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Welcome

Welcome to the 5th annual HMAA student Balatonfured meeting! It is hard to believe that another year has gone by. This meeting has taken on great importance for our organization. I hope that you take the time to get to know what the HMAA is all about and what we have to offer for you. There will be numerous officers and members of the society here at the meeting for you to interact with.

I urge you to attend all the presentations and social events. Each year we have built on the successes of past meetings and this year's meeting promises to be the best yet. A full schedule of events and fun-filled activities await you. The professors, educators, and organizers have generously donated their time to allow you the opportunity to present your work in a friendly and collegial environment.

I wish you all good luck to every one of you and have a great time. Remember that there are awards for the best presentations including travel money to attend our 44th annual meeting in sunny Sarasota, Florida October 28-November 2, 2012.

Istvan Somkuti MD, PhD
President HMAA

Dear Guests, Colleagues, Lecturers, past and future Participants in our Student Exchange program, all who participated in this Congress, Ladies and Gentlemen,

As president of this Congress it is my honor to greet you all who participate at this meeting of the Hungarian Chapter of the Hungarian Medical Association of America (the HMAA) here at Balatonfured. This Meeting is our sixth, and with a pride may I mention this Congress has become a tradition. The presentations cover such a wide field of medical knowledge of 2012 that I call this meeting interdisciplinary. At this point I should be repetitious to the former presidents by expressing the hope that the presentations should not only widen the wisdom of those present but shall awake the desire for new research and help to amalgamate professional collaboration in mutual areas. We certainly hope that the scientific information will not be worded here only but new acquaintances, exchange of local experiences will enrich a concerted result.

Last but not least at this beautiful surrounding of the Lake Balaton, the nectars coming from the hillside products and the social programs should be such a pleasant memory for you that you will return for the meetings in the years to come.

This year we made a minor change in the format of the presentations.

Instead leaving the discussions to the end of a session we shall discuss each presentation at the end of the lecture, hoping this will make each presentation more memorable.

I hope you all will enjoy coming here, staying here and be with us at this Institute of memorable history.

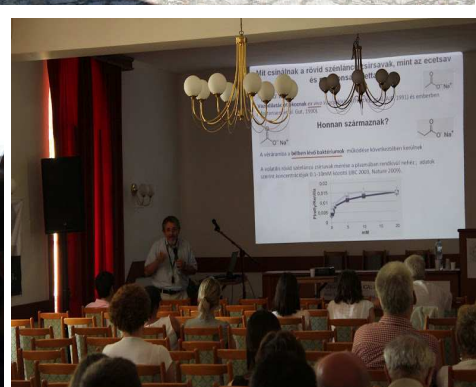
With all these thoughts I wish a successful meeting and hope to see you all added with those you will convince to come and participate in the years of the future.

László Csáthy MD PhD
President of HMAA Hungary Chapter



Pictures

Pictures of HMAA Füred2011 meeting











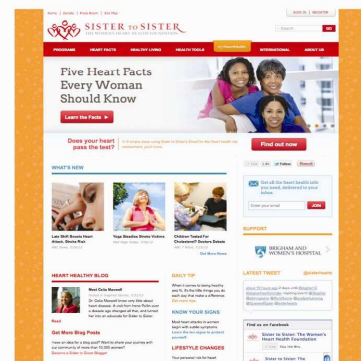
The Sister to Sister Foundation has been a pioneer in preventing heart disease, the #1 killer of women, through the development of heart-health programs, educational materials, and awareness and advocacy campaigns. Sister to Sister was the first US organization to provide free cardiovascular screening interventions to fight heart disease in women.

Since its founding in 1999, Sister to Sister has developed a record of successful community-based programs dedicated to prevention through education and behavior change. Through the Sister to Sister Five-Step Screening Intervention, we have provided over 80,000 free cardiovascular screenings for women, with immediate results.

JUST LAUNCHED

We just launched a refreshed website at
www.sistertosister.org/myhearthealth

Tools for *your* heart | Women Bloggers | Inspiring Stories



Our Partnerships:

- Brigham and Women's Hospital: our primary partner and host/manager of our founder's Pollin Wellness Program.
- Harvard Medical School: partners on the research on cardiovascular disease in women based upon data from our longitudinal database.
- Million Hearts: a national initiative of the Centers for Disease Control and the US Department of Health and Human Services to prevent a million heart attacks and strokes over five years.
- National Heart, Lung, and Blood Institute and the National Institute of Health's (NIH) Heart Truth Campaign to raise awareness among women about heart disease and disseminate heart health messages to American women.

Our Programs:

- SMART FOR THE HEART, an interactive free online wellness program with powerful assessment and tracking tools for participants to better understand and improve their cardiovascular health, in partnership with Brigham and Women's Hospital. Participants receive personalized, preventative tips and follow-up to lower their cardiac risk. It is available at www.sistertosister.org/myhearthealth.
- Community Outreach Screening Events, which include education and awareness, biometric health screenings and risk assessments, lifestyle modification counseling, outcomes tracking and evaluation in partnership with Brigham and Women's Hospital and Harvard Medical School. These events include speaking programs to educate women on the signs and symptoms of heart disease and how to lower your risk, stress reduction tips, healthy eating and cooking, physical activity demos, and information to keep the entire family fit and healthy.



- The Capitol Hill Advocacy Program, in its ninth year, educates and raises awareness of cardiovascular disease and its risk factors among key policymakers by providing free cardiovascular screenings to all Senators, Representatives and staff members directly at their workplace. Combined with education and comprehensive online tools, the screenings offer a complete action plan for preventive care. Other valuable services include stress-reducing massages, reiki and nutrition consultations, personal fitness demonstrations, materials and giveaways.



- Global Workplace Wellness Programs: a one week program held September 12, 2011 at the World Bank Group cafeterias to promote the benefits of a natural and healthy diet. Our mission is to support and educate women by providing heart-healthy nutrition at their workplace in order to help them control and prevent obesity - a major risk of heart disease. Participating embassies included Bulgaria, Denmark, Hungary, Sweden and Thailand.
- Since 2005, the International Woman's Heart Day Screenings for members of the Washington D.C. diplomatic community, who act as Heart Ambassadors by raising awareness of heart disease risk and prevention in their home countries. In February 2011, Sister to Sister hosted an international executive luncheon and cardiovascular screening in which over 42 countries took the first step to help combat the global crisis of women and heart disease.
- The development of hands on, patient centered educational materials to help women understand the factors that can increase their risk for heart disease, and what heart-healthy changes they can make to manage that risk. The materials are also available in Spanish.



A-B Multidisciplinary Session I.

A. Radiology-anatomy Session

A/1. COMPARATIVE MAGNETIC RESONANCE IMAGING (MRI) STUDY OF THE BRAIN IN PATIENTS AFTER CAROTID ARTERY STENTING AND CAROTID ENDARTERECTOMY

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Keywords: internal carotid artery (ICA) stenosis, carotid artery stenting (CAS), carotid endarterectomy (CEA), restricted diffusion areas, FA

Introduction: The stenosis of the internal carotid artery (ICA) is a worldwide cause of cerebral ischemic events. The two major therapeutical approaches of an ICA stenosis are carotid artery stenting (CAS) and carotid endarterectomy (CEA).

Materials and methods: Our patients (n=20, selected from the Department of Vascular Surgery) had no actual neurological symptoms at the time of CAS (n=10) and CEA (n=10). The MRI was brought out within 3 days before and within 7 days after the treatment. Conventional T2, FLAIR, T2*, 3D T1, 3D time-of-flight sequences, and diffusion tensor imaging (DTI) from 32 directions were acquired on a 1.5T Philips Achieva scanner. We compared the number of restricted diffusion (rDWI) areas and the FA and ADC values on the pre- and postoperative images.

Results: Preoperatively we found 4 rDWI lesions in the CEA group and we didn't find any in the CAS group. Postoperatively 38 new rDWI lesions were found in the CAS group in 3 patients and 2 new rDWI lesions in 2 patients in the CEA group. The size of the lesions ranged 2-6 mm. There were significant differences within the affected group between the pre- and postoperative status in the left parietal region's FA data (preop: 0.444 ± 0.0348 , postop: 0.364 ± 0.0494 , $p=0.04$).

Conclusion: The number of new ischaemic lesions was significantly higher in the CAS

group which is in accordance with the literature. We didn't notice any minor and major neurological symptoms postoperatively. According to the size and localisation of the lesions we assume microembolization as a background.

A/2. SOCIAL INFLUENCES OF ADOLESCENT SMOKING: CLASSIFICATION OF HUMAN CORONARY ATHEROSCLEROTIC PLAQUES WITH HIGH-RESOLUTION MRI: IMAGING AT 9.4 TESLA

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Keywords: atherosclerosis, coronary artery disease, magnetic resonance imaging, ultra-short echo time, plaque classification

Introduction: Magnetic Resonance Imaging (MRI) has been used to classify carotid plaque but its capability to characterize coronary plaque remains unknown. In addition, the detection of plaque calcification by MRI remains challenging. We sought to determine the accuracy of human coronary atherosclerotic plaque characterization with 9.4T MRI as compared to histology. We hypothesized that the addition of ultra-short TE (UTE) sequence to T1 and T2 weighted MRI allows accurate differentiation of calcified and lipid-rich (LRNC) plaque components.

Methods: three human ex-vivo LAD specimens were imaged at 9.4 Tesla with a T1 3D FLASH sequence (250 μ m resolution), a T2 Rare sequence (resolution 0.156mm) and an UTE sequence (300 μ m resolution). Histological characterization of the plaques was performed according to the American Heart Association criteria.

Results: We have co-registered 59 MRI cross-sections with histology, 31 plaques were used as training, 28 plaques as validation datasets. Plaques showing

selective hypointensity on T2-weighted MRI were classified as lipid-rich. Areas of hypointensity on the T1-weighted images but not the UTE images were classified as calcified. MRI showed high sensitivity and specificity for the detection of calcification (100% and 90%) and LRNC (90% and 75%). Inter-observer correlation for calcium and LRNC detection was excellent (0.80 and 0.82, respectively, $p < 0.0001$). In addition, MRI based classification of plaque was in good agreement with histology ($n = 22/28$; weighted $\kappa = 0.6945$, $p < 0.0001$). Inter-observer agreement for MRI plaque classification was high ($\kappa = 0.78$, $p < 0.0001$). Conclusions: High-resolution MRI with T1, T2 and UTE contrast enables accurate classification of human coronary atherosclerotic plaques.

A/3. CORONARY CT ANGIOGRAPHY WITH 256-SLICE SCANNER IN PATIENTS WITH ATRIAL FIBRILLATION

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Keywords: 256-slice CT, atrial fibrillation, CCTA

Background: Atrial fibrillation (AF) is considered a relative contraindication to coronary computed tomography angiography (CCTA) due to the irregular heart rates resulting in motion artifacts. Thus, the aim of this study was to evaluate the performance of 256-slice CCTA (256-CCTA) for the visualization of coronary arteries in a population with atrial fibrillation (AF) and to explore the impact of patients' mean heart rate (HR) on image quality (IQ).

Methods: Thirty-six consecutive patients (25 male, 64.2 ± 10.2 years old) with permanent AF were examined on 256-slice CT scanner (120 kV, 300 mAs/rot, 0.27 s rotation time, $2 \times 128 \times 0.625$ mm collimation, Philips Brilliance iCT) to evaluate the coronary arteries. Patients were divided into two groups: low/medium HR [LHR] group (mean HR < 80 bpm, $n = 22$) and high HR [HHR] group (mean HR ≥ 80 bpm, $n = 14$). The IQ assessment was based on the

American Heart Association's coronary segment classification scheme using a four-point likert-type scale from excellent (1) to non-assessable (4).

Results: We have analyzed 467 coronary segments. The mean IQ score was 1.9 ± 0.7 and 86.1% (402/4657) of the segments had a diagnostic image quality, resulting in 50.3% (235/467) excellent, 25.9% (121/467) good and 9.9% (46/467) moderate IQ. Image quality of LHR group was better than that of HHR group (mean score 1.6 ± 0.6 versus 2.4 ± 0.7 ; $p = 0.0014$). The mean HR of LHR group and HHR group were 68.5 ± 8.5 beats per minute (bpm) and 94.6 ± 12.7 bpm ($p < 0.0001$). There was no difference between the range of the variation of HR between the LHR group and HHR group (mean difference between minimum and maximum HR: 53.1 ± 26.9 versus 63.1 ± 35.8 bpm; $p = 0.34$). The average radiation dose was 6.9 ± 2.6 mSv (range: 3.5-15.0 mSv).

Conclusion: Due to the sophisticated arrhythmia detection algorithm, wide detector coverage and high temporal resolution of the 256-slice CT, it provides diagnostic image quality in patients with AF, which otherwise would be excluded from CCTA examinations. Patients' mean HR has a significant impact on IQ. The radiation of 256-CCTA in AF is lower than other reported values of CCTA in AF (30% of dual-source CT).

A/4. DIAGNOSTIC EFFICACY OF NEUROIMAGING METHODS IN BRAIN TUMORS WITH SPECIAL REGARD TO THE CLINICAL IMPACT OF METHIONINE PET/CT

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4: Euromedic Diagnostics Hungary Ltd.

Keywords: methionine, PET/CT, neuroimaging, brain tumor, clinical impact

Introduction: The purpose of our retrospective study was to compare the diagnostic value of methionine, FDG PET/CT (MET, FDG) and MRI in the detection of intracranial tumors. In addition, we evaluated the clinical impact of MET on patient management.

Methods: MET, FDG and MRI findings were collected between February 2007 and January 2011. ROC analyses were performed to assess the diagnostic performance of MET and MRI. Neurosurgeons estimated the clinical impact of MET.

Results: Altogether we analyzed 99 MET, 50 FDG and 91 MRI findings of 95 patients including 78 MET studies of 74 patients with neuroglial neoplasms. Sensitivity, specificity and accuracy of MET were 94%, 91% and 93%, whereas these values of MRI were 93%, 86% and 91% and that of FDG were 88%, 83% and 88%, respectively. Histological subgroup analyses revealed that the sensitivity of MET and MRI in gliomas including oligodendroglial component was 95% and 90%, respectively, whereas in astrocytomas MET and MRI had 95% vs. 86% sensitivity. In grade II gliomas, the sensitivity of MET and MRI was 94% vs. 75%, respectively. Retrospectively, the clinical impact of MET was estimated in 82 cases. Altogether the therapeutic management was changed after 62 examinations (76%).

Conclusion: We can state that the diagnostic efficacy of both MET and MRI are high in the detection of intracranial tumors. The diagnostic power of MET is superior to MRI in cases of recurrent/residual and low grade tumors. Our study indicate that MET might have major impact on patient management.

A/5. CORONARY ARTERY STENOSIS QUANTIFICATION WITH 256-SLICE COMPUTED TOMOGRAPHY

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Keywords: 256-slice CT, CT-coronarography, stenosis quantification

Introduction: Multidetector row computed tomography (MDCT) allows noninvasive visualization of the coronary arteries. We sought to determine the accuracy of 256-slice coronary CT angiography (256-CCTA) stenosis quantification compared to the invasive quantitative coronary angiography (QCA). We investigated the reproducibility of 256-CCTA plaque characterization too.

Methods: 71 atherosclerotic lesions were analyzed with CCTA and QCA. Cross-sectional images, perpendicular to the axis of the coronary artery, were created by multi-planar reformation. We measured the minimum lumen area (MLA), the reference diameter (RD) and the plaque length. Cross-sectional area (CSA) stenosis was calculated. The reproducibility of plaque characterization was examined by calculating interobserver agreement and kappa value.

Results: Mean MLA was 1.7 mm² (IQR: 1.1 to 2.6) measured with CCTA; 1.6 mm² (IQR: 0.6 to 2.5) with QCA. A strong correlation was observed between the CCTA and QCA MLA values and CSA values. (%). Regarding the plaque length we found a significant difference between the CCTA (18.1 mm, IQR: 10.7 to 26.9) and the QCA (12.1 mm, IQR: 9.9 to 18.0) measurements ($p = 0.0006$). Among 71 plaques, 27 calcified, 31 mixed and 13 non-calcified were identified. The inter-reader agreement was 82% (kappa = 0.68).

Conclusion: For stenosis quantification and plaque analysis 256-CCTA proved to be a reliable tool. A strong correlation was detected between the 256-CCTA and QCA measurements regarding the percentage of CSA stenosis. The plaque length was significantly higher according to 256-CCTA as compared to the QCA measurements. The plaque characterization showed a good reproducibility.

B. Physiology-pathophysiology session

B/1. ASSOCIATIONS OF ENDOGENOUS ERYTHROPOIETIN LEVEL WITH MARKERS OF INFLAMMATION AND IRON DEFICIENCY AMONG KIDNEY TRANSPLANT RECIPIENTS

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Keywords: acute leukemia, mTOR, ELISA, rapamycin

Introduction: Acute lymphoblastic leukemia (ALL) is the most common malignancy in children. Recently, the mammalian target of rapamycin (mTOR) has gained more attention as a potential therapeutical target in different tumor types including hematological malignancies.

Methods: In our present work we studied the mTOR activity in bone marrow/peripheral blood samples from pediatric ALL patients and in lymphoma/leukemia cell lines. The expression of mTOR activity dependent

proteins (p-4EBP1, p-S6) were examined by ELISA. We statistically analyzed the expression results in clinical samples during the therapy and at the possible relapses based on minimum 2 years follow up. The p-4EBP1 and p-S6 expression and the in vitro effect of rapamycin treatment on lymphoblasts were also studied by flowcytometry and immunocytochemistry.

Results: Lymphoblasts from ALL patients and leukemia/lymphoma cell lines showed significantly increased mTOR activity compared to normal lymphoid cells. The p-4EBP1 expression levels showed significant correlation with the prognosis of the patient. In vitro rapamycin inhibited proliferation but could not induce apoptosis in all examined cases.

Conclusions: Our results confirm that pediatric ALL cells have high mTOR activity, which could be detected by measuring the p-4EBP1 expression. Recent results suggest that mTOR activity measurements could be useful methods to identify ALL patients with poor prognosis at the diagnosis and to recognize early relapses. However further studies are required to define the best way to sort ALL and other lymphoma patients for future rapalog treatments based on rapalog sensitivity prediction.

B/2. THE PHOSPHOINOSITIDE 3-KINASE B REGULATES OSTEOCLAST DEVELOPMENT AND IN VIVO BONE HOMEOSTASIS

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Keywords: osteoclast, PI3K, bone, bone homeostasis

Background: Osteoclasts are the unique bone resorbing cells of myeloid origin. Their development is directed by macrophage colony-stimulating factor (M-CSF), receptor activator of nuclear factor kappa-B ligand (RANKL) and integrin-mediated adhesive interactions. The phosphoinositide 3-kinases (PI3K) have crucial roles in regulating a variety of cellular functions, but their role in osteoclast biology is poorly understood.

Methods: Murine bone marrow cells were isolated from wild-type and PI3K β mice and differentiated into osteoclasts in vitro in the presence of M-CSF and RANKL. For survival assays cells were stained with annexin-V-phycoerythrin and 7-aminoactinomycin-D, necrosis and apoptosis markers, and analysed by fluorescence-activated cell sorting. For actin ring formation assays, cells were fixed, permeabilized and stained with Alexa488-Phalloidin. MicroCT analysis was used to study the trabecular bone of the distal femoral metaphysis of the mice.

Results: In vitro differentiation of murine progenitors to multinucleated osteoclasts was strongly reduced in case of the PI3K β -/- cultures. Disruption of PI3K β decreased the resorptive capacity of osteoclasts too. PI3K β was not required for the survival of preosteoclasts, but it was needed for actin ring formation in mature osteoclasts. PI3K β -/- mice had significantly higher trabecular bone volume than wild type mice. The number of trabecules was higher in the KO mice, there was no significant difference in the trabecular thickness between the two genotypes.

Conclusion: Based on our results we can state that the PI3K β is important for osteoclast development, function and in vivo bone resorption likely by regulating the organization of the osteoclast cytoskeleton.

B/3. EFFECTS OF MUSICAL ENVIRONMENTAL ENRICHMENT IN NEW BORN RATS

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Keywords: musical enriched environment, monosodium-glutamate, neurobehavioral development, retina

Introduction: Our research group examined several neuroprotective agents and some environmental factors in nervous system lesions previously. We already described the positive effects of environmental enrichment in some animal models. About musical enrichment we have not found any results on the early neurobehavioral development, so we started to examine it. The aim of the present study was to investigate whether musical enriched

environment has any effects on the neurobehavioral development of newborn rats, and is able to attenuate retinal injury induced by neonatal monosodium glutamate (MSG) treatment.

Methods: We used two types of musical enrichment: classical and heavy-metal music from 6PM till 6AM daily. We examined the animals every day to investigate their neurobehavioral development: eye opening, incisor eruption, negative geotaxis, and some reflex performances: placing, grasping, crossed extensor, sensory reflexes. Retina degeneration was induced by early postnatal subcutaneous MSG injection.

Results: Our results show that musical enriched environment has no significant effects on the normal development. We found only slight differences between the two music groups: the heavy-metal group showed some reflex earlier than the classic. On the other hand we found significant differences between the groups in the glutamate-induced retina degeneration: the metal animals had more severe degeneration than the classical music rats.

Conclusion: These results show that musical environmental factors just slightly influence the early development of the nervous system, but in case of injuries the effects of the musical environmental influences will have significant effects in the size of the injury and the dynamism of the regeneration. We hope that our results could be bridge between the rehabilitation, clinical practice and base science in the future.

B/4. ROLE OF THE SOMATOSTATIN SST4 RECEPTOR IN INFLAMMATORY, NEUROPATHIC AND POSTOPERATIVE PAIN MODELS OF THE MOUSE

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Keywords: sst4 receptor, J-2156, acute inflammation, neuropathic hyperalgesia, chronic postoperative hyperalgesia

INTRODUCTION: Inhibitory effects of somatostatin on hormone production and tumor growth are well known, however, its

anti-inflammatory and analgesic effects were proved by our workgroup. These effects are mediated through the activation of the somatostatin receptor subtype 4 (sst4). Our research aimed at exploring the role of the sst4 receptor in mouse models of acute inflammation, chronic postoperative and neuropathic hyperalgesia.

METHODS: Acute inflammation was induced by intraplantar injection of carrageenan, traumatic mononeuropathy was produced by partial ligation of the sciatic nerve and chronic postoperative pain was evoked by meniscectomy in sst4 receptor gene-deleted (sst4^{-/-}) and wildtype (sst4^{+/+}) mice. The mechanonociceptive threshold of the paw was determined with dynamic plantar aesthesiometry. The role of the selective sst4 receptor agonist J-2156 was examined in these models.

RESULTS: Carrageenan caused 40% decrease of the mechanonociceptive threshold in wildtype mice, this hyperalgesia was significantly greater among sst4^{-/-} animals. J-2156 inhibited hyperalgesia