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MITRAL REGURGITATION AS A COFACTOR IN MITRAL VALVE PROLAPSE
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OBJECTIVE: To assess whether mitral regurgitation in the setting of mitral valve prolapse identifies a subset of individuals at higher risk for arrhythmias.
DESIGN: Case series study
SETTING: Referral center for evaluating aviators with possible heart disease
PATIENTS: Military aviators (n=198) known to have mitral valve prolapse; evaluated and followed in the period from June 1983 to February 1991.
MEASUREMENTS: History, physical examination, echocardiography, Holter monitor, and other testing (including subspecialty evaluation) as required for a thorough aeromedical evaluation. Mitral regurgitation was considered present if there was a late systolic/holosystolic murmur that behaved appropriately with maneuvers and/or color-flow/continuous wave evidence for mild-/moderate/severe regurgitation on at least one evaluation.
RESULTS: The 198 aviators underwent 320 evaluations averaging 1.62 visits per subject. MR was noted on physical exam and/or echocardiography in 133 of these aviators. Some degree of MR (mild/moderate/severe) was noted on Doppler study in 31 aviators; 25 of these 31 aviators had auscultatory MR as well as MR by echo. The only arrhythmia significantly more common in individuals with MVP and MR was supraventicular pairs (12.7% with MR vs. 1.5% without MR, p=.01). Ventricular pairing, ventricular or supraventricular tachycardia, atrial fibrillation/flutter, etc. did not show a significant association with the MR group.
CONCLUSION: In this group of 198 aviators with MVP only PAC pairing was significantly more common in the subjects with MR as compared to those without MR. MR is not useful for identifying aviators with MVP who are at risk for tachyarrhythmias.

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ASPECIFIC NASAL HYPERREACTIVITY IN AN AIR FORCE POPULATION AND ITS RELATIONSHIP WITH BRONCHIAL HYPERREACTIVITY AND ATOPY. L. Urbani*, R. Berti*, C. De Angelis, G. Petrelli, S. Farrace*, P.M. Matricardi, R. Nisini and F. Filiaci°. IAF, DASRS, Dept. of Aerospace Medicine and °ENT Clinic, University of Rome, Italy.

INTRODUCTION. Nasal function is of paramount importance for aircrew. Aspecific nasal hyperreactivity (ANH) prevalence in a young IAF population was investigated and compared to the prevalence of aspecific bronchial hyperreactivity (ABH) and atopy. METHODS. 90 healthy males (17-24 yrs) were administered cold water and methacholine nasal provocation tests (NPTs). ANH was evaluated by computerized rhinomanometry and, only for the methacholine NPT, by measurement of nasal secretions. A methacholine bronchial provocation test (BPT) was also performed, as well as a screening test for inhalant allergy (Phadiatop). RESULTS. 25% was positive to cold water NPT, 38% to methacholine NPT and 8% to both. BPT was positive in 18% and in more than 2/3 of cases ABH was associated with ANH to either NPTs. 24% was positive to Phadiatop and 91% in this group was positive to either NPT or BPT. CONCLUSION. ANH is more frequent than ABH, which is often associated to the former condition. Atopy seems to match very often with aspecific upper and/or lower airway hyperreactivity. Implications for selection of aircrew can follow.

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Tissue oxygen tension in patients with peripheral occlusive arterial disease during simulated altitude exposure.
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INTRODUCTION. Tissue oxygen pressure values were determined in the tibial anterior muscles of the diseased legs of 10 patients suffering from intermittent claudication due to chronic occlusive arterial disease before and after 20 min. of exposure to an oxygen reduced gas mixture (115 mmHG $pO_2$) simulating an altitude of 8500 feet. METHODS. Oxygen pressure values (medians) were determined with a polarographic method according to Ehrly and Schröder using atraumatic micro-PT-needle electrodes. In addition transcutaneus $pO_2$ and $pCO_2$ (Radiometer, Kopenhagen), pulsoximetric $O_2$-saturation (Pulsox 7, Minolta) and blood gas analysis were performed (AVL, Schaffhausen, Switzerland). RESULTS. Arterial $pO_2$ decreased from 80.2 ±15,1 mm HG to 59,9 ±10,4 mm Hg, O2-saturation from 95 ±2,5 to 90 ±5,6%. Accordingly tissue oxygen tension in the tibial ant. muscle decreased from 6,5 mm Hg to 2,4 mm Hg. The pooled histograms were markedly shifted to the hypoxic to anoxic range. None of the patients complained of rest pain in the diseased leg. CONCLUSIONS. Exposure of patients with at rest compensated peripheral occlusive arterial disease of the leg led to a marked decrease of tissue $pO_2$ values without any evidence of clinical worsening, especially no rest pain. It may be discussed if rest pain in ischemic legs is due to low $pO_2$-values or to disturbed microcirculatory perfusion.

