, Silvia Ulrich1, Konrad E Bloch1. 1Department of Respiratory Medicine, University Hospital of Zurich, Zurich, Switzerland, 2Department of Respiratory Medicine, National Center for Cardiology and Internal Medicine, Bishkek, Kyrgyz Republic, 3HP2 laboratory, Université Grenoble Alpes, Inserm (U1300), CHU Grenoble Alpes, Grenoble, 38000, France

BackgroundThere are no reliable means to identify patients with COPD at risk of altitude-related adverse health effects (ARAHE) during altitude travel. Therefore, diagnostic tests that predict ARAHE in COPD would be desirable.MethodsThis prospective diagnostic accuracy study included patients with COPD (FEV1 40-80%pred.), pulse oximetry (SpO2) ≥92% and PaCO2 <6kPa at low altitude. After baseline evaluation at 760m, patients traveled by bus to a clinic at 3100m and stayed there for 2 days. During this period, they performed structured self-monitoring (SSM) using a symptom checklist and pulse oximetry. They reported occurrence of at least moderate symptoms of acute mountain sickness (AMS) and/or SpO2 <85% (=positive index test). Patients remained at 3100m to observe whether ARAHE (=positive reference test), i.e. severe AMS symptoms, SpO2 <80% for >30min or any condition requiring medical intervention subsequently developed or not. ClinicalTrials.gov NCT03957759.Results158 COPD patients (80 women), mean±SD age 57±9yrs, participated. At 3100m, 98(62%) remained SSM negative, 55(35%) became SSM positive; ARAHE occurred in 112 of 153 (73%), ARAHE was indeterminate in 5(3%) participants. Most common ARAHE were severe hypoxemia 85(56%) and AMS 17(11%). Diagnostic accuracy of SSM quantified by C-statistic (95%CI) was 0.66 (0.59 to 0.73), sensitivity 45%, specificity 88% and positive and negative predictive value 91% and 37%, respectively.ConclusionIn lowlanders with moderate to severe COPD ascending to 3100m, ARAHE are common. SSM of symptoms and pulse oximetry is highly positive predictive of imminent ARAHE. Therefore, COPD patients testing positive in SSM may timely descend or take preventive treatment to reduce the risk of ARAHE.

Poster #: 20 .SLEEP AND BLOOD PRESSURE DURING A 12-MONTH STAY AT CONCORDIA STATION (3233 M), ANTARCTICA. Michael Furian1, Paul Robach2, Stijn Thoolen3, Sarah Rommel3, Sebastien Baillieul1, Stephane Doutreleau1, Pierrick J Arnal4, Samuel Verges1. 1HP2 laboratory, Université Grenoble Alpes, Inserm (U1300), CHU Grenoble Alpes, Grenoble, 38000, France, 2Ecole Nationale des Sports de Montagne, 74400 Chamonix, France, 3French Polar Institute Paul-Émile Victor, Brest, 4Dreem, Paris, France

IntroductionSleep architecture remains impaired when staying at the Concordia Station (3233m), Antarctica. The purpose of this study was to investigate sleep and blood pressure, and the pathophysiological role of hypoxia.MethodProspective cohort study in 23 subjects staying for 12 months at 3233m (N=11, mean±SD age 36±10y, BMI 24.3±3.1kg/m2) or in Dumont d'Urville, 20m (N=12, age 31±12y, BMI 22.3±3.1kg/m2), Antarctica. Before departure (BL) and

in the 1st and 12th month at the Stations, sleep assessment (DREEM) and 24h ambulatory blood pressure (BP) monitoring was performed.ResultAt 3233m, subjects had less stage 3 sleep (%total sleep time, TST) in the 1st (mean±SE 18±2%TST) and 12th (18±2%TST) month vs BL (24±3%TST, both P<0.05). In contrast, proportion of stage 2 sleep and micro-arousals were higher in the 1st (50±2%TST, 10.1±1.0/h) and 12th (51±2%TST, 11.5±1.0/h) month vs BL (43±3%TST, 7.1±1.2/h, both P<0.05). At 20m, no changes occurred. At 3233m, nocturnal mean BP was higher in the 1st (85±2mmHg) and 12th (80±2mmHg) month vs BL (76±2mmHg, both P<0.05). The higher nocturnal BP was caused by a higher proportion of non-dipping defined by <10% Δnight-day BP, which was 0% at BL, 45% in 1st and 27% in 12th month at 3233m (P<0.05, 1st month vs BL). At 20m, no changes occurred. ConclusionA 12-month stay at the Concordia Station at 3233m was associated with worse sleep and nocturnal BP compared to pre-departure. Since these impairments were not observed at Dumont d'Urville, preventive measures against hypoxia might be considered to improve outcomes in these crewmembers.

Poster #: 21 .PRELIMINARY OBSERVATIONS ON THE EFFECT OF ACUTE INTERMITTENT HYPOXIA ON POSTPRANDIAL PLASMA LIPID LEVELS IN PREMENOPAUSAL WOMEN. Nicholas Goulet1, Caroline Marcoux1, Vincent Bourgon2, Jean-François Mauger1, Ruwan Amaratunga3, Pascal Imbeault1, 3. 1University of Ottawa, Canada, 2Université du Québec en Outaouais, Canada, 3Institut du Savoir Montfort, Canada

Introduction: Hypoxia impairs lipid metabolism in multiple tissues, resulting in increased circulating blood lipid levels. Despite well-characterized differences in lipid metabolism between men and women, research into the relationship between hypoxia and lipid metabolism has been conducted almost exclusively in men thus far. Therefore, we investigated whether acute moderate intermittent hypoxia, previously demonstrated to increase postprandial blood lipid levels in men, has similar effects in women. Methods: Using a randomized crossover design, six young women (mean age [SD], 21.5 years [3.6]) were exposed to 6 hours of normoxia (~98% SpO2) and intermittent hypoxia (~15 hypoxic cycles per hour: 100% nitrogen, ~85% SpO2) following the consumption of a high-fat meal (59% fat) during the early follicular phase. Plasma levels of total triglycerides (TG), buoyant triglyceride-rich lipoprotein TG (TRL-TG), denser TRL-TG, and non-esterified fatty acids (NEFA) were analyzed using colorimetric assays at 0, 30, 60, 90, 120, 180, 240, 300, and 360 minutes after meal ingestion. Oxyhemoglobin saturation (SpO2) was monitored continuously with pulse oximetry. Results: Mean SpO2 was lower during intermittent hypoxia compared to normoxia ($p = 0.045$). Plasma levels of total TG, buoyant TG, and denser TG increased similarly over time in both conditions (time: $p \leq 0.047$, $\eta p2 \geq 363$; time x condition: $p \geq 0.365$). Across time, plasma NEFA levels were higher during intermittent hypoxia, however, this fell short of statistical significance (time x condition: $p = 0.057$, $\eta p2 = 0.352$). Conclusion: While not definitive, our findings indicate that acute intermittent hypoxia does not alter the postprandial TG response in premenopausal women. Funding: Natural Sciences and Engineering Research Council of Canada, and Association Médicale Universitaire de l'Hôpital Montfort.

Poster #: 22 .ACUTE INTERMITTENT HYPOXIA IS NOT ASSOCIATED WITH CHANGES IN PLASMA BIOMARKERS OF ACUTE KIDNEY INJURY IN HEALTHY YOUNG ADULTS AND INDIVIDUALS WITH OBSTRUCTIVE SLEEP APNEA. Nicholas Goulet1, Emily J. Tetzlaff1, Renée Morin1, Jean-François Mauger1, Ruwan Amaratunga2, Glen P. Kenny1, Pascal Imbeault1, 2. 1University of Ottawa, Canada, 2Institut du Savoir Montfort, Canada

Introduction: It is currently proposed that obstructive sleep apnea (OSA) can induce kidney dysfunction by causing ischemia-reperfusion injury in proximal tubular cells. However, it remains unclear whether a single exposure to intermittent hypoxia can increase circulating biomarkers of acute kidney injury (AKI). Therefore, we conducted an exploratory study aimed at evaluating the relationship between intermittent hypoxia and AKI. Methods: Using a randomized crossover design, 24 healthy young adults (18 men, 6 women; mean age [SD], 22 years [3]) and 7 middle-aged adults with OSA (6 men, 1 woman; 54 years [6]) were exposed to normoxia (~98% oxyhemoglobin saturation (SpO2)) and intermittent hypoxia (~15 hypoxic cycles per hour: 100% nitrogen, ~85% SpO2) for 6 hours following a meal. Plasma concentrations of neutrophil gelatinase-associated lipocalin (NGAL), interleukin 18 (IL-18), liver-type fatty acid-binding proteins (L-FABP), and kidney injury molecule-1 (KIM-1) were measured at baseline, and after 3 and 6 hours of exposure. SpO2 was monitored continuously. Results: Mean SpO2 (%) and time spent under 90%, 85%, and 80% were lower during intermittent hypoxia compared to normoxia ($p < 0.001$, $\eta p2 \geq 771$). No differences in plasma concentrations of NGAL and KIM-1 were observed. Irrespective of group, plasma IL-18 concentrations increased over time during normoxia (time x condition: $p = 0.033$, $\eta p2 = 0.122$) and plasma L-FABP concentrations transiently decreased after 3 hours in both conditions (time: $p = 0.008$, $\eta p2 = 0.152$). Conclusion: We did not observe a clear relationship between intermittent hypoxia and biomarkers indicative of AKI. Further studies looking at intensity-dependent effects are needed to elucidate the mechanisms underlying this relationship. Funding: Natural Sciences and Engineering Research Council of Canada, Association Médicale Universitaire de l'Hôpital Montfort.

Poster #: 23 .CHARACTERIZING THE RESPONSE TO INTERMITTENT HYPOXIA DURING THE POSTPRANDIAL STATE IN IMMUNE CELLS FROM YOUNG ADULTS. Nicholas Goulet1, Vincent Bourgon2, Caroline Marcoux1, Jean-François Mauger1, James J. McCormick1, Ruwan Amaratunga3, Glen P. Kenny1, Pascal Imbeault1, 3. 1University of Ottawa, Canada, 2Université du Québec en Outaouais, Canada, 3Institut du Savoir Montfort, Canada

Introduction: Growing evidence shows that postprandial inflammation occurs in immune cells following a high-fat meal. However, little is known about how inflammatory responses are modulated by intermittent hypoxia during the postprandial state, which is important considering that individuals with obstructive sleep apnea are exposed to chronic intermittent hypoxia. Additionally, it remains unclear if postprandial inflammation occurs synchronously with changes in autophagy, an important component of the cytoprotective responses. Methods: Four young adults (2 men, 2 women; mean age [SD], 22 years [5]) were randomly exposed to normoxia (~98% SpO2) and intermittent hypoxia (~15 hypoxic cycles per hour, 100% nitrogen, ~85% SpO2) for 6 hours following a high-fat meal (59% fat). Plasma non-esterified fatty acid (NEFA)

concentrations were measured using colorimetric assays, and proteins associated with autophagy (microtubule-associated protein 1 light chain 3 [LC3]-II) and inflammation (interleukin-6 [IL-6]) were assessed in peripheral blood mononuclear cells at baseline, and after 3 and 6 hours of exposure via Western blot (data presented as a relative quantity (RQ) to the respective baseline). Results: NEFA changed over time, decreasing after 3 hours, but increasing above baseline after 6 hours ($p = 0.012$, $\eta p2 = 0.891$), with higher elevations observed during intermittent hypoxia ($p = 0.036$, $\eta p2 = 0.819$). During normoxia only, IL-6 increased after 3 hours (1.5RQ [0.4], $p = 0.046$). When comparing between conditions, a trend towards higher LC3-II during normoxia was observed relative to intermittent hypoxia ($p = 0.063$, $\eta p2 = 0.735$). Conclusion: Due to a small sample size, our preliminary observations remain inconclusive with the additional caveat that complex cellular processes cannot be assessed with a single biomarker, highlighting the need for larger studies. Funding: Natural Sciences and Engineering Research Council of Canada, Association Médicale Universitaire de l'Hôpital Montfort.

Poster #: 24 .CHARACTERIZATION OF THE INFLAMMATORY RESPONSE TRIGGERED BY NORMOBARIC HYPOXIA. Sonja Hersel1, Frank Splettstoesser1, Katrin Reiners2, Sarah Zaffarana2, Laura de Boni3, Henning Weis3, 4, Fabian Hoffmann3, 5, Jan-Niklas Hoenemann3, 5, Jens Jordan3, Ulrich Limper3, Jens Tank3, Stilla Frede1. 1Department of Anesthesiology and Intensive Care Medicine, University Hospital Bonn, Germany, 2Institute of Clinical Chemistry and Clinical Pharmacology, University Hospital Bonn, Germany, 3Department of Cardiovascular Aerospace Medicine, Institute for Aerospace Medicine, German Aerospace Center, Cologne, Germany, 4Department of Nuclear Medicine, University of Cologne, Germany, 5Department of Internal Medicine III, Division Cardiology, Pneumology, Angiology and Intensive Care, University of Cologne, Germany

Objective: Hypoxia and inflammation share interlinked cellular pathways. We investigated the hypothesis that exposure to hypoxia is sufficient to trigger pro-inflammatory processes in human immune and endothelial cells, which could be involved in inflammatory signaling at high altitudes. Methods: White blood cells (WBCs) were collected from normoxic healthy donors. Primary human pulmonary microvascular endothelial cells (HPMECs) were purchased from PromoCell. Cells were incubated for up to 24h under normoxic or hypoxic conditions with 10% or 1% oxygen (O2). Regulation of pro-inflammatory and hypoxia-inducible genes and proteins was evaluated by RT-PCR, ELISA and immunoblot (HIF-2α stabilization). Plasma samples were taken from participants of the MyoCardioGen 3 (MCG3) study who were exposed to sustained severe hypoxia (35 days, lowest O2 concentration 9.5%). The study included three participants who had suffered myocardial infarction and one healthy subject. Plasma from the MCG3 participants was analyzed by Luminex assay. In addition, extracellular vesicles (EVs) were investigated using nanoparticle tracking analysis (NTA). Results: WBCs and HPMECs exposed to 1% O2 showed a slight elevation of tested pro-inflammatory cytokines, which was absent under normoxic or 10% hypoxic conditions. A cellular response to hypoxia could be proven in all in vitro experiments. Luminex results showed changes in pro-inflammatory cytokine concentrations in plasma of MCG3 study participants. NTA analysis confirmed a change in EV numbers in in vitro and in vivo hypoxia experiments. Conclusion: Our study indicates that 1% O2 slightly increases the pro-inflammatory state in WBCs and HPMECs. Since donors exposed to sustained hypoxia showed a more pronounced regulation of

inflammatory cytokines, we conclude that inflammatory processes in vivo are influenced by communication between different cell types. Unidentified humoral factors or EVs secreted by cells under hypoxic stress may represent a possible connection.Funding: No external funding.

Poster #: 25 .Measuring the effects of supplemental oxygen on inspired oxygen fraction at extreme simulated altitude.. Matthew M. Howrey1, Denis J. Wakeham1, 2, Peter Hackett3, Murugappan Ramanathan1, Marcus Payne1, Dean Palmer1, Renie Guilliod1, 2, James Berry1, 2, Tony G. Babb1, 2, Benjamin D. Levine1, 2, Christopher M. Hearon Jr.1, 2, Andrew R. Tomlinson1, 2. 1Institute for Exercise and Environmental Medicine, Texas Health Presbyterian Hospital Dallas, Dallas, Texas, USA, 2The University of Texas Southwestern Medical Center, Dallas, Texas, USA, 3Altitude Research Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

Most extreme altitude climbers use supplemental oxygen when climbing above 8000m. Despite its common use, the fraction of inspired oxygen (FiO2) delivered and its effects on oxygen saturation (SpO2) during extreme hypobaric hypoxia are unknown.Therefore, we measured gas fractions (via mass spectrometry) in six unacclimatized or partially acclimatized individuals using a capillary within the Summit Oxygen mask. Continuous measurements of gas fractions were made during 4-minute exposures at nominal flows of 6, 4, 2, 1 and 0 L/min. Measurements were made at rest and during cycling at 60 and 120 Watts at extreme simulated altitude (282 mmHg; 8100m), as well as at rest at 253 mmHg (8848m). Dynamic mixing of ambient air with supplemental oxygen within the mask as well as a reservoir effect produced distinct patterns of oxygen fractions that were not amenable to standard assessments of FiO2. Thus, we quantified the time-averaged mean oxygen fraction during inspiration (TA-mean) and the end-tidal (alveolar) oxygen fraction (taken as the end-expiratory plateau) and performed exploratory regression analyses between these oxygen fractions and SpO2 to assess their physiological relevance and utility in this setting.With decreasing supplemental oxygen flow (6, 4, 2, 1 and 0 L/min) during rest at 282 mmHg, there were stepwise decreases in TA-mean oxygen fraction (0.659, 0.425, 0.405, 0.272, 0.215, P=0.004) and end-tidal oxygen fraction (0.697, 0.489, 0.391, 0.276, 0.153, P=0.0004). Similar stepwise decreases were observed during exercise and at 253 mmHg. There were exponential relationships between both TA-mean and end-tidal oxygen with SpO2 (R2=0.67 and R2=0.78, respectively) across all conditions.These data provide the first assessments of oxygen fractions at extreme simulated altitude when using supplemental oxygen. Based upon our results, TA-mean and end-tidal oxygen can provide insight into oxygen fractions when assessments of FiO2 are not possible during studies delivering supplemental oxygen via a mask.

Poster #: 26 .ACTIVE ASCENT INDUCES PLASMA VOLUME RETENTION THAT LIKELY EXACERBATES ACUTE MOUNTAIN SICKNESS AT 3600M. Reed Hoyt1, Janet Staab1, Peter Figueiredo1, Steven Landspurg1, Jon Femling2, Jason Williams2, Aaron Reilly2, Trevor Mayschak2, Mark Buller1, J Philip Karl1, Emma Atkinson1, Tim Mesite1, Beth Beidleman1. 1US Army Research Institute of Environmental Medicine, 2University of New Mexico

Objective: Plasma volume (PV) typically decreases following passive ascent to high altitude (HA), but strenuous exercise may alter this response due to greater arterial desaturation with exercise. Methods: To determine the impact of active versus passive ascent on PV changes at HA, 78 healthy Soldiers (mean±SD; age=26±5yr) were tested at baseline residence (BLR), transported to Taos, NM (2845m), then hiked (n=39) or were driven (n=39) to HA (3600m), and stayed for 4 days. AMS-Cerebral factor score (AMS-C) was assessed using the Environmental Symptoms Questionnaire (ESQ) at HA twice on day 1 (HA1), five times on days 2 and 3 (HA2 and HA3) and once on day 4 (HA4). Pulse arterial oxygen saturation (SpO2) was measured immediately after the ESQ. If AMS-C was ≥0.7 at any assessment, individuals were categorized as AMS-susceptible (AMS+; n=33); others were non-susceptible (AMS−; n=45). Hemoglobin and hematocrit were measured in the morning at BLR, HA2, HA3 and HA4 and at 18:00 on HA1 to calculate PV changes. Results: The SpO2 did not differ between active and passive ascent cohorts in the AMS- group at any HA time point. SpO2 (%), however, was lower in the active vs. passive ascent cohort in the AMS+ group, on HA1 (85.0±7.9 vs. 87.9±7.9, p=0.04) and HA4 (87.8±4.6 vs. 89.0±3.1, p=0.03). In the passive ascent cohort, PV changes were similar in the AMS+ and AMS− groups at all HA time points. In the active ascent cohort, PV changes (%) were lower in the AMS+ vs. AMS− group at HA1 (+1.7±6.5 vs. −4.3±6.0, p=0.04) and HA4 (−1.3±5.1 vs. −7.3±7.8, p=0.04). The PV changes were positively correlated with AMS-C scores at HA1 (r=0.22, p=0.05) and HA2 (r=0.21, p=0.04). Conclusion: Active ascent induced a retention of plasma volume in AMS+ individuals early in the exposure likely due to a reduction in blood oxygen saturation and associated antidiuresis. Authors' views not official U.S. Army or DoD policy. Funding: USAMRDC

Poster #: 27 .AMBULATORY BLOOD PRESSURE IN OLDER ADULTS AT LOW VERSUS HIGH ALTITUDE: THE COLORADO HIGH ALTITUDE MONITORING BLOOD PRESSURE STUDY (CHAMPS) . Greta Kreider-Carlson 1, Andrew C Burns2, Ilaria Ferrari2, Cameron Niswander2, Linda E Keyes3. 1Hennepin, 2University of Colorado School of Medicine, 3University of Colorado, Anchutz Campus

Introduction: Blood pressure (BP) after acute high altitude exposure varies between individuals and is most accurately measured by 24-hour ambulatory BP (ABP) monitoring. Understanding impacts of altitude on BP is essential in the creation of evidence-based travel guidelines.Objective: Compare 24-hour ABP at low versus high altitude in participants with and without preexisting hypertension.Methods: This was a prospective observational cohort study of adult lowlanders, comparing 24-hour ABP at low (<1,000 m) versus high altitude (2,800-3,000 m). BP was monitored every 30 minutes while awake and hourly overnight for 24 hours using Welch-Allyn 6100 ABP monitors.Results: 19 participants completed the high altitude study (mean age 64, 11 with underlying hypertension). 12 participants completed low and high altitude measurements. We found no difference in average 24-hour mean arterial pressure (MAP) between low and high altitude in all-comers, mean diff 4 mmHg, [95% CI:-4-11 mmHg], p=0.3. Participants without preexisting hypertension had a greater increase in 24-hour MAP from low to high altitude on average versus those with preexisting hypertension (average change +11 mmHg vs -2 mmHg, respectively, p=0.042). Asymptomatic severely elevated BP was common at both altitudes.Conclusions: In these older adults, BP was similar at low and high altitude, with high individual variation. Our data suggest that BP is more likely to increase at

high altitude in those without underlying hypertension, and to stay the same or decrease in those with hypertension.

Poster #: 28 .ACUTE MOUNTAIN SICKNESS DOES NOT IMPACT VENTILATORY ACCLIMATIZATION FOLLOWING ACTIVE AND PASSIVE ASCENT TO 3600M. Steven Landspurg1, Peter Figueiredo1, Emma Atkinson1, Janet Staab1, Mark Buller1, Reed Hoyt1, Philip Karl1, Tim Mesite1, Beth Beidleman1, Jon Femling2, Jason Williams2, Aaron Reilly2, Trevor Mayschak2. 1US Army Research Institute of Environmental Medicine, 2University of New Mexico Health Sciences Center

Introduction: Whether acute mountain sickness (AMS) differentially impacts the magnitude or time course of ventilatory acclimatization at high altitude (HA) remains controversial. Methods: To determine whether AMS impacts ventilatory acclimatization following both passive and active ascent to HA, 78 healthy Soldiers (mean±SD; age=26±5yr) were tested at baseline residence (BLR), transported to Taos, NM (2845m), then hiked (n=39) or were driven (n=39) to 3600m, and stayed for four days. AMS-C was assessed using the Environmental Symptoms Questionnaire at HA twice on day 1 (HA1), five times on days 2 (HA2) and 3 (HA3) and once on day 4 (HA4). If AMS-C was ≥0.7 at any timepoint, individuals were categorized as AMS-susceptible (AMS+, n=33); others were categorized as non-susceptible (AMS-, n=45). Portable real-time capnography was used to measure resting partial pressure of end-tidal carbon dioxide (PETCO2 mmHg) at ~09:00 at BLR, and after 19h (HA2), 43h (HA3), and 67h (HA4) at HA. Resting pulse arterial oxygen saturation (SpO2, %) was measured immediately after PETCO2. Results: Ascent conditions did not differentially impact ventilatory responses. PETCO2 and SpO2 did not differ between AMS+ and AMS- groups at BLR or any time point at HA. The PETCO2(mmHg) in AMS+ vs. AMS- groups, decreased($p<0.05$) from BLR (37.2±3.6 vs. 36.9±3.1) on HA2 (33.5±4.1 vs. 33.7±4.0), remained stable from HA2 to HA3 (33.4±4.1 vs. 33.8±3.9) and decreased($p<0.05$) from HA3 to HA4 (31.8±4.4 vs. 31.4±4.1). SpO2(%) decreased($p<0.05$) in both AMS+ and AMS-, from BLR (97.3±1.5 vs. 96.9±1.5) on HA2 (87.9±3.1 vs. 88.8±2.9) and remained stable from HA2 to HA3 (88.8±3.1 vs. 89.1±2.9) and HA4 (88.9±3.1 vs. 89.6±2.1). Conclusions: Ventilatory acclimatization occurred at HA, but AMS-susceptibility did not impact the magnitude or time course of acclimatization following active or passive ascent to 3600m. Authors' views not official U.S. Army or DoD policy. Funding: USAMRDC

Poster #: 29 .VENTILATORY ACCLIMATIZATION OBTAINED AT MODERATE ALTITUDE (1190M) DOES NOT CARRY OVER FOLLOWING ACTIVE OR PASSIVE ASCENT TO A HIGHER ALTITUDE (3600M) . Steven Landspurg1, Peter Figueiredo1, Emma Atkinson1, Janet Staab1, Mark Buller1, Reed Hoyt1, Philip Karl1, Tim Mesite1, Beth Beidleman1, Jon Femling2, Jason Williams2, Aaron Reilly2, Trevor Mayschak2. 1US Army Research Institute of Environmental Medicine, 2University of New Mexico Health Sciences Center

Introduction: Previous research has demonstrated that ventilatory acclimatization obtained at moderate altitude (1800-2200m) carries over following ascent to a higher altitude, but whether a lower altitude threshold (1190m) is also effective at inducing ventilatory acclimatization

following ascent to a high altitude (HA) is unknown. Methods: To determine the impact of moderate- versus low-altitude residence (MAR vs. LAR) and ascent conditions on ventilatory acclimatization following ascent to HA, 78 healthy Soldiers (mean±SD; age=26±5yr) were tested at baseline residence (BLR) at 331m (LAR; n=41) or 1190m (MAR; n=37), transported to Taos, NM (2845m), then hiked (n=39) or were driven (n=39) to HA (3600m), and stayed for four days. Portable real-time capnography was used to measure resting partial pressure of end-tidal carbon dioxide (PETCO2, mmHg) at ~09:00 on BLR, and after 19h (HA2), 43h (HA3), and 67h (HA4) at HA. Resting pulse arterial oxygen saturation (SpO2, %) was measured immediately after the PETCO2 assessment. Results: Ascent conditions did not differentially impact ventilatory responses. PETCO2 (mmHg) did not differ between MAR versus LAR, at any time point but decreased($p<0.05$) from BLR (36.6±3.2 vs. 37.5±3.3) on HA2 (34.1±3.7 vs. 33.3±3.7), remained stable from HA2 to HA3 (34.1±4.4; 33.3±3.7) and decreased($p<0.05$) from HA3 to HA4 (32.4±4.3 vs. 31.1±4.2). SpO2 (%) was lower in MAR versus LAR, at BLR (96.5±1.1 vs. 97.6±1.2, $p=0.001$) but did not differ between groups at HA2, HA3 or HA4. SpO2(%) decreased($p<0.05$) in both MAR and LAR, from BLR on HA2 (89.1±3.2; 87.9±3) and remained stable from HA2 to HA3 (89.4±3.7; 88.7±3.1) and HA4 (89.6±3.3; 89.1±3.0). Conclusion: Ventilatory acclimatization occurred in both LAR and MAR at 3600m, but the magnitude and time course did not differ between altitude-residence groups or ascent conditions. Authors' views not official U.S. Army or DoD policy. Funding: USAMRDC

Poster #: 30 .ACCURACY OF WRIST WORN OXYGEN SATURATION MONITORS IN HYPOXIC AND HYPOXIC AND COLD CONDITIONS. . Floris Paalman1, Carmen Possnig1, Hendrik Mugele1, Justin Lawley1, 2. 1Department of Sport Science, Division of Performance Physiology and Prevention, University of Innsbruck, 2Institute of Mountain Emergency Medicine, Eurac Research, Bolzano, Italy

Introduction: Wrist-worn oxygen saturation (SpO2) monitors could provide valuable information if accurate, especially in comparison to fingertip devices in cold environments where a reduction in finger cutaneous blood flow impairs signal quality. Methods: Study 1: Seven participants were exposed to a simulated altitude of 4500m, and then SpO2 was clamped at 85%, 90% & 95% based on a clinical Nellcor N600x monitor with a forehead sensor. SpO2 was simultaneously recorded on a Nonin 9590 finger sensor, the Apple Watch 6 and the Garmin Venu 2S. Study 2: Nineteen participants were exposed to a simulated altitude of 4500m for 2 hours, and on a separate occasion combined with whole body cooling to a target skin temperate of 27°C. SpO2 was recorded with the Nellcor N600x, Nellcor 9590 fingertip sensor and the Apple Watch 6. Results: Study 1: The Apple Watch 6 showed good validity (typical error of the estimate (TEE) = 2.4%, $r=0.82$, $p<0.0001$, CV=3.3%, Bias -0.33) compared to the clinical forehead sensor, which was similar to the Nonin fingertip sensor (data not shown). The validity of the Garmin Venu 2S was inferior (TEE = 3.8%, $r=0.66$, $p<0.0001$, CV =4.6%, Bias 1.92). Study 2: The Apple Watch 6 showed acceptable validity when free breathing (TEE = 3.01%, $r=0.75$, $p<0.0001$, CV =3.8%) over a SpO2 range of 75 to 95%. In the cold, the validity was reduced on the Apple watch (TEE = 4.34%, $r=0.71$, $p<0.0001$, CV =5.6%) similar to the Nonin fingertip sensor (TEE = 3.68%, $r=0.80$, $p<0.0001$, CV =4.6%). Conclusion: SpO2 can be obtained by a wrist-worn monitor with similar validity to a clinical SpO2 forehead monitor in hypoxic conditions. However, its validity is reduced during cold exposure like a fingertip sensor.

Poster #: 31 .HIGH-ALTITUDE PULMONARY EDEMA IN COLORADO CHILDREN: A CROSS-SECTIONAL SURVEY AND RETROSPECTIVE REVIEW.

Timothy Kelly1, Maxene Meier2, Jason Weinman2, Dunbar Ivy2, John Brinton2, Deborah Liptzin2. 1University of Indiana, 2University of Colorado

Introduction: Few studies of high-altitude pulmonary edema (HAPE) are specific to the pediatric population. The purpose of this investigation was to further characterize the radiographic patterns of pediatric HAPE, and to better understand ongoing risk following an initial pediatric HAPE episode.Methods: This study uses both a retrospective chart review and cross-sectional survey. Pediatric patients with HAPE at a single quaternary referral center in the Rocky Mountain Region were identified between the years 2013 and 2020. Patients were eligible if they presented with a clinical diagnosis of HAPE and had a viewable chest radiograph (CXR). Surveys were sent to eligible patients/families to gather additional information relating to family history, puberty, and HAPE recurrence.Results: Forty-two individuals met criteria for clinical diagnosis of HAPE with a viewable CXR. A majority of CXRs (24/42, 57.1%) demonstrated predominant right-sided involvement. Similarly, 24 CXRs (24/42, 57.1%) demonstrated predominant upper lobe involvement. Twenty-one (21/42, 50%) surveys were completed. Many children went on to experience at least one other HAPE episode (8/19, 42.1%).Conclusion: The most common radiographic pattern seen in pediatric HAPE is pulmonary edema that favors the right lung and upper lobes. After an initial HAPE presentation, over 1/3 of children will experience additional HAPE episodes. One family reported "We have not been back to higher altitudes in fear of this [HAPE] happening again;" clearly, pediatric HAPE is an anxiety provoking, and potentially deadly disease that requires ongoing efforts to better understand pediatric HAPE physiology, treatment, and recurrence risk. Funding: DI is supported by NIH/NCATS Colorado CTSA Grant Number UL1 TR002535. DRL is supported by NIH/ECHO UG1OD024952. Contents are the authors' sole responsibility and do not necessarily represent official NIH views.

Poster #: 32 .ASSESSING LOOP GAIN VIA VOLUNTARY END-EXPIRATORY BREATH HOLDS IN STEADY-STATE HYPOXIA: A METHODOLOGICAL CHARACTERIZATION.

Benjamin Mackenzie1, Courtney Taylor1, Anthony Marullo1, Jordan Bird1, Scott Thrall1, Alexandra Skalk1, Britta Byman1, Brandon Pentz1, Trevor Day1. 1Mount Royal University

Introduction: Central sleep apnea (CSA) occurs in 50-60% of heart failure (HF) patients, and is universal with high altitude (HA) ascent. HF patients with CSA have higher peripheral chemoreflex (PCR) gain than those without CSA. Hypoxic exposure during HA ascent increases PCR gain via carotid body sensitization. Loop gain (LG) is defined as the responsiveness of the chemoreflex feedback loop. In sleep studies, LG is quantified as the ratio of the ventilatory response following a ventilatory disturbance, with values over 1.0 representing susceptibility to ventilatory instability during sleep and CSA. We aimed to characterize a novel method to quantify LG using a standardized series of short, voluntary, end-expiratory breath holds (EEBH) in a background of steady-state hypoxia, to simulate CSA. We hypothesized that LG would be similar in magnitude to that quantified during sleep studies

(Range:0.2-2.0).Methods: Fifteen heathy participants (6F) were instrumented with a calibrated pneumotachometer to measure breath-by-breath ventilation and underwent a baseline period of 10-min under steady-state hypoxia (FIO2≈0.145, PO2≈96mmHg), followed by five consecutive ~15-sec EEBHs separated by ~1-min recovery. LG was quantified as the ventilatory response immediately following EEBH breakpoint, indexed against the ventilatory disturbance, taken as the absolute reduction in ventilation to apnea from baseline values. LG was then quantified using either (a) the 1st, (b) an average of the 1st+2nd and (c) an average of the 1st+2nd+3rd breaths following EEBH, with the five LG calculations averaged to obtain a representative within-individual value.Results: Mean LG ratios were 1.77±0.70 (1st), 1.31±0.56 (1st+2nd), and 0.96±0.46 (1st+2nd+3rd; P<0.00001). These three LG calculations were well-correlated, within-individual (r>0.99, P<0.00001).Conclusions: We suggest that this simple voluntary EEBH protocol can be used to quantify LG in those susceptible to CSA, as a predictor of CSA severity in contexts such as HF or HA ascent. Funding: NSERC Discovery

Poster #: 33 .VASCULAR REACTIVITY TO RHYTHMIC HANDGRIP AT ALTITUDE. Lauren Maier1, Emily Vanden Berg1, Lydia Simpson2, Michiel Ewalts3, Jenna Wowdzia1, 4, Travis Gibbons5, Katharine Foster6, Jared Baylis7, Christopher Gasho6, David Macleod8, Sean van Diepen9, Philip Ainslie5, James Anholm6, Michael Stembridge10, Jonathan Moore3, Craig Steinback1. 1Neurovascular Health Laboratory, Faculty of Kinesiology, Sport, and Recreation, University of Alberta, 2University of Innsbruck, 3Bangor University, 4Program for Pregnancy and Postpartum Health, Faculty of Kinesiology, Sport, and Recreation, University of Alberta, 5University of British Columbia - Okanagan, 6Loma Linda University, 7Southern Medical Program, University of British Columbia, 8Duke University, 9Faculty of Medicine and Dentistry, University of Alberta, 10Cardiff Metropolitan University

Objectives: We aimed to examine sympathetic reactivity of the vasculature to handgrip exercise at altitude, determine the direct contribution of adrenergic receptors to the exercise response, and explore any sex-based differences.Methods: 8 young, healthy participants (4M/4F) were tested at low (Kelowna, BC; 344m) and high (Barcroft Station, White Mountain 3800m) altitude (days 3-12). Participants performed 3 minutes of rhythmic handgrip exercise at 25% of their maximal voluntary contraction during local infusions of saline, propranolol (beta-blockade), and propranolol plus phentolamine (combined alpha- and beta-blockade). Doppler ultrasound was used to examine brachial artery blood flow (FBF) and calculate forearm vascular conductance (FVC).Results: There was a main effect of blockade on resting FVC (p<0.001), but it was not different between low- and high-altitude (main effect p=0.606). The FVC response to rhythmic handgrip was also different between conditions [low-altitude (control, +10.1±6.5 a.u.; beta-blockade, +13.9±3.4 a.u.; alpha-beta-blockade, +3.1±5.1 a.u.); and high-altitude (control, +11.0±3.8 a.u.; beta-blockade, +13.0±4.8 a.u.; alpha-beta-blockade, +2.9±6.8 a.u.) p=0.009], but was not different between locations (p=0.989). There was a main effect of blockade on FBF during exercise [low-altitude (control, 17.8±5.7 mL/min/100mLx102; beta-blockade, 20.7±7.2 mL/min/100mLx102; alpha-beta-blockade, 25.9±5.3 mL/min/100mLx102); and high-altitude (control, 16.4±4.5 mL/min/100mLx102; beta-blockade, 27.3±6.1 mL/min/100mLx102; alpha-beta-blockade, 31.2±6.9 mL/min/100mLx102) p=0.0007], but it was not different between locations (p=0.095). No differences between males and females existed in baseline FVC or response to handgrip exercise at low- or high-altitude.Conclusions: This evidence supports that there is alpha-mediated restraint of exercising blood flow in the vasculature. However, it does

not differ between low- and high-altitude, suggesting the response to low to moderate-intensity exercise is preserved at altitude. Despite evidence indicating females have differing control of the vasculature due to beta-receptor sensitivity, these results suggest no difference in resting conductance or response to rhythmic exercise at altitude.Funding: NSERC

Poster #: 34 .Pulsatile cerebrovascular hemodynamics in response to pharmacologically altered cerebral perfusion following acclimation to high altitude.

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Background: Cerebral blood flow (CBF) at high altitude (HA) increases to maintain oxygen(O_2) delivery; however, since HA also increases systemic hemodynamic factors (i.e., blood pressure [BP] and heart rate [HR]) we aimed to characterize the impact of HA cerebral perfusion on cerebral hemodynamic pulsatilities (PI) and damping (DF = PIICA / PIMCAv), both of which are considered indexes of cerebrovascular compliance. Because the brain acts as a high pass filter, we hypothesized that acute pharmacologically-induced elevations and reductions in PI and CBF would elicit robust increases and decreases in DF, respectively.Methods: Six males were studies following 2-weeks acclimatization to 5050m. Extracranial hemodynamics (velocity, diameter, flow, PI) were measured proximally in the internal carotid artery (ICA), while velocity (MCAv) and pulsatility (PIMCAv) were measured in the distal middle cerebral artery using ultrasound. DF was calculated using proximal and distal PI's. BP, HR, and arterial blood gases were also measured. Dobutamine (DOB-2-5 μg/kg/min + acetazolamide (ACZ-10mg/kg) and indomethacin (INDO 1.45 mg/kg) trials were randomized. Results: DOB+ACZ significantly increased HR (78±14bpm vs 83±14bpm), MCAv (74±15cm.s-1 vs 91±17cm.s-1), ICAdiameter (5.0±0.02 mm vs 5.3±0.03 mm), ICAflow (271±115ml.min-1 vs 360±68.9ml.min-1), and PIICA(1.0±0.28a.u. vs 1.2±0.29a.u), but did not alter DF. In contrast, INDO decreased ($p<0.05$) ICAflow (225±66ml.min-1 vs 184±55ml.min1) and DF (1.9±0.59a.u vs 1.38±0.29a.u), but increased PIMCAv (0.65±0.11a.u vs 0.83±0.11a.u; $p<0.05$). Neither drug altered BP or arterial blood gases.Conclusion: Our findings indicate that a compliant cerebral vasculature may be protected from enhanced hemodynamic pulsatile stress (i.e., preserved DF) when perfusion is pharmacologically increased at HA. This protective benefit appears to be diminished (reduced DF) when perfusion is pharmacologically reduced. Future studies exploring whether these cerebrovascular compliance mechanisms underlie the etiology of altitude-related illness are required.

Poster #: 35 .DIFFERENTIAL CLAMPING OF HYPOXIA INDUCES DISTINCT CHANGES IN INTRACORTICAL AND SPINAL NEURAL NETWORKS. Daniel McKeown1, 2, 3, Glenn Stewart2, 3, Justin Kavanagh1, 2, 3. 1Neural Control of Movement Laboratory, 2Menzies Health Insitute Queensland, 3Griffith University

The purpose of this study was to examine how two common methods of continuous hypoxia impact the activity of intracortical circuits responsible for inhibition and facilitation of motor output, and spinal excitability. Ten participants were exposed to 2 hr of hypoxia at 0.13 fraction of inspired oxygen (FIO2 clamped protocol) and 80% of peripheral capillary oxygen saturation (SpO2 clamped protocol) using a simulating high-altitude device on two visits separated by a week. Using transcranial magnetic and peripheral nerve stimulation, unconditioned motor evoked potential (MEP) area, short intracortical inhibition (SICI) and facilitation (ICF), and F-wave persistence and area, were assessed in the first dorsal interosseous muscle before titration, 1 and 2 hr of hypoxia, and at reoxygenation. The clamped protocols resulted in differing reductions in SpO2 by 2 hr (FIO2 clamped protocol: 90.6 ± 2.5%, SpO2 clamped protocol: 81.9 ± 1.3%). Although unconditioned MEP area did not differ between the protocols, SICI was significantly lower at 2 hr ($P < 0.001$) and ICF was higher throughout ($P = 0.005$) the FIO2 clamped protocol compared to the SpO2 clamped protocol. Furthermore, a negative correlation between SICI and SpO2 ($r = 0.31$) and a positive correlation between ICF and SpO2 ($r = 0.30$) were determined, where greater reductions in SpO2 resulted in less inhibition and less facilitation of MEP responses. Although F-wave area progressively increased similarly throughout the protocols ($P = 0.036$), persistence of responses was reduced at 2 hr and reoxygenation ($Ps < 0.01$) during the SpO2 clamped protocol compared to the FIO2 clamped protocol. This study demonstrates that activity in intracortical networks responsible for facilitating and inhibiting motor output from the motor cortex, and activity of spinal motoneurones, are dependent on the degree of hypoxia, where greater severities of exposure lead to reduced excitability of these networks.

Poster #: 36 .DIFFERENCES IN DNA METHYLATION BETWEEN ALTITUDE EXPERIENCED AND ALTITUDE NAÏVE HEALTHY VOLUNTEERS ON EXPOSURE TO HYPOBARIC HYPOXIA. Kay Mitchell1, Emma Garratt1, Michael Natoli2, Elie Antoun1, Matthew Hewitt1, Negusse Kitaba1, Andrew Cumpstey1, Thomas Smedley1, Nelson Diamond2, Timothy Beck2, Denny Levett1, Michael Mythen3, Andrew Murray4, Hugh Montgomery3, Daniel Martin5, Keith M Godfrey1, Richard Moon2, Karen Lillycrop1, Michael Grocott1. 1University of Southampton, 2Duke University, 3University College London, 4University of Cambridge, 5University of Plymouth

Objectives: We investigated skeletal myocyte DNA methylation patterns in altitude experienced (AE) and altitude naïve (AN) lowlander volunteers on exposure to hypobaric hypoxia and subsequent return to normoxia. Methods: Twenty-one healthy male volunteers were exposed to environmental hypoxia over 3 days in a hypobaric chamber (maximum altitude equivalent to 3500m, PaO2 8 kPa). Vastas lateralis skeletal muscle biopsies were taken at baseline, at the end of hypoxia, and 3 hours after return to normoxia. Following quality control and normalisation procedures methylation levels of cytosine-guanine sequences (CpGs), generated using an Illumina HumanMethyaltion EPIC bead array, were compared between baseline and hypoxia, and between hypoxia and subsequent normoxia using paired t-tests.

Associations between sites of methylation change and all known biological pathways were sought. Results: Methylation patterns altered in response to hypoxia in all participants, with further changes following return to normoxia. The number of differentially methylated CpGs (dmCpGs) was greater in AE than AN participants following exposure to hypoxia (ratio 2.06:1, $p<0.001$), and subsequent return to normoxia (ratio 4.14:1, $p<0.001$), and differed between them. DmCpGs were enriched in MAPK and PI3K-Akt signalling pathways following exposure to hypoxia, and subsequent return to normoxia. Conclusions: Altered DNA methylation patterns were associated with hypoxic exposure and subsequent return to normoxia in healthy humans with differences in methylation patterns between AE and AN individuals. Methylation changes were associated with signalling pathways that may underpin the skeletal muscle response to hypoxia.

Poster #: 37 .HEMORHEOLOGY DURING ACCLIMATIZATION TO HIGH ALTITUDE (3800 m). Justin A Monteleone1, Andrew R Steele1, Connor A Howe1, Katharine Foster2, Hannah G Caldwell1, L Madden Brewster1, Jennifer Duffy1, Prajan Subedi2, James D Anholm2, Philip N Ainslie1, Joshua C Tremblay3. 1University of British Columbia Okanagan, 2Loma Linda University School of Medicine, 3Cardiff Metropolitan University

OBJECTIVE: High altitude causes numerous hematological changes to maintain oxygen delivery to tissues. Hemoconcentration occurs at high altitude causing a substantial increase in whole blood viscosity. However, it remains unresolved if changes in specific red blood cell properties – red blood cell deformability and aggregation – contribute to these hematological changes. Therefore, we aimed to characterize hemorheology at baseline (BL) (344m), during EARLY (days 1-2) and LATE (days 11-14) acclimatization to high altitude (Barcroft Field Station, 3800m). METHODS: Participants (9M/10F; age = 27±4 years) arrived in the lab fasted, where blood was taken from the antecubital vein to assess hemorheology (whole blood viscosity, plasma viscosity, hematocrit, red blood cell deformability and aggregation). Viscosity was determined using a temperature-controlled cone/plate viscometer at a physiological shear rate of 225 s-1, hematocrit using a microcentrifuge and red blood cell deformability and aggregation using a laser-optical rotational red cell analyzer. RESULTS: Whole blood viscosity and hematocrit were elevated during EARLY (4.87±0.3 cP $p < 0.01$ and 48.0±3.6 % $p = 0.03$) and remained elevated during LATE (4.87±0.8 cP $p < 0.01$ and 48.5±3.6 % $p < 0.01$) compared to BL (4.07±0.3 cP and 46.4±3.0 %). Plasma viscosity was not different between BL (1.45±0.2 cP) and EARLY (1.44±0.07 cP $p = 0.93$); however, plasma viscosity was higher at LATE compared to EARLY (1.51±0.10 $p = 0.02$), but not when compared to BL ($p = 0.17$). Red blood cell deformability and aggregation were unchanged across all conditions. CONCLUSION: Hypoxic mediated hyperviscosity is caused by rapid increases in hematocrit without changes in red blood cell properties. Plasma viscosity may also contribute to this increase after 11-14 days of acclimatization. The mechanisms and implications of changing plasma viscosity remains to be established.Funding: This work was funded by an NSERC Discovery grant and University Research Chair to PNA.

Poster #: 38 .Heart Rate Responses to End-Expiratory Apneas During Simultaneous Hypercapnia and Hypoxia. Ben O'Croinin1, Desmond Young1, Lauren Maier1, Trevor Day2, Craig Steinback1. 1Faculty of Kinesioloyg, Sport, and Recreation; University of Alberta, 2Mount Royal University

Objective: We have previous observed bradyarrythmias during voluntary apneas during hypoxia (HX). We sought to examine the influence of concurrent hypercapnia on apnea induced bradycardia during hypoxia. We hypothesized that there would be a greater bradycardic response to apneas during apneas in concurrent hypoxic hypercapnia (HCHX) when compared to HX or hypercapnia (HC) alone. Methods: 13 participants (10M/3F) were exposed to three gas conditions: HC (+5 mmHg above baseline end tidal partial pressure of CO2), HX (decrease to 50 mmHg end tidal partial pressure of O2), and HCHX (combination of HC and HX gas exposures), control apneas were performed during interspaced periods of normoxic normocapnia (NX). Heart rate and rhythm (3-lead ECG), blood pressure, gas concentrations, and oxygen saturation were measured continuously. Results: Apneas during concurrent HCHX (-17.2 ± 18.9 bpm; p=0.015) and HX (-17.9 ± 16.4 bpm; p=0.004) elicited a significantly larger bradycardia than NX apneas (-11.0 ± 15.3 bpm).Although HC apneas (-15.7 ± 12.6 bpm) did not show a significantly larger bradycardic response compared to NX apneas (p=0.069), there were no significant differences between the HX, HC, and HCHX responses (main effect p=0.892). A comparison between the arithmetic sum of the bradycardic responses to apneas during HX and HC (-33.6 ± 28.0 bpm) was larger than the actual HCHX response (p=0.0016) demonstrating a hypoadditive influence on heart rate during the combined condition. Conclusion: Our data suggests that a combination of HC and HX produces a non-additive heart rate response during apneic conditions. The apnea response to the HC stimulus was similar to that during HCHX and HX are greater. The application of this research is primarily to sleep apnea which is characterized by concurrent HC, HX, and apneas.Funding: NSERC

Poster #: 39 .MODERATE- AND LOW-ALTITUDE RESIDENTS EXPIENCE SIMILAR DECREMENTS IN PLASMA VOLUME FOLLOWING PASSIVE BUT NOT ACTIVE ASCENT TO 3600M . Stefan Pasiakos1, Reed Hoyt1, Janet Staab1, Peter Figueiredo1, Steven Landspurg1, Jon Femling2, Jason Williams2, Aaron Reilly2, Trevor Mayschak2, Mark Buller1, J Philip Karl1, Emma Atkinson1, Tim Mesite1, Beth Beidleman1. 1US Army Research Institute of Environmental Medicine, 2University of New Mexico

Objective: Previous research has demonstrated both similar and smaller decrements in plasma volume (PV) in moderate (>1500m) compared to low-altitude residents (MAR vs. LAR) following ascent to high altitude (HA) due to previously acquired hematologic acclimatization. Whether a lower altitude threshold (1190m) induces a similar response following active versus passive ascent to HA is unknown. Methods: To determine the impact of MAR versus LAR and ascent conditions on PV changes following ascent to HA, 78 healthy Soldiers (mean±SD; age=26±5yr) were tested at baseline residence (BLR) at 331m (LAR; n=41) or 1190m (MAR; n=37), transported to Taos, NM (2845m), then hiked (n=39) or were driven (n=39) to HA (3600m), and stayed for four days. AMS-Cerebral factor score (AMS-C) was assessed using the Environmental Symptoms Questionnaire at HA twice on day 1 (HA1), five times on days 2 and 3 (HA2 and HA3) and once on day 4 (HA4). Hemoglobin and hematocrit were measured at 07:00 at BLR, HA2, HA3 and HA4 and 18:00 on HA1 to calculate changes in PV. Results: In the

passive ascent group, there were no differences in PV changes at HA between MAR and LAR. In the active ascent group, PV changes (%) were different in MAR versus LAR, respectively, on HA1 (-4.8±7.5 vs. +5.2±6.8, p=0.001), HA2 (-5.3±10.0 vs. -0.05±6.5, p=0.04), HA3 (-6.5±9.2 vs -0.47±7.2, p=0.02) and HA4 (-6.7±6.6 vs. 0.64±8.5, p=0.01). PV changes (%) were positively correlated with AMS-C scores on HA1 (r=0.22; p=0.05) and HA2 (r=0.21; p=0.04). Conclusion: Our data suggest that residents living at a lower altitude threshold (1190m) demonstrate similar changes in PV as LAR following passive ascent to 3600m. More importantly, active ascent in LAR compared to MAR induced retention of PV at 3600m which may have resulted in more AMS. Authors' views not official U.S. Army or DoD policy. Funding: USAMRDC

Poster #: 40 .MANIPULATION OF IRON STATUS ON CEREBRAL BLOOD FLOW AT HIGH ALTITUDE IN LOWLANDERS AND ADAPTED HIGHLANDERS . Alexander Patrician1, Christopher Willie1, Ryan Hoiland2, Christopher Gasho3, Prajan Subedi3, James Anholm3, Michael Tymko1, Philip Ainslie1. 1Centre for Heart, Lung & Vascular Health, University of British Columbia Okanagan, 2Department of Anesthesiology, University of British Columbia, 3Pulmonary/Critical Care, Loma Linda University

Objective: Cerebral blood flow (CBF) increases during hypoxia to counteract the reduction in arterial oxygen content. The onset of tissue hypoxemia coincides with the stabilization of hypoxia-inducible factor (HIF) and transcription of downstream HIF-mediated processes. It has yet to be determined, whether HIF down- or upregulation can modulate hypoxic vasodilation of the cerebral vasculature. Therefore, we examined whether: 1) CBF would increase with iron depletion (via chelation) and decrease with repletion (via iron infusion) at high-altitude, and 2) explore whether genotypic advantages of highlanders extend to HIF-mediated regulation of CBF. Methods: In a double-blinded and block-randomized design, CBF was assessed in 82 healthy participants (38 lowlanders, 20 Sherpas and 24 Andeans), before and after the infusion of either: iron(III)-hydroxide sucrose, desferrioxamine or saline. Results: Across both lowlanders and highlanders, baseline iron levels contributed to the variability in cerebral hypoxic reactivity at high altitude (R^2=0.174, P<0.001). At 5,050 m, CBF in lowlanders and Sherpa were unaltered by desferrioxamine or iron. At 4,300m, iron infusion led to 4±10% reduction in CBF (main effect of time p=0.043) in lowlanders and Andeans. Conclusion: Iron status may provide a novel, albeit subtle, influence on CBF that is potentially dependent on the severity and length-of-stay at high altitude. Funding: The 2016 UBC Mt Everest Expedition and the 2018 Global REACH expedition to Peru was funded as a whole, by a Canada Research Chair (CRC) and the Natural Sciences and Engineering Research Council (NSERC) Discovery Grant and the Canadian Foundation for Innovation to P.N.A. A.P., M.M.T., R.L.H., were supported by an NSERC Doctoral Grants.

Poster #: 41 .HIGH-ALTITUDE EXPOSURE INDUCES UPREGULATION OF KEY PROINFLAMMATORY IMMUNE CELL MOBILIZATION FACTORS THAT ARE POTENTIALLY LINKED TO PHYSIOLOGICAL RESPONSES TO HYPOXIA.

Kathy Pham1, Shyleen Frost1, Erica Heinrich1. 1University of California, Riverside

Objective: We hypothesize that proinflammatory gene expression increases in response to high-altitude hypoxia, and exacerbates high-altitude pathologies. Methods: We compared the inflammatory profile in whole blood samples collected in the morning during fasting at sea level and after one and three nights at high altitude (3800m elevation). Basic physiological measurements (oxygen saturation, blood pressure, Acute Mountain Sickness (AMS) Scores) were taken every night at high altitude. RNA samples were collected in 15 healthy sojourners. RNA sequencing was coupled with a nanoString Human Inflammatory Panel. In a separate expedition, plasma was isolated from fasting whole blood in 20 healthy sojourners. A bead-based immunoassay was used to quantify inflammatory cytokines and chemokines (LEGENDPlex Inflammatory Panel 1). Results: Previously, we have identified upregulation of key components of the innate immune toll like receptor 4 pathway (TLR4) following acute high-altitude exposure. Several chemotactic factors were found to be significantly differentially expressed in plasma collected at high altitude. This includes IL-8, a chemotactic cytokine responsible for neutrophil mobilization ($p<0.05$) and IL-18, a cytokine involved in regulation of T cell populations ($p<0.05$). Conclusions: Our study indicates that, even in the absence of a pathogen infection, high-altitude hypoxia alone is enough to stimulate proinflammatory immune cell mobilization in healthy unacclimatized sojourners. This may have consequential implications in the development of high-altitude pathologies, where individuals who have a chronic inflammatory profile may have an exacerbated response to subsequent inflammatory stimuli. Funding: The study was supported by WMRC Mini-Grant 2022 and Mildred E. Mathias Grant.

Poster #: 42 .EXPEDITION 5300 : EXCESSIVE ERYTHROCYTOSIS IS NOT ASSOCIATED WITH ALTERED IRON HOMEOSTASIS IN MEN FROM THE WORLD'S HIGHEST CITY .

Aurélien Pichon1, Gaetano Cairo2, Benoit Champigneulle3, Margherita Correnti2, Elena Gammella2, Stefania Recalcati2, Domenico Girelli2, Annalisa Castagna2, Anne-Kristine Meinild-Lundby4, Ivan Hancco3, Carole Chirica5, Dorra Guergour5, Laura Oberholzer6, Emeric Stauffer7, Carsten Lundby8, Julien V Brugniaux3, Stéphane Doutreleau3, Samuel Vergès3, Paul Robach9. 1University of Poitiers, Laboratory Mobility, Aging & Exercise-ER 20296, Faculty of Sport Sciences-STAPS, Poitiers, France, 2Department of Biomedical Sciences for Health, University of Milan, Italy, 3HP2 Laboratory, University Grenoble Alpes, INSERM, CHU Grenoble Alpes, Grenoble, France, 4Department of Clinical Biochemistry, Nordsjællands Hospital, Hillerød, Denmark, 5Platform of Biochemistry, University Hospital of Grenoble, Grenoble, France, 6Norwegian School of Sports Sciences, Oslo, Norway, 7Laboratoire Interuniversitaire de Biologie de la Motricité EA7424, Team Vascular Biology and Red Blood Cell, Université Claude Bernard Lyon 1, Université de Lyon, CMSMR, Hôpital Croix Rousse, Hospices Civils de Lyon Lyon, France, 8Innland Norway University of Applied Sciences, Lillehammer, Norway, 9National School for Mountain Sports, Site of the National School for Skiing and Mountaineering, Chamonix, France

Objective: Despite continuously high erythropoiesis and iron demand, high-altitude residents appear to keep iron stores within the normal range. However, the mechanisms enabling iron

stores to be maintained have not been described. This study explores how iron homeostasis adapts in polycythemic residents from the world's highest city (5,100 m), with and without chronic mountain sickness (CMS). Methods: This study involved 100 male participants: 57 were permanent residents in La Rinconada (5,100 m) with no CMS, mild CMS or moderate-to-severe CMS; 26 were permanent residents in Puno (3,800 m), with no CMS, mild CMS or moderate-to-severe CMS; and 17 were healthy residents from Lima (sea level). Total hemoglobin mass (Hbmass) was assessed by carbon-monoxide rebreathing. Erythropoiesis and iron homeostasis were examined from serum samples. Results:Hbmass progressively increased with altitude, reaching extremely high values at 5,100 m. Excessive erythrocytosis was accompanied by increased erythropoietin and soluble transferrin receptor (sTfR) levels. However, healthy residents at 5,100 m did not modify iron metabolism, as erythroferrone and hepcidin concentrations remained similar to those in sea-level residents. Furthermore, iron deficiency was absent as indicated by unaltered transferrin saturation and ferritin, while ceruloplasmin was found increased. Similar high levels of Hbmass and erythropoietin were found in CMS patients and healthy individuals at 5,100 m, although moderate-to-severe CMS patients displayed trends toward even higher levels, suggesting a stronger erythropoietic response, substantiated by higher sTfR levels. In this subpopulation, excessive erythrocytosis was accompanied by erythroferrone induction and hepcidin inhibition, however without reduction in iron stores. Conclusion: Male residents from the world's highest city experience excessive erythrocytosis and massive Hbmass expansion without concomitant iron deficiency, presumably since iron regulation reaches equilibrium at a different level of erythropoiesis, through optimization of iron transport mechanisms not involving the erythroferrone/hepcidin axis.Funding: The study was sponsored by Grenoble Alpes University foundation and the French National Research Agency

Poster #: 43 .Feasibility of polysomnography sleep study among high altitude acclimatized shift workers in an industrial setting at 5050 m. Matiram Pun1, Bradley Hansen1, Ivan Lopez2, Marc Poulin3. 11. Department of Physiology & Pharmacology, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada 2. Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada, 2Safety Group, Atacama Large Millimeter Submillimeter Array (ALMA), Calama, Chile, 31. Department of Physiology & Pharmacology, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada 2. Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada 3. O'Brien Institute for Public Health, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada 4. Faculty of Kinesiology, University of Calgary, Calgary, Alberta, Canada 5. Libin Cardiovascular Institute of Alberta, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada.

Feasibility of polysomnography sleep study among high altitude acclimatized shift workers in an industrial setting at 5050 m Matiram Pun1,2, Bradley Hansen1,2, Ivan Lopez3, Marc Poulin1,2,4,5,6 1Department of Physiology & Pharmacology, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada2Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada3Safety Group, Atacama Large Millimeter Submillimeter Array (ALMA), Calama, Chile4O'Brien Institute for Public Health, Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada5Faculty of Kinesiology, University of Calgary, Calgary, Alberta, Canada6Libin Cardiovascular Institute of

Alberta, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada. Corresponding author:Marc J. Poulin, PhD, DPhilProfessor and Brenda Strafford Foundation Chair in Alzheimer ResearchDepartment of Physiology & Pharmacology, Hotchkiss Brain Institute, Cumming School of Medicine, University of CalgaryHeritage Medical Research Building Room 210, University of Calgary3330 Hospital Drive NW, Calgary Alberta, T2N 4N1, CanadaTel.: +1 403-220-8372, Fax: +1 403-210-8420 Email: poulin@ucalgary.ca
AbstractObjective: Very few studies have exploited the use of full overnight polysomnography (PSG) for high-altitude sleep studies. Published studies have been limited by small sample sizes, lower sleeping altitudes and lack of data from high-altitude workers. Here, we investigate the feasibility of using full PSG sleep studies among high-altitude acclimatized shift workers from an astronomical observatory, the Atacama Large Millimeter Array (ALMA) in the Atacama Desert in Northern Chile.Methods: High-altitude acclimatized workers at ALMA Array Operations Site (AOS, 5050 m) typically spend a week of high-altitude shift work followed by another week of rest at or near sea level (~500 m). During the week of high-altitude shift work, workers sleep at the ALMA Operation Support Facility (OSF, 2900 m) and go to work at the AOS during the day. AOS workers were recruited for a full PSG assessment during their week of shift work at high-altitude. The sleep data were analysed using Michele Sleep Scoring System (MSS).Results: We have successfully recruited a total of fifty-three high-altitude acclimatized workers (36.5±10.6 years old, male/female=36/17, body mass index=27.3±3.8kg/m2). Traditional sleep parameters such as total sleep time (TST), sleep efficiency (SE), wake after sleep onset (WASO), sleep onset latency (SOL), awakenings and periodic limb movement index were assessed and will be presented. Similarly, we will present results for sleep apnea indices (apnea-hypopnea index (AHI), central and obstructive sleep apnea indices (CSA, OSA), hypoxia burden (oxygen desaturation index (ODI) and TST below blood oxygen saturation 90% (TST90)) and sleep depth parameters (deep sleep, transitional sleep, drowsy awake and full wakefulness).Conclusion: Gold-standard sleep assessments using full PSG are feasible in industrial settings at high-altitude. Preliminary analyses show that the sleep data from high-altitude are as high quality as in-home PSG and in-hospital PSG studies at lower altitude.
Acknowledgements: We acknowledge support from ALMA, Alberta Innovates (MP), Canadian Institutes of Health Research (MJP, MP), NSERC CREATE (BRAIN CREATE; MJP, MP) and DISCOVERY (MJP) programs, and the Brenda Strafford Chair in Alzheimer Research (MJP).

Poster #: 44 .THE RELATIONSHIP BETWEEN SLEEP DURING THE FIRST NIGHT OF EXPOSURE TO 3600M ON ACUTE MOUNTAIN SICKNESS THE NEXT MORNING. Bradley Ritland1, Peter Figueiredo1, Steven Landspurg1, Jon Femling2, Jason Williams2, Janet Staab1, Reed Hoyt1, Mark Buller1, J Philip Karl1, Aaron Reilly2, Trevor Mayschak2, Emma Atkinson1, Tim Mesite1, Beth Beidleman1. 1US Army Research Institute of Environmental Medicine, 2University of New Mexico

Objective: Sleep disturbances are common at high altitude (HA) (> 3500m), but the relationship between sleep and the incidence and severity of acute mountain sickness (AMS) is debated. The objective was to investigate whether sleep on the first night at HA was associated with AMS the next morning following active and passive ascent to 3600m. Methods: 78 healthy Soldiers (mean±SD; age=26±5yr) were transported from their baseline residence (BLR) to Taos, NM (2845m), where they hiked (n=39) or were driven (n=39) to HA (3600m) and assessed for two days (HA1 and HA2). Sleep was measured via actigraphy on the first night of

sleep at HA (HA1) and used to calculate sleep awakenings (events/hr), duration (min), onset latency (min), wakefulness after sleep onset (WASO, min), and sleep efficiency (%). Mean pulse oxygen saturation (SpO2) was measured using pulse oximetry during sleep. AMS-Cerebral factor score (AMS-C) was assessed using the Environmental Symptoms Questionnaire on day 2 at HA (HA2). If AMS-C values were ≥0.7 on HA2, individuals were classified as AMS-susceptible (AMS+, n=23); others as non-susceptible (AMS-, n=55). Results: Ascent conditions did not differentially impact sleep measurements. There were no differences in sleep awakenings, onset latency, WASO, or sleep efficiency between the AMS+ and AMS- groups. In the AMS+ group compared to the AMS- group, sleep duration (min) was lower (392±57 vs. 433±63, p=0.009) and mean SpO2 (%) was lower (79.7±6.1 vs 82.0±3.9, p=0.05). Sleep duration (r=-0.32, p=0.004) and mean SpO2 (r=-0.32, p=0.005) values on the first night at HA were negatively correlated with AMS-C values the following morning on HA2. Conclusion: When Soldiers passively or actively ascend to high altitude (3600m), sleep duration and arterial oxygen saturation during the first night at HA is associated with AMS the next morning. Authors' views not official U.S. Army or DoD policy. Funding: USAMRDC

Poster #: 45 .SEX, BLOOD PRESSURE, AND ALTITUDE: A PROSPECTIVE OBSERVATIONAL COHORT STUDY. T Douglas Sallade1, Charles Duke2, Jennifer Starling3, 4, Alison Sheets5, Sushil Pant6, David Young7, David Twillman4, Nirajan Regmi8, Benoit Phelan9, Purshotam Paudel10, Matthew McElwee11, Luke Mather12, 13, Devlin Cole14, Theodore McConnell15, Buddha Basnyat16, 17, Linda Keyes4, 5. 1Geisinger Lewistown Hospital, Lewistown, Pennsylvania, 2Department of Emergency Medicine, Yale School of Medicine, New Haven, Connecticut, 3Colorado Permanente Medical Group, Saint Joseph Hospital, Denver, Colorado, 4Department of Emergency Medicine, University of Colorado, Aurora, Colorado, 5Longmont United Hospital, Longmont, Colorado, 6Mountain Medicine Society of Nepal and Kunde Hospital, Kathmandu, Nepal, 7Department of Emergency Medicine, Rush University Medical Center, Chicago, Illinois, 8Mountain Medicine Society of Nepal, Kathmandu, Nepal, 9Saint John Regional Hospital, Saint John, Canada, 10Mountain Medicine Society of Nepal and District Hospital, Dhading, Nepal, 11Department of Medicine, University of Minnesota, Minneapolis, Minnesota, 12Family Medicine Residency of Idaho, Boise, Idaho, 13University of Washington School of Medicine, Seattle, Washington, 14Kapiolani Women and Children's Hospital, Honolulu, Hawaii, 15McGill University, Montreal, Canada, 16Oxford University Clinical Research Unit - Nepal, Nepal, 17Nepal International Clinic, Kathmandu, Nepal

Objective: A recent study found blood pressure (BP) increased more in men than women upon acute high altitude exposure. We sought to confirm these sex differences in a cohort of Himalayan trekkers.Methods: We reanalyzed data from our previously published cohort comparing mean BP and change in BP in male (M) versus female (F) trekkers ascending from 2860 m to 3400 m and 4300 m.Results: We analyzed 658 trekkers, 60 with preexisting hypertension (M=387, F=271). In those without preexisting hypertension, systolic BP (mean (mmHg), 95% CI) was greater in men than women at 2860 m (M:130, 128.7-131.7; F:122, 120.4-124.2) and 3400 m (M:129, 127.4-130.9; F:124, 122.2-126.6), but not 4300 m (M:129, 127.2-131.2; F:126, 123.6-128.6). In men and women with preexisting hypertension, BP was similar at 2860 m (M:150, 144.0-155.7; F:153, 141.4-163.6), 3400 m (M:150, 141.8-157.3; F:153, 139.8-165.6) and 4300 m (M:143, 134.1-152.8; F:139, 122.0-156.0). From 2860 m to 3400 m the

proportion of trekkers without preexisting hypertension whose BP increased (F=25%, M=18%), decreased (F=17 %, M=21%) or did not change >10 mmHg (F=58%, M=61%) was similar between sexes (p=0.2). Similar results were found among those with preexisting hypertension and between 3400 m to 4300 m (data not shown).Conclusion: Normotensive men had higher BP than women at 2860 m and 3400 m. BP changed little with altitude and changes did not differ by sex. Our study is limited by the lack of a low altitude measurement. Funding: Nepal International Clinic, Wilderness Medicine Society.

Poster #: 46 .TRANSIENT HYPOXIA-INDUCED DEOXYHEMOGLOBIN FORMATION SERVES AS AN MRI CONTRAST FOR PERFUSION IMAGING IN PATIENTS WITH STENO-OCCLUSIVE DISEASE. Ece Su Sayin1, 2, Vittorio Stumpo3, 4, Jacopo Bellomo3, 4, Julien Poublanc2, Marco Piccirelli3, 4, James Duffin1, Vepeson Wijeya2, Athina Pangalu 3, 4, Andrea Bink3, 4, Bence Nemeth3, 4, Zsolt Kulcsar3, 4, David Mikulis1, 2, Olivia Sobczyk2, Jorn Fierstra3, 4, Joseph Fisher1, 2. 1University of Toronto, 2University Health Network, 3University Hospital Zurich, 4University of Zurich

Background: Susceptibility agents are required to generate contrast for calculating resting perfusion measures (such as mean transit time, cerebral blood volume, and cerebral blood flow) using dynamic susceptibility contrast (DSC) MR perfusion. Currently this requires the intravascular injection of gadolinium (Gd), engendering medical risks, cost, along with image, and environmental drawbacks. Hypoxia-induced deoxyhemoglobin (dOHb) is intrinsic, reversibly paramagnetic, and relatively low-cost.Objective: Here we use hypoxia-induced dOHb as a suitable agent for DSC perfusion and validate against a clinical standard, Gd, in patients with steno-occlusive disease (SOD).Methods: We studied 10 patients between the ages of 39 and 74 (8 M) with known steno occlusive disease in a 3-Tesla scanner running-BOLD acquisition sequences. Transient hypoxia was induced via an automated gas blender running feed-forward gas algorithm targeting 2 consecutive reductions of pulmonary PO2 from 95 mmHg to 40 ± 3 mmHg followed by full reoxygenation within a single inhalation. A second BOLD sequence was acquired following an intravenous injection of 5 ml of Gd. All images were analyzed, and resting perfusion measures were calculated using a standard tracer kinetic model.Results: The calculated perfusion measures and their distribution showed similar voxel-wise proportional changes in BOLD signal throughout the brain. Bland-Altman analysis indicated little bias or difference in hemodynamic measures between methods.Conclusions: The resting perfusion measures obtained from brief transient hypoxia are spatially and quantitatively comparable to those obtained using Gd in the same patients with varying patterns of SOD. The main advantages of transient hypoxia as a contrast agent include it being non invasive; reduced risk of allergy, renal or fetal toxicity; no accumulation in organs, and no environmental damage, making it a suitable contrast for DSC perfusion imaging.Funding: Dr Joseph Fisher Critical Care Research Fund

Poster #: 47 .Hyperoxia improves exercise capacity in cardiopulmonary disease. A series of RCT's. Julian Müller1, Mona Lichtblau1, Saxer Stéphanie1, Simon Raphael Schneider1, Paula Appenzeller1, Bauer Meret1, Elisabeth Hasler1, Esther Irene Schwarz1, Konrad Ernst Bloch1, Silvia Ulrich1. 1Department of Pulmonology, University Hospital Zurich, Zurich, Switzerland ; University of Zurich, Zurich, Switzerland

Background: To study the overall and differential effect of breathing hyperoxia (FiO2 0.5) vs. placebo (ambient air, FiO2 0.21) to enhance exercise performance in healthy people, patients with pulmonary vascular disease (PVD) with precapillary pulmonary hypertension (PH), chronic obstructive pulmonary disease (COPD), PH due to heart failure with preserved ejection fraction (HFpEF) and cyanotic congenital heart disease (CHD) using data of five RCTs performed with identical protocols.Methods: 91 subjects (32 healthy, 22 PVD with pulmonary arterial or distal chronic thromboembolic PH, 20 with COPD, 10 with PH in HFpEF and 7 with CHD) performed 2 cycle incremental (IET) and 2 constant work-rate exercise tests (CWRET) at 75% of maximal load (Wmax), each with ambient air and hyperoxia in single blinded, randomized-controlled cross-over trials. The main outcomes were differences in Wmax (IET) respectively cycling time (CWRET) with hyperoxia vs ambient air.Results: Overall, hyperoxia increased Wmax by +12 W (95%CI: 9 to 16, p<0.001) and cycling time by +6:13 min (4:50 to 7:35, p<0.001), with improvements being highest in patients with PVD: (Wmax/min: +18%/+118% vs. COPD: +8%/+60%, healthy: +5%/+44%, HFpEF: +6%/+28%, CHD: +9%/+14%).Conclusion: This large collective of healthy and patients with various cardiopulmonary disease confirms that hyperoxia significantly prolongs cycling exercise with improvements being highest in endurance CWRET and patients with PVD. These results call for studies investigating optimal oxygen levels to prolong exercise time and effects on training.

Poster #: 48 .ACUTE HYPOXIA ELICITS LASTING REDUCTIONS IN THE SYMPATHETIC ACTION POTENTIAL TRANSDUCTION OF ARTERIAL BLOOD PRESSURE IN MALES. . Brooke Shafer1, Massimo Nardone2, Anthony Incognito 2, Tyler Vermeulen1, Andre Teixeira2, Philip Millar2, William Sheel1, Christopher West1, Najib Ayas1, Glen Foster1. 1University of British Columbia, 2University of Guelph

Objective: Acute hypoxia leads to lasting sympathoexcitation without corresponding changes in vascular tone, suggesting reduced sympathetic transduction. We hypothesized that (1) changes in mean arterial pressure (MAP) evoked by sympathetic action potential (AP) activity would be blunted during acute hypoxia but restored in recovery and (2) that asynchronous APs would elicit a smaller change in MAP compared with synchronous APs. Methods: Seven healthy males (age: 24 (3) yrs; BMI: 25 (3) kg/m2) underwent 20-min isocapnic hypoxia (PETO2: 47 (2) mmHg) and 30-min recovery. MAP (photoplethysmography) and muscle sympathetic nerve activity (MSNA; fibular microneurography) were acquired during baseline, hypoxia, early (first 7-min) and late recovery (last 7-min). A continuous wavelet transform with matched mother wavelet was used to detect sympathetic APs. AP groups were classified as cardiac cycles associated with synchronous (APs with MSNA burst), asynchronous (APs outside MSNA burst), and no sympathetic AP activity. Sympathetic transduction of MAP was quantified using signal-averaging and DMAP was tracked following AP group activity. Results: Following synchronous APs, DMAP was reduced in hypoxia (+1.8 (0.9) mmHg, P = 0.041) and early recovery (+1.5 (0.7) mmHg, P = 0.009) compared with baseline (+3.1 (2.2) mmHg). At rest, MAP reductions

following asynchronous APs was attenuated compared with no AP activity (-0.4 (1.1) vs. -2.2 (1.2) mmHg, respectively; P = 0.003) but did not differ between AP groups in hypoxia, early, or late recovery. Conclusion: Sympathetic transduction of MAP is blunted in hypoxia and early recovery. At rest, asynchronous sympathetic APs contribute to neural regulation of MAP by attenuating nadir pressure responses. Funding: NSERC, HSFC

Poster #: 49 .THE EFFECTS OF ACUTE INTERMITTENT HYPERCAPNIA ON VENTILATORY LONG-TERM DEPRESSION AND CARDIOVASCULAR FUNCTION. Conan Shing1, Scott Thrall1, Megan Lance1, Jordan Bird1, Brooke Shafer1, Mohammad Soltani1, Glen Foster1. 1Centre for Heart, Lung, and Vascular Health, School of Health and Exercise Sciences, University of British Columbia, Kelowna, British Columbia, Canada

The ventilatory and cardiovascular effects of intermittent hypercapnia (IHc) in the absence of hypoxia is unknown. This study investigated if IHc led to long-lasting effects on ventilation, blood pressure, and vascular conductance. Thirteen healthy participants (age: 23±4 years; BMI: 22±2 kg/m2) underwent a 10-minute baseline, 40-minutes of IHc (40 seconds end-tidal PCO2 +5 mmHg from baseline and 20 seconds of normocapnia), followed by 30-minutes of room-air recovery. Ventilation and mean arterial pressure (MAP) were measured continuously, while arm and leg blood flow were measured via strain gauge plethysmography at the end of baseline and every 10 minutes throughout recovery. Limb vascular conductance was calculated as the sum of arm and leg blood flow multiplied by two and divided by MAP. Data were compared statistically (P<0.05) using mixed effects linear modeling with time (baseline, 10-, 20-, and 30-minutes recovery) as a fixed factor and participants as a random factor. Ventilation (P=0.05) and tidal volume (P=0.06) tended to be reduced throughout recovery while breathing frequency (P=0.2) was unchanged. There was a time effect for MAP (P<0.001) and post hoc analysis indicated that MAP was increased at 10-minutes (7.2 mmHg, CI95%: 3.7 – 10.7, P<0.001), 20-minutes (7.7 mmHg, CI95%: 4.2 – 11.2, P<0.001), and 30-minutes (8.6 mmHg, CI95%: 5.1 – 12.1, P<0.001) following IHc. There was a time effect for limb vascular conductance (P=0.001) and post-hoc analysis found conductance was reduced throughout recovery (0.03 ml/min/100ml/mmHg, CI95%: -0.05 – -0.01, P<0.01) following IHc. In conclusion, IHc attenuated minute ventilation and limb vascular conductance and led to long-lasting increases in arterial pressure. This suggests IHc may contribute to the long-lasting sympathoexcitatory effects of intermittent hypoxia in obstructive sleep apnea.Funding Sources: American Physiological Society, Natural Sciences and Engineering Research Council of Canada.

Poster #: 50 .24-HOUR AMBULATORY BLOOD PRESSURE AT LOW VERSUS HIGH ALTITUDE BEFORE AND AFTER PARTIAL ACCLIMATIZATION: THE COLORADO HIGH ALTITUDE MONITORING PRESSURE STUDY (CHAMPS). .
Lukas Sloan1, Andrew Burns1, Greta Carlson1, Ilaria Ferrari1, Diana Biggs1, Linda Keyes1. 1University of Colorado School of Medicine

Andrew C. Burns; Greta Kreider-Carlson MD; Ilaria Ferrari BS; Lukas Sloan BS; Diana Biggs MD; Linda E. Keyes MD; University of Colorado School of Medicine Aurora, Colorado; andrew.c.burns@colorado.edu24-HOUR AMBULATORY BLOOD PRESSURE AT LOW VERSUS HIGH ALTITUDE BEFORE AND AFTER PARTIAL ACCLIMATIZATION: THE COLORADO HIGH ALTITUDE MONITORING PRESSURE STUDY (CHAMPS).Abstract:Objective: Acute high altitude exposure may increase 24-hour ambulatory blood pressure (ABP), but change in blood pressure with acclimatization is poorly understood. [LK1] We compare 24-hour ABP at low altitude versus the first 24 hours at high altitude and after 72 hours.Methods: This is a prospective observational cohort study of adult lowlanders, comparing 24-hour ABP at low (<1,000m) versus high-altitude (2,500-2,800m). BP was monitored every 30 minutes while awake and every hour overnight for 24 hours using Welch-Allyn6100 ABP monitors. High altitude data was collected during the first and third days at high altitude.Results: We present preliminary data on 8 participants (f=5, m=3) with complete matched data for all three time points (mean age 48 (range 34-70), 2 [LK2] with underlying hypertension). We found an increase in average 24-hour SBP between low and high altitude (121 [91-150] mmHg vs 132 [96-169] mmHg, respectively), with a mean SBP increase of 12 [-16-40] mmHg, p=0.049. Diurnal SBP was greater at high altitude (123 [94-151] vs 136 [100-172], p=0.02), but nocturnal SBP did not differ (112 [72-151] vs 121[79-163], p=NS). Results were similar for DBP. Comparing the first 24h versus 72h at high altitude, we found no differences in average 24-hour (132 [96-169] mmHg vs 132 [92-172] mmHg, p=NS), diurnal SBP (136 [100-172]) mmHg vs 136 [95-177] mmHg, p=NS) or nocturnal SBP (121 [79-163] mmHg vs 113 [84-142] mmHg.Conclusions: In our cohort, BP was elevated at high altitude compared to low altitude due to increases in diurnal BP, and remained so after 72-hours of acclimatization. The clinical importance and the long-term effects of elevated BP during high altitude sojourns remain to be determined.Funding: Wilderness Medical Society Hultgren Grant.

Poster #: 51 .SLEEP QUALITY, AMBULATORY BLOOD PRESSURE AND ACUTE MOUNTAIN SICKNESS. Lukas Sloan1, Diana Biggs1, Andrew Burns1, Greta Carlson1, Ilaria Ferrari1, Linda Keys1. 1University of Colorado School of Medicine

SLEEP QUALITY, AMBULATORY BLOOD PRESSURE AND ACUTE MOUNTAIN SICKNESSLukas Sloan, Diana Biggs, Andrew Burns, Greta Carlson, Ilaria Ferrari, and Linda E. KeyesObjectiveHigh altitude may negatively affect sleep quality, but the association between poor sleep and acute mountain sickness (AMS) is controversial. BP measured at the time of altitude-related symptoms has no association with AMS, but nocturnal BP might. Thus, we compared sleep quality and 24h-ambulatory blood pressure (ABP) in high altitude travelers with and without AMS.MethodsThis is a prospective observational cohort study of lowlanders visiting 2500-2800m during their first 24h at high altitude, and at 72h. We measured sleep quality with the Groningen Sleep Quality Scale (GSQ), AMS by the 2019 Lake Louise Questionnaire (LLS) and 24-hour ABP with Welch-Allyn 6100 ABPM. ResultsWe enrolled 28

participants (mean age 58, range 32-77, m=18, f= 10), 3 with AMS and 23 without AMS (missing data, n=2)). Baseline GSQ did not differ in AMS+ vs AMS- (p=NS), however, AMS+ had higher 24-h GSQ scores, (ie, worse sleep quality) vs AMS- (mean GSQ AMS+= 10.7 [95%CI:8.88-12.4] vs AMS-= 5.5 [95%CI:3.89-7.16], p=0.04). In a subset (n=8), baseline GSQ did not differ versus 24-h GSQs or 72-h scores (p=NS); however, sleep quality was worse on the first night vs the third (GSQ 6.9 vs 1.9, p=0.02). Mean 24-hour SBP (129 mmHg vs 140 mmHg) and mean daytime SBP (136 mmHg vs 150 mmHg) did not differ by AMS status (p=NS), however, AMS+ had lower mean nocturnal SBP versus AMS- (96 mmHg vs 127 mmHg, p=0.01).ConclusionThose with AMS had worse sleep quality, supporting the inclusion of a sleep quality question in the LLS. Sleep quality improved after time at high altitude. Surprisingly, mean nocturnal SBP was lower in those who develop AMS. We need more participants to validate this finding.Funding: Wilderness Medical Society Hultgren Grant

Poster #: 52 .Effect of Aymara Enriched Genetic Variants in Austrians Exposed to Acute Hypoxia.. Jihyun Song1, Martin Burtscher2, Ricardo Amaru3, Maria Wille2, Soo Jin Kim1, Josef T. Prchal1. 1Division of Hematology and Hematologic Malignancies, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA, 2Dept. of Sport Science of the University of Innsbruck, A-6020 Innsbruck, Austria, 3Cell Biology Unit, School of Medicine, San Andres University, La Paz, Bolivia

Objective: The evolutionary adaptation to the high-altitude hypoxia is best defined in Tibetans and Andean natives. We reported evolutionary selected genetic variants of Andean Aymaras identified by whole genome analysis (Crawford, AJHG, 2017, Sundar, Blood, 2022). These variants are not unique to Aymaras and are present also in other populations, but at lower frequencies. We postulated that they likely modify hypoxic responses in non-Aymaras, and we attempted to define their functional consequences in non-Aymara population upon acute hypoxia exposure.Methods: We genotyped 6 Aymara enriched single nucleotide polymorphisms (SNPs) - BRINP3(rs11578671), NOS2(rs34913975), SH2B1(rs12448902), TBX5(rs487105), PYGM(rs487105), and NFKB1(rs230511) in 74 fit Austrians. Physiological parameters including SpO2, PaCO2, PaO2, SaO2, blood pressure (BP), heart rate (HR), lactate, and Lake Louis Score (LLS) were measured at 0, 3, and 6 hours of hypoxic exposure (~4500m). Hemoglobin was measured before hypoxic exposure. We interrogated associations of these genotypes with these physiological responses to acute hypoxia.Results: 6 hours-hypoxic exposure decreased SpO2, PaCO2, PaO2, SaO2, systolic and diastolic BP, while increased HR, but did not alter lactate.Heterozygotes for NOS2 SNP and SH2B1 SNP had lower SpO2 while homozygotes for NFKB1 SNP had higher SpO2. Systolic and diastolic BP were more decreased in homozygotes for NOS2 SNP and heterozygotes for PYGM SNP. After hypoxia, the BP was the highest in NFKB1 SNP heterozygotes. HR was highest in NOS2 SNP heterozygotes but negatively correlated with PYGM SNP. BRINP3 SNP heterozygotes had lower lactate compared to wild type after hypoxia. LLS at 3 hour-hypoxia was lower in SH2B1 SNP heterozygotes. NFKB1 SNP homozygotes had the lowest LLS at 6 hour-hypoxia, while hemoglobin measured before hypoxia positively correlated with NFKB1 SNP in females. Only NFKB1 SNP negatively correlated with severity of AMS.Conclusion: We report that these genetic variants enriched in Aymaras modify hypoxic responses also in Europeans.

Poster #: 53 .Expedition 5300 - Reduced red blood cell deformability is associated with excessive erythrocytosis in the highest city of the world . Emeric STAUFFER1, 2, Aurélien PICHON3, Benoit CHAMPIGNEUL4, Michaël Furian5, Lars KARSTNER6, 7, Ivan HANCCO4, Paul ROBACH4, 8, Julien V. BRUGNIAUX4, Mélanie ROBERT1, Elie NADER1, Philippe CONNES1, Samuel VERGES4. 1Laboratoire Interuniversitaire de Biologie de la Motricité (LIBM) EA7424, Team « Vascular Biology and Red Blood Cell », Université Claude Bernard Lyon 1, Université de Lyon, France, 2Explorations Fonctionnelles Respiratoires, Médecine du sport et de l'Activité Physique, Hospices Civils de Lyon, Hôpital Croix Rousse, Lyon, France, 3Université de Poitiers, Laboratoire MOVE, Poitiers, France , 4Univ. Grenoble Alpes, Inserm, CHU Grenoble Alpes, HP2, 38000 Grenoble, France, 5Pulmonary Division, University Hospital Zurich, 8092 Zurich, Switzerland, 6Theoretical Medicine and Biosciences, Saarland University, Homburg, Germany., 7Experimental Physics, Saarland University, Saarbrücken, Germany, 8National School for Mountain Sports, Site of the National School for Skiing and Mountaineering (ENSA), Chamonix, France

Introduction: Excessive erythrocytosis (EE) is a frequent condition observed in highlanders leading to blood hyperviscosity, which can favour the onset of clinical complications. Blood viscosity is highly dependent on haematocrit (and haemoglobin concentration) but also on red blood cell rheological properties. However, very few studies investigated RBC rheological properties in individuals residing at high altitude and suffering from EE. The present study investigated blood viscosity and RBC rheological parameters in residents of the highest city in the world (La Rinconada, Peru, 5,100 m) with (EE group) and without EE (non-EE group).Methods: Seventy-two Andean highlanders living at 5,100 m were included in this study (38 with EE and 24 without). Blood viscosity at native haematocrit, RBC deformability and aggregation, reticulocytes count and free haemoglobin were measured.Results: EE group exhibited lower arterial oxygen pressure ($p=0.01$) and higher percentage of reticulocytes ($3.37\pm1.6\%$ vs $2.64\pm1.1\%$; $p=0.02$) than subjects without EE. Blood viscosity at 22.5 s-1 shear rate at native haematocrit was higher in the EE group than in non-EE group (38.3 ± 1.7 vs 27.43 ± 1.1 cP; $p <0.001$). RBC deformability was lower in EE subjects ($p<0.01$). Free haemoglobin concentration was higher in subjects suffering from EE (24.35 ± 13.41mg/dL vs 12.13 ± 4.32 mg/dL; $p<0.001$). No difference was observed for RBC aggregation.Conclusion: The lower arterial oxygen pressure in EE subjects resulted in increased erythropoietic activity, marked by higher percentage of reticulocytes. Reticulocytes are immature RBCs that are less deformable than mature RBCs that could explain why the EE group had a lower RBC deformability. Indeed, both the higher haematocrit and the lower RBC deformability could be at the origin of the greater blood viscosity in EE individuals. The greater amount of less deformable RBCs in the EE group could have increased haemolysis and accumulation of free haemoglobin.

Poster #: 54 .THE INFLUENCE OF PENTOXIFYLLINE ON HEMORHEOLOGY AND PULMONARY ARTERY PRESSURE AT 3800M. Andrew R Steele1, Connor A Howe1, Katharine Foster2, Alexandra M Williams3, Hannah G Caldwell1, L Madden Brewster1, Jennifer Duffy1, Justin A Monteleone1, Prajan Subedi2, James D Anholm2, Philip N Ainslie1, Joshua C Tremblay4. 1University of British Columbia Okanagan, 2Loma Linda University School of Medicine, 3University of British Columbia, 4Cardiff Metropolitan University

OBJECTIVE: Pentoxifylline, a non-selective phosphodiesterase inhibitor, reduces blood viscosity and directly vasodilates and is used for the treatment of peripheral vascular disease. High altitude pathologies relate to rises in blood viscosity and pulmonary artery pressure. METHODS: We conducted a double-blinded, placebo-controlled study to test the hypothesis that pentoxifylline would reduce blood viscosity and pulmonary pressure in lowlanders after 11-14 days at Barcroft Field Station (3800m). Participants (6M/10F; age = 27 ± 4) were administered placebo or 400 mg of pentoxifylline orally the preceding night and the two hours before testing. An arterial blood sample was acquired to assess blood gases and venous sample for hemorheology (viscosity, hematocrit, plasma viscosity, red blood cell deformability and aggregation). Pulmonary artery systolic pressure (PASP) was estimated using echocardiography during room air breathing and following 8-10 minutes of isocapnic hypoxia (end tidal partial pressure of oxygen: 40 mmHg). RESULTS: Pentoxifylline did not alter arterial blood gases, red blood cell deformability or aggregation compared to placebo. Blood viscosity was reduced at high shear rates (>150 s-1) in males (Cohen's d = 1.41-1.83, P= 0.02-0.008) but not females. Plasma viscosity (d = 2.06, P = 0.01) and hematocrit (d = 2.43, P = 0.002) were also reduced in males. PASP conversely, was reduced with pentoxifylline in females during room air (d = 1.05, p = 0.02) and isocapnic hypoxia (d = 0.971, p = 0.03), but not in males. CONCLUSION: Therefore, acute pentoxifylline administration appears to influence both hemorheological properties and PASP in lowlanders without high altitude-related illnesses at 3800m; however, these effects may be sex specific. Pentoxifylline may be useful for the prevention or treatment of high altitude-related illnesses and merits further investigation in individuals susceptible for high altitude pulmonary edema and with excessive erythrocytosis.Funding: This work was funded by NSERC.

Poster #: 55 .MECHANISTIC INSIGHTS INTO NORMOTHERMIC REGIONAL PERFUSION (NRP) FOR THE TREATMENT OF HYPOXIA INDUCED LIVER DAMAGE PRIOR TO TRANSPLANTATION.. Andrew Sutherland1, Bansal Sukhchain 2, Carolyn Cairns1, Brian Conway1, Emma Morrison1, Chris Watson3, James Dear1, Gabriel Oniscu1. 1University of Edinburgh, 2University of Birmingham, 3University of Cambridge

Introduction: Normothermic regional perfusion (NRP) is a transplant procurement technique that can reverse the deleterious effects of hypoxia associated with donors after circulatory death (DCD). A number of studies have demonstrated NRP improves clinical outcomes and organ utilization. However, little is known about the mechanism of action. We hypothesised that DCD livers are preconditioned during the initial period of hypoxia and then reconditioned during NRP. Furtherrmore NRP provides a period of organ assessment prior to transplantation.Methods: NRP was commenced following cardiac arrest in DCD donors for 2 hours and liver biopsies and serum samples were taken at 0 and 120 minutes. mRNA expression of 6 common HIF target genes; erythropoietin (EPO), haemoxygenase-1 (HMOX-1),

pyruvate dehydrogenase kinase-1 (PDK1), glucose transporter-1 (SLC2A1) , vascular endothelial growth factor (VEGFA), and VEGF receptor (FLT-1) was assessed. ADP/ATP ratio was assessed using bioluminescence and serum miR-122 concentration (a marker of liver injury) was determined by quantitative real time RT-PCR. Two-sample t tests were run to compare groups.Results: HIF target genes were up-regulated following 2 hours NRP (NRP2) compared to the start of NRP (NRP0). The mean up-regulation ranged from 1.3 fold (EPO) to 2.4 fold (FLT-1). The up-regulation of 4 genes reached significance ($p<0.05$). At the end of NRP serum miR-122 was significantly lower in the donors whose livers were successfully transplanted compared to those deemed not suitable. ATP/ADP ratio was restored and lactate reduced.Conclusions: Upregulation of HIF target genes suggests that hypoxic preconditioning may play a role in the mechanism of NRP. Reconditioning likely occurs through replenishment of `ATP and normalization of lactate. miR-122 is a sensitive and specific marker of liver injury that was able to differentiate transplantable from non-transplantable livers.

Poster #: 56 .A PILOT STUDY INVESTIGATING THE EFFECT OF POSITIVE PRESSURE VENTILATION ON OXYGEN SATURATION AT ALTITUDE DURING RECREATIONAL AVIATION. Jenna L Taylor1, J. Hunter Downs III1, Joshua D Donkor1, Jessica I Johnston1, Aidan K Downs1, Crystal L Marshall2, Elias Smirlis2, Alex R Carlson1, Douglas Rozendaal3, Peter Larsen2, Bruce D Johnson1, Douglas T Summerfield2. 1Mayo Clinic Rochester, 2MercyOne North Iowa Medical Center, 3None

Objective: We investigated whether positive pressure ventilation (PPV), using a commercial bilevel positive airway pressure (BIPAP) device, would improve oxygen saturation during recreational aviation up to 12500ft without supplemental oxygen. Methods: In this pilot study, ten healthy adults with recreational flight experience (age:47±14; female=5; flight hours=1450±2105) completed a standardized flight profile in an unpressurized aircraft, involving randomized crossover design at 8000ft and 12500ft with BIPAP or control. Peripheral oxygen saturation (SpO2), middle cerebral artery velocity (MCAv), and mean arterial pressure (MAP) were measured continuously on the ground and during flight. Subjects completed a 3-min psychomotor vigilance test (PVT) during flight taxi and halfway through each 15-min altitude period. Data were analyzed for the effect of altitude or BIPAP using two-tailed paired t-tests. Results: There was a large significant effect of altitude on mean SpO2 [ground:97±1%; 8000ft:92±1%; 12500ft:86±4%; mean difference (MD)=-8±2%; $p<0.001$; effect size (ES)=3.3], SpO2 nadir [ground:95±2%; 8000ft:87±3%; 12500ft:78±3%; MD=-12±3%; $p<0.001$; ES=4.0], and MCAv [ground:57±9cm/s; 8000ft:53±9cm/s; 12500ft:52±9cm/s; MD=-5±5cm/s; $p=0.01$; ES=1.0]. There was no effect of altitude ($p>0.05$) on MAP or PVT reaction time. There was a large significant effect of BIPAP on mean SpO2 at 8000ft [Control:92±1%; BIPAP:94±2%; MD=2±1; $p=0.003$; ES=1.3] and 12500ft [Control:86±4%; BIPAP:89±4%; MD=2±3%; $p=0.03$; ES=0.8]. There was also a large significant effect of BIPAP on MCAv at 8000ft [Control:53±9%; BIPAP:50±9cm/s; MD=-4±3cm/s; $p=0.005$; ES=1.4] but not 12500ft ($p>0.05$). There was no effect of BIPAP ($p>0.05$) on SpO2 nadir, MAP, or PVT reaction time. Conclusion: This small pilot study provides preliminary results that BIPAP may improve mean oxygen saturation for recreational aviators up to 12500ft without supplemental oxygen. BIPAP appears to reduce MCAv, however, reaction time was unaffected. Future adequately powered studies are needed to further investigate the potential utility of PPV to optimize oxygen saturation and cognition in recreational aviation.Funding: Mayo Clinic and MercyOne North Iowa Medical Center

Poster #: 57 .ACUTE MOUNTAIN SICKNESS NEGATIVELY IMPACTS MOOD STATE FOLLOWING BOTH ACTIVE AND PASSIVE ASCENT TO 3600M. William Tharion1, Peter Figueiredo1, Steven Landspurg1, Janet Staab1, Mark Buller1, J Philip Karl1, Reed Hoyt1, Jon Femling2, Jason Williams2, Aaron Reilly2, Trevor Mayschak2, Emma Atkinson1, Tim Mesite1, Beth Beidleman1. 1US Army Research Institute of Environmental Medicine, 2University of New Mexico

Objective: Mood state is known to change following acute exposure to high altitude (HA) but it is unknown whether acute mountain sickness (AMS) and ascent conditions exacerbate this response. Methods: To determine if AMS impacts mood state following active and passive ascent to HA, 78 healthy Soldiers (mean±SD; age=26±5yr) were tested at baseline residence (BLR), transported to Taos, NM (2845m), then hiked (n=39) or were driven (n=39) to HA (3600m), and stayed for four days. AMS-Cerebral factor score (AMS-C) was assessed using the Environmental Symptoms Questionnaire at HA twice on day 1 (HA1) and five times on days 2 and 3 (HA2 and HA3). If AMS-C was ≥0.7 on any assessment, individuals were categorized as AMS-susceptible (AMS+, n=33); others were non-susceptible (AMS-, n=45). Seven mood states (anger, anxiety, depression, fatigue, happiness, vigor, and restlessness) were assessed using the Automated Neuropsychological Assessment Metrics at BLR, and after 19h (HA2) and 43h (HA3) at HA. Results: Ascent conditions did not differentially impact mood state. In the AMS- group, none of the mood states changed from BLR to HA. In the AMS+ group, however, anger and anxiety increased ($p<0.05$), respectively, from BLR (0.07±0.15; 0.06±0.17) to HA2 (0.51±0.80; 0.39±0.59) and decreased ($p<0.05$) from HA2 to HA3 (0.39±0.69; 0.21±0.61). Depression and fatigue increased ($p<0.05$), respectively, from BLR (0.02±0.08; 0.50±0.67) to HA2 (0.41±0.67; 1.89±1.20) and decreased ($p<0.05$) from HA2 to HA3 (0.18±0.57; 1.25±1.17). Happiness and vigor decreased ($p<0.05$), respectively, from BLR (3.27±1.62; 2.14±1.53) to HA2 (2.27±1.64; 1.48±1.24) and remained unchanged from HA2 to HA3 (2.54±1.70; 1.66±1.50). Restlessness increased ($p<0.05$) from BLR (0.19±0.36) to HA2 (0.85±1.02) and decreased ($p<0.05$) from HA2 to HA3 (0.46±0.20). All mood states (both positive and negative) remained different at HA3 compared to BLR. Conclusions: Mood was negatively impacted by rapid ascent to 3600m in AMS-susceptible individuals for the first three days at HA which may negatively impact operational effectiveness. Authors' views not official U.S. Army or DoD policy. Funding: USAMRDC

Poster #: 58 .ACUTE INTERMITTENT HYPERCAPNIC HYPOXIA AUGMENTS LEFT VENTRICULAR END-SYSTOLIC ELASTANCE. Scott Thrall1, Alexandra Williams2, Philip Millar3, Megan Lance1, Brooke Shafer1, Conan Shing1, Jordan Bird1, Christopher West2, Glen Foster1. 1University of British Columbia Okanagan, 2University of British Columbia, 3University of Guelph

Objective: Acute intermittent hypercapnic hypoxia (IHH) elicits persistent increases in peripheral sympathetic activity – termed sympathetic long-term facilitation (sLTF) – leading to high blood pressure without affecting heart rate. Whether sLTF signals the myocardium to augment left ventricular contractility is unknown. We hypothesized that IHH would augment load-independent metrics of cardiac contractility, improving left ventricular systolic function.

Methods: 15 healthy participants (4F; age: 25±4 yrs; BMI: 23±2 kg/m2) underwent 40 consecutive 1-min bouts of 40-sec hypercapnic hypoxia (PETO2: 45 mmHg; PETCO2: +4 mmHg) and 20-sec normocapnic normoxia. Ventilation, end-tidal gases, blood pressure, heart rate, muscle sympathetic nerve activity (fibular nerve), end-systolic and end-diastolic volumes, and isovolumic contraction time were measured at rest and during conditions of heightened sympathoexcitation using 5-min stages of progressive lower body negative pressure (LBNP; -15, -30, and -45 mmHg) before and after IHH. End-systolic elastance was estimated noninvasively according to validated standards using echocardiography-derived parameters of ventricular volumes, contraction timings, and arterial pressure as an assessment of load-independent left ventricular contractile performance. Results: As expected, IHH elicited sustained increases in ventilation, mean and diastolic blood pressure both at rest (all $P < 0.01$) and across progressive LBNP (all $P < 0.001$). End-systolic elastance at rest was similar before and after IHH (+0.11 [-0.10, 0.31] mmHg/mL, $P = 0.301$) but tended to be greater across all stages of LBNP following IHH (+0.11 [0.00, 0.21] mmHg/mL, $P = 0.055$) irrespective of cardiac loading, with LBNP-mediated reductions in end-diastolic volume unchanged between conditions (-0.4 [-4.4, 3.6] ml, $P = 0.841$). Conclusions: In addition to the well-established effects of IHH on ventilation and blood pressure, IHH appears to influence cardiac contractility during orthostatic stress, suggesting sLTF may exert a positive inotropic effect on the left ventricular myocardium.Funding: NSERC; Stober Foundation; APS

Poster #: 59 .EXPEDITION 5300 – ANDEAN HIGHLANDERS WITH EXCESSIVE ERYTHROCYTOSIS PERMANENTLY LIVING ABOVE 5000M EXHIBIT A HYPOCOAGULABLE PROFILE: A THROMBOELASTOMETRIC STUDY. Samuel Verges1, François Caton2, Landry Seyve3, Emeric Stauffer4, Aurélien Pichon5, Julien Brugniaux1, Michael Furian1, Ivan Hancco1, Blandine Deschamps1, Lars Kaestner6, Paul Robach1, 7, Philippe Connes4, Pierre Bouzat1, Benoit Polack3, Raphael Marlu3, Benoit Champigneulle1. 1HP2 laboratory, Univ. Grenoble Alpes, INSERM, CHU Grenoble Alpes,Grenoble, France, 2LRP, University Grenoble Alpes, CNRS, Grenoble INP, Grenoble, France, 3Therex, TIMC-IMAG, Univ. Grenoble Alpes, CNRS, CHU Grenoble Alpes, Grenoble, France, 4LIBM, Université de Lyon 1, Hospices Civils de Lyon, Lyon, France, 5Laboratoire MOVE, Université de Poitiers, Poitiers, France, 6Saarland University, Homburg, Germany, 7National School for Mountain Sports, Site of the National School for Skiing and Mountaineering (ENSA), Chamonix, France

Objective: Excessive erythrocytosis (EE, consensually defined as a hemoglobin concentration ([Hb]) ≥ 21 g·dL-1 in men) is highly prevalent in Andean highlanders (HL) chronically exposed to hypobaric hypoxia. How EE impacts the coagulation system remains poorly investigated. We sought to assess the whole-blood coagulation, using a thromboelastometry point-of-care device (ROTEM® delta, Werfen, France), in high-altitude dwellers permanently living in La Rinconada (5100-5300 m, Peru).Methods: A cross-sectional study including 10 lowlanders acclimatized to high-altitude (LL; 80% males; 33±7 years; [Hb], 17.4±1.2 g·dL-1) and 45 HL (100% males; 45±11 years), including 30 HL without EE ([Hb], 19.4±1.2 g·dL-1) and 15 HL with EE ([Hb], 23.5±1.6 g·dL-1). ROTEM® assays (EXTEM, INTEM, FIBTEM, APTEM) were performed at native and at corrected (40%) hematocrit (Hct) by dilution of whole blood samples using autologous platelet-poor plasma (PPP) in the three groups of participants.Results: HL with EE exhibited longer clotting times (CT) as well as lower clot firmness (i.e., smaller clot amplitude at 20 min (A20))

than HL without EE and LL in EXTEM, INTEM and FIBTEM assays (all p-values <0.01) at native Hct. No hyperfibrinolysis was highlighted by APTEM assay. At corrected Hct, no significant difference persisted regarding CT in EXTEM, INTEM and FIBTEM assays between the 3 groups of participants (all p-values >0.05). Significant differences between groups in A20 persisted at corrected Hct (all p-values <0.01) in EXTEM and INTEM assays but not in FIBTEM assay (p-value >0.05).Conclusion: Compared to acclimatized LL and HL without EE, HL with EE exhibited significant delayed clot initiation (CT) and weaker clot stiffness (A20), partially corrected after hemodilution with PPP. These findings indicate a hypocoagulable profile in EE Andeans highlanders permanently living at extreme altitude.

Poster #: 60 .RETINAL VASCULAR CHANGES AT HIGH ALTITUDE. Jessica Westwood1, 2, Ciaran Simpkins1, 2, India Mayhook-Walker1, 3, Andrew Darby-Smith1, Eduardo Normando1, Daniel Morris4. 1Imperial College London, 2University of Birmingham, 3University of Sheffield, 4University Hospital of Wales

Objective: This study aimed to evaluate retinal vascular changes throughout an expedition to 4167 metres. Methods: 10 healthy participants summitted Mount Toubkal, Morocco. Fundus images were taken on a handheld camera pre-departure, daily throughout the expedition, and one-month post-return. Diameter and tortuosity of four vessels was assessed, in addition to vessel density and the presence of HAR. Results: Significant ($p \leq 0.05$) increases in tortuosity and diameter were observed in some vessels on high-altitude exposure days. There was a significant increase in vessel density on summit day only. This is the first study to report no evidence of high-altitude retinopathy. Conclusion: This is the first study to report increased vessel density and no incidence of HAR. These results are likely attributable to relatively low altitude exposure, a conservative ascent profile, and the young, healthy demographic profile of participants. However, the study is limited by its small sample size, environmental confounding factors and semi-subjective diameter measurements. Physiological but not pathological changes were seen in this cohort, which gives insight to the state of the cerebral vasculature throughout this expedition and builds on current understanding of retinal vascular changes in hypoxia. Future work must include daily retinal images of larger sample sizes at higher altitude and take steps to mitigate against environmental confounders. This work is relevant to altitude tourists, patients with diabetic retinopathy or retinal vein occlusion, and critically ill patients at sea level.

Poster #: 61 .SEX DIFFERENCES IN THE LEFT VENTRICULAR RESPONSES TO ORTHOSTATIC STRESS AT 3800 M. Alexandra M Williams1, 2, Jennifer S Duffy2, 3, Liisa Wainman2, 3, Travis D Gibbons4, Mike Stembridge5, Elliot Jenkins5, Philip N Ainslie4, Christopher R West1, 2, 3. 1Cellular & Physiological Sciences, Faculty of Medicine, University of British Columbia, Canada, 2International Collaboration on Repair Discoveries, University of British Columbia, Canada, 3Centre for Chronic Disease Prevention & Management, Faculty of Medicine, University of British Columbia, Canada, 4Centre for Heart, Lung and Vascular Health, School of Health and Exercise Science, University of British Columbia, Canada, 5Cardiff School of Sport and Health Sciences, Cardiff Metropolitan University, Cardiff, United Kingdom

Objective. While the left ventricular (LV) responses to reductions in preload are known to differ between males and females, any potential impacts of hypoxia on sex-related differences in

LV function have not been examined. Methods. 9 females (28±4yrs) and 8 males (29±4yrs) were tested near sea level (SL) and following 3-5 days arrival at 3800m (high-altitude, HA). In both settings, participants were assessed while resting supine, then during sequential levels of head-up tilt (HUT; 20°, 40° and 60°). LV volumes and hemodynamics (i.e. end-diastolic volume, EDV; stroke volume, SV; ejection fraction, EF; cardiac output, Q), mean arterial blood pressure (MAP) and heart rate (HR) were assessed with 2-dimensional echocardiography, automated brachial pressure cuff and electrocardiogram, respectively. Results. At HA, MAP and HR were elevated at baseline compared to SL baseline in both sexes ($p<0.05$ for all). Overall, HA led to shifts in EDV, SV and Q (main effects $p<0.01$), and the profile of LV hemodynamic adjustments to altitude differed between the sexes. First, baseline EDV was reduced ($p=0.012$) and Q was augmented ($p=0.003$) in males at HA, while baseline SV was reduced in females (HA:42±9ml vs. SL:50±7ml, $p=0.01$). Next, sex x HUT interactions were not detected for EDV, SV, Q or EF at SL; however, significant sex x HUT interactions were detected for EDV ($p=0.005$) and SV ($p=0.031$) at HA. Specifically, males had greater reductions to EDV (males:-37±7ml vs. females:-20±11ml, $p=0.004$) and SV (males:-24±6ml vs. females:-12±7ml, $p=0.006$) from baseline to 60° HUT. Nonetheless, both males and females were able to maintain EF, Q and MAP during HUT at HA. Conclusion. Males and females appear to have distinct LV hemodynamic adjustments to hypoxic environments, both at rest and during orthostatic challenges. The specific physiological factors contributing to such sex differences (e.g. cardiac autonomic control) remain to be determined.

Poster #: 62 .DYNAMICS OF THE CEREBRAL BLOOD FLOW RESPONSE TO HYPOXIA . Harrison T. Levine1, 2, Ece Su Sayin1, 2, Olivia Sobczyk3, 4, Julien Poublanc4, David J. Mikulis4, James Duffin1, 3, Joseph A. Fisher1, 3. 1Department of Physiology, University of Toronto, Toronto, Canada, 2Joint Department of Medical Imaging and the Functional Neuroimaging Lab, University Health Network, Toronto, ON, Canada, 3Department of Anaesthesia and Pain Management, University Health Network, Toronto, Canada , 4Joint Department of Medical Imaging and the Functional Neuroimaging Lab, University Health Network, Toronto, Canada

DYNAMICS OF THE CEREBRAL BLOOD FLOW RESPONSE TO HYPOXIA Harrison T. Levine, Ece Su Sayin, Olivia Sobczyk, Julien Poublanc, David J. Mikulis, James Duffin, Joseph A. Fisher University of Toronto, Toronto, Ontario, Canada, harrison.levine@mail.utoronto.caIntroduction: While steady-state measurements have determined the extent of the increase in cerebral blood flow during hypoxia, how fast the changes occur is unknown. Objective: To quantify the dynamic changes in cerebral blood flow on exposure to hypoxia. Methods: In 21 healthy volunteers we precisely controlled arterial oxygen tensions in a 3 min square wave pattern of 85 - 40 - 85 mmHg while maintaining resting isocapnia. We recorded trans-cranial Doppler (TCD) measurements of cerebral blood flow velocities in the middle cerebral artery (MCAv) and the posterior cerebral artery (PCAv). Beat-by-beat heart rate (HR) was calculated from these recordings, and mean arterial blood pressure (MAP) was recorded in 9 subjects. Results: The cerebral blood flow increase with hypoxia varied considerably among the volunteers (mean (SD) range (%) 22.6 (10.2) 9.4 - 41.4 MCAv; 27.7 (13.8) 0 – 50.9 PCAv). The increase in MCAv was fitted with an exponential rise in 11 volunteers; mean (SD) cm/s 26.45 (9.25), and for PCAv in 9 volunteers; mean (SD) cm/s 34.14 (10.92). Increases in HR and MAP also occurred. Discussion: The exponential time constants

characterizing the speed of the cerebral blood flow velocity changes in response to hypoxia were much smaller than previously published values. Although the resting MCAv and PCAv differ, the dynamic responses to hypoxia do not, suggesting similar vessel wall characteristics. Finally, TCD responses during hypoxia may be affected by HR and MAP changes and possibly those of vessel diameter during hypoxia. Conclusion: The amplitude and speed of MCAv and PCAv responses to hypoxia vary widely between people, with rates of response considerably faster than previously thought.

Poster #: 63 .HIMALAYA AIR QUALITY IMPACTS FROM COVID-19 LOCKDOWN ACROSS THE INDO-GANGETIC PLAIN. G.W.K. Moore1, John Semple1. 1University of Toronto

Objective: The COVID-19 lockdown within the heavily polluted Indo-Gangetic Plain (IGP) provided a unique opportunity to assess the impact and the path of pollution from this region into the Himalaya. Unique communities in high-altitude regions, such as those in the Himalaya, are unexpectedly exposed to pollution levels that approximate those reported in industrialized cities and other polluted environments. Little is known about the source of this pollution and its cross-border pathways. Methods: To characterize the impact of the lockdown on the spatial and temporal variability in air quality across the IGP and the Himalaya, we use daily tropospheric NO2 column retrievals from the OMI instrument on NASA's Aura satellite as well as higher spatial resolution data from the TROPOMI instrument on ESA's Sentinel 5P satellite. Mass-weighted wind data from the European Centre for Medium-Range Weather Forecasts' ERA5 Reanalysis were used to characterize the atmospheric circulation during April 2020. Results: In-situ and satellite observations show that there was a step function decrease in two key indicators of air quality, nitrogen dioxide and airborne particulates, in locations within the Indo-Gangetic Plan (IGP) secondary to the Spring 2020 lockdown. Based on anomaly patterns, we find a dipole response with a statistically significant reduction in air pollution along the western IGP and Himalaya and an increase in air pollution in the eastern IGP and Himalaya. We show that spatial variability in the reductions in economic activity across northern India and the adjoining countries of Nepal, Pakistan and Bangladesh contributed to this dipole as did a persistent atmospheric circulation anomaly across the region during the lockdown. Conclusions: The COVID-19 lockdown within the heavily polluted IGP provided a unique opportunity to assess the impact of pollution from this region on the Himalaya.