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BLOOD VOLUME AND ORTHOSTATIC RESPONSES OF MEN AND WOMEN TO A 13-DAY BEDREST. *S. Fortney, T. Driscoll, L. Steinmann, and C. Alfrey. NASA Johnson Space Center, KRUG Life Sciences, and the Baylor College of Medicine.

INTRODUCTION. Changes in blood volume during space flight are thought to contribute to decrements in postflight orthostatic function. The purpose of this study was to determine whether gender affects red cell mass and plasma volume during a short exposure to simulated microgravity, and whether gender differences in orthostatic tolerance ensure. METHODS. Ten men (31.5 ± 5.2 yrs, STD) and eleven normally-menstruating women (33.3 ± 6.0 yrs, STD) underwent 13 days of 6° head-down bedrest. Plasma volume ($^{125}$I-labelled human serum albumin) and red cell mass ($^{51}$C-labelled red blood cells) were measured before bedrest and on bedrest day 13. On the same days, orthostatic tolerance (OT) was determined as the maximal pressure during a presyncopal-limited lower body negative pressure test. RESULTS. Plasma volume (PV) and red cell mass (RCM) decreased ($P < 0.01$) during bedrest in both groups, with a greater PV decrease ($P < 0.05$) in men (6.3 ± 0.6 ml/kg) than in women (4.1 ± 0.6 ml/kg). Decreases in red cell mass were similar (1.7 ± 0.2 ml/kg in men and 1.7 ± 0.2 ml/kg in women). OT was similar for men and women before bedrest (-78 ± 6 mmHg in men vs. -70 ± 4 mmHg in women) and decreased by a similar degree (by an average of 11 mmHg in both groups) after bedrest. The changes in OT did not correlate with changes in plasma volume during bedrest ($r^2 = 0.002$). CONCLUSION. Thus, although female hormones may protect PV during bedrest, they do not appear to offer an advantage in terms of loss of orthostatic function.

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EFFECT OF ANTIORTHOSTATIC BEDREST (BR) ON GASTROINTESTINAL MOTILITY (GIM) OF NORMAL SUBJECTS L. Putcha[1*], R.P. Hunter[2], K.J. Tietze[3], and N.M. Cintrón[1*] [1]Biomedical Operations and Research Branch, NASA/Johnson Space Center, Houston, TX, [2]KRUG Life Sciences, Inc., Houston, TX and [3]Philadelphia College of Pharmacy and Science, Philadelphia, PA

INTRODUCTION. The combined effect of postural changes, fluid shifts, and diuresis associated with the absence of the gravity vector may decrease GIM during space flight. GIM can be estimated from the mouth-to-cecum transit time (MCTT) of orally administered lactulose (LAC); this test is used to assess changes in GIM in normal subjects and in patients with GI pathology and related disease conditions. Since BR mimics some of the physiological changes that occur during space flight, the effect of ten days of BR on GIM was evaluated from the MCTT of LAC. METHODS. Subjects were 12 nonsmoking males between the ages of 35 and 50. After an 8-10 h fast, subjects ingested Cephulac® (20g solution) with a low-fiber breakfast on four different days (45, 30, 25, and 20) before BR and on three separate days (4, 7, and 10) during BR. Breath-$H_2$ concentrations were measured before and at 10-min intervals for 4 h after breakfast using a Quintron breathalyzer® and MCTT was determined from these data. RESULTS. MCTT ranged between 50 and 100 min during ambulation and 80 and 210 min during BR with means of 79 min and 122 min, respectively. CONCLUSIONS. Mean MCTT during BR was 54% longer than during ambulation, suggesting that absorption and availability of orally administered medications and nutrients may be delayed or impaired as a result of decreased GIM during bedrest.

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THE EFFECTS OF LYPRESSIN ON HEMODYNAMIC RESPONSES TO HEAD-DOWN TILT AND ORTHOSTATIC STRESS. D.F.Ward* and R.W.Gotshall*. Wright State University School of Medicine, Dayton, OH 45401.

INTRODUCTION. This study was conducted to assess the effects of the synthetic drug lysine-8-vasopressin (lypressin) on specific hemodynamic variables during nascent (4 hours) head-down tilt (HDT) and subsequent orthostatic stress. METHOD. Seven healthy male subjects, ages 23-37, participated in a blinded, cross-over study of lypressin versus the control, normal saline nasal spray, administered intranasally immediately before and two hours after beginning a 6 degree head-down tilt. Plasma volume, urine flow and cardiovascular dynamics were assessed by venous hemoglobin/hematocrit, urine volumes, electrocardiography, impedance cardiography and plethysmography measurements before, during, after tilt, and in response to a 10 minute stand test. RESULTS. In the lypressin trial, stroke volume, cardiac output and index, basal impedance, and pulse pressure were significantly decreased ($p<0.05$) while total peripheral resistance was increased at the end of tilt. Plasma volume change showed a significant increase of 5.9% by the end of tilt in the lypressin trial ($p<0.005$), while in the placebo group there was no significant change. Clinical observations included pre-syncopal symptoms in three of the seven control trial subjects versus none of the lypressin trial subjects during post-tilt stand testing. Post-tilt stand tests showed that mean arterial pressure was maintained at a higher value in the lypressin trial compared to baseline stand test. The pulse time index and cardiovascular index of deconditioning showed a significant increase for placebo subjects after tilt and no significant change from pre-tilt with lypressin subjects. CONCLUSIONS. The cardiovascular system adapts to a new steady-state during 4 hours HDT that is maladaptive when provoked with orthostatic stressors. Exogeneous vasopressin analogue ameliorates the deleterious effects of post-tilt stand testing by maintaining the intravascular volume at greater than pre-tilt values and increasing mean arterial pressure via peripheral resistance.

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DOBUTAMINE, A BETA AGONIST, REDUCES MUSCLE AND BONE LOSS IN DENERVATED HINDLIMBS. M.L. Walker, K. Prater, R. Herz, S. Whittenberger and B. Girten*. Wright State University School of Medicine, Dayton, OH 45435.

INTRODUCTION. Hindlimb denervation produces alterations in skeletal muscle and bone similar to those observed in animals exposed to microgravity. The objective of this experiment was to determine if dobutamine (DOB), a synthetic catecholamine and a beta agonist, could effectively attenuate bone and muscle changes induced by 12 days of hindlimb denervation. METHODS. Adult male Sprague-Dawley rats (n=14) underwent unilateral sciatic nerve transection on the right hindlimb. After surgery rats were randomly assigned to either control saline (SAL) or DOB treatment groups. Each animal received two intraperitoneal injections per day, given approximately one hour apart, for 11 of the 12 days. Bone mineral content (BMC) of the proximal head (PH) and shaft (PS) of the tibia from both the innervated (INNERV) and denervated (DENERV) hindlimbs of each rat were measured by a bone densitometer (SP-2 Lunar). Muscle weights of the soleus (SOL) and plantaris (PLT), and citrate synthase (CS) enzyme levels of the SOL muscle were examined. RESULTS. ANOVA and Tukey's post hoc tests ($p<0.05$) indicated a significant reduction in wet weight of the SOL and PLT muscles in the DENERV SAL group when compared with their INNERV hindlimb counterparts. BMC of the PH and PS of the tibia and CS levels of the SOL were also significantly reduced in the DENERV animals that received SAL. Although animals which received DOB treatment did have decreases in muscle mass, BMC and CS in the DENERV hindlimb, these decreases were not significant when tested against their INNERV values. DOB treatment appeared to be most effective in bone, where the decrease in BMC produced by DENERV in SAL animals was almost entirely eliminated in rats receiving the drug. CONCLUSION. These data indicate that DOB is able to effectively attenuate alterations in muscle and bone which are induced by hindlimb denervation. This information suggests that DOB may be effective as a countermeasure for some of the deconditioning like changes which result from exposure to a microgravity environment.

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**CHANGES IN LEFT VENTRICULAR FUNCTION AS DETERMINED BY THE MULTI-WIRE GAMMA CAMERA AT NEAR PRE-SYNCOPAL LEVELS OF LOWER BODY NEGATIVE PRESSURE.** **+R. Pinter, *S. Fortney, **S. Mulvagh, #J. Lacy. +KRUG Life Sciences, *NASA Johnson Space Center, **Universities Space Research Association and #Baylor College of Medicine.**

At presyncopal levels of lower body negative pressure (LBNP), we have frequently observed electrocardiographic responses that may be due to changes in cardiac position and/or shape, but could be indicative of altered myocardial function. To further investigate this, we evaluated cardiac function using a nuclear imaging technique in 21 healthy subjects (17 men and 4 women) after 30 minutes of supine rest and near the end of a presyncopal-limited LBNP exposure (LBNP averaged 65 ± 3 mmHg at injection). Cardiac first pass images were obtained using a Multi-Wire Gamma Camera following an intravenous bolus injection of 30-50 millicurries of $^{178}$Tantalum. Manual blood pressures and electrocardiograms were obtained throughout the 3-minute graded LBNP protocol. Between rest and injection during LBNP, heart rate increased ($P<001$) from 67 ± 3 bpm to 99 ± bpm, systolic blood pressure decreased ($P<0.01$) from 119 ± 3 mm Hg to 107 ± 3 mm Hg and left ventricular ejection fraction (EF) decreased ($P<0.01$) from 0.57 ± 0.02 to 0.48 ± 0.02. During LBNP, ST segment depression of at least 0.5 mm occurred in 7 subjects. Subjects with ST segment depression had greater reductions ($P = 0.05$) in EF than subjects without ST depression (0.15 ± 0.07 vs. 0.05 ± 0.03), but also tolerated greater levels ($P<0.05$) of negative pressure (88 ± mm Hg vs. 69 ± 5 mm Hg). There was a significant relationship between presyncopal LBNP level and EF ($R^2 = 0.50$, $P< 0.05$). Our findings suggest there may be a decrease in systolic myocardial function at high levels of LBNP.

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**EFFECT OF LBNP ON CEREBRAL CIRCULATION**

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**INTRODUCTION** The purpose of our study is to determine the effects of lower body negative pressure(LBNP) on cerebral circulation. **METHODS** Oxygenation and hemodynamics of the brain were measured continuously and noninvasively in eight cases who were exposed to 30mmHg LBNP for 25min by using a carotid doppler, a transcranial doppler, a cutaneous laser doppler, and a near infrared spectrophotometry. **RESULTS** The carotid blood flow and the mean velocity of the middle cerebral artery decreased in almost every cases, even though the systemic blood pressures were well maintained. Oxygenated hemoglobin and cerebral blood volume of the brain typically increased while deoxygenated hemoglobin showed variable small changes. **CONCLUSION** The results of the carotid doppler and the transcranial doppler indicate that the cerebral blood flow might decrease during LBNP. From the increase of oxygenated hemoglobin and cerebral blood volume, it is suggested that the dilatation of the cerebral vessels occur at the arterial side. Taken together, it can be said that exposure to moderate LBNP typically produces a decrease of the cerebral blood flow with a compensatory vasodilatation of the arterial side of the brain.

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EAR OPACITY SHOWS HEAD-LEVEL BLOOD FLOW CYCLING DURING STEADY-STATE EXPOSURE TO +Gz. F. Buick* and J. Maloan. Defence and Civil Institute of Environmental Medicine, North York, Canada, M3M 3B9.

INTRODUCTION. The generally accepted +Gz time/tolerance curve (Stoll, 1951) shows a smooth and horizontal band through discrete points of tolerance up to 20 sec after the "trough". While this suggests cardiovascular steady-state, head-level blood flow, and arterial pressure at heart and head level are known to increase and decrease with regular frequency (Wood and Lambert, 1989). If so, +Gz tolerance capacity may vary during this time. METHODS. Continuous head-level perfusion indices were obtained from measurement of ear opacity, a technique developed in the Mayo Centrifuge Laboratory in the '40s. 7 relaxed subjects were exposed to 1 +Gz/s onset rate centrifuge profiles with 2 min of sustained +Gz. +Gz level increased in successive 0.5 +Gz increments beginning at +2.5 Gz until visual blackout. RESULTS. In the first 5 s of +Gz exposure, ear opacity and ear opacity pulse amplitude decreased. The decrease was more marked at increased +Gz levels. Cardiovascular compensation occurred over the next 5 s which increased opacity and opacity pulse. For the remainder of the 2 min exposure, ear opacity and ear opacity pulse increased and decreased with a mean cycling period of 10.4 s. The mean difference in the opacity levels within cycles was 17.1% of the +1 Gz opacity value. CONCLUSIONS. These results suggest head-level perfusion is not constant during the supposed cardiovascular steady-state period of sustained +Gz exposure. It follows that the physiological ability to avoid loss of consciousness may also fluctuate.

The advice of Dr. E.H. Wood is gratefully acknowledged.

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**ASSESSMENT OF CEREBRAL BLOOD FLOW BY TRANSCRANIAL DOPPLER METHOD DURING +Gz ACCELERATION IN HUMAN.** G. OSSARD, J.M. CLERE*, F. MELCHIOR, A. RONCIN, J. SEYLAZ. Laboratoire de Médecine Aérospatiale, Centre d'Essais en Vol, F91228 Brétigny sur Orge Cedex; France.

INTRODUCTION. Limit of human tolerance to $+G_z$ acceleration is attributed to cerebral perfusion failure. A study using transcranial Doppler (TCD) was conducted in order to evaluate changes in cerebral blood flow (CBF) under $+G_z$ stress. METHOD. 9 relaxed volunteers were exposed to 30 sec $+G_z$ plateaus of 2, 3, 4 and 5 G (G-onset rate=1G/s). CBF changes were assessed by transcranial Doppler recording of middle cerebral artery (MCA) blood flow velocity. Arterial pressure (heart level) was monitored with a continuous non-invasive method (Finapres 2300). From these data, mean cerebral artery perfusion pressure was computed. RESULTS. Mean blood flow velocity (MBFV) was significantly decreased during G-onset and during 2 and 4 $+G_z$ plateaus. MBFV ± S.E.M. decreased from 11.5 ± 5.2 % (2 $+G_z$) to 44.5 ± 24.% (5 $+G_z$). Three main intolerance cases were observed correlated with transient or extended blood flowing back in MCA. DISCUSSION. The sensitivity of TCD method is adequate to evaluate small variations of CBF at 2 +Gz. The method shows that CBF is insufficient at certain 5 +Gz profiles, explaining intolerance symptoms.

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HEMODYNAMIC RESPONSES OF THE SWINE TO G-SUIT INFLATION, THE AGSM AND PRESSURE BREATHING DURING +Gz (PBG). JW Burns*, JW Fanton and JL Desmond. Crew Technology and Veterinary Sciences Divisions, Armstrong Laboratory, Brooks AFB, TX 78235-5000.

INTRODUCTION The G-protective benefits of PBG have been well demonstrated. A swine model has been developed to investigate the physiologic bases for these benefits. METHODS A mask and a chest counterpressure garment have been fabricated for application of PBG to the swine. G-suit protection was supplied by an extended coverage suit which provided nearly complete body coverage caudal to the rib cage. Left and right ventricular pressure, left and right ventricular stroke volume (SV) and cardiac output (CO), aortic pressure, eye-level blood pressure (ELBP), heart rate (HR), central venous pressure, esophageal pressure, mask pressure, and G-suit pressure were measured during +Gz with and without PB and during PB without +Gz. RESULTS During a 130 sec exposure to a 5-9 +Gz SACM mean ELBP was maintained above 55 mmHg without PBG and above 70 mmHg with PBG by an increase in total peripheral resistance, even though SV, CO and HR decreased by 57%, 63% and 5%, respectively, without PBG and by 45%, 60% and 2%, respectively, with PBG. The combination of G-suit inflation, the AGSM and PB during +Gz resulted in significantly increased intravascular pressures. However, a similar increase in intrathoracic pressure resulted in minimal transmural vascular pressure changes. CONCLUSIONS Elevated ELBP with PBG compared to without PBG supports the finding in man of extended time at +Gz and a reduction in the physical effort to maintain vision during sustained +Gz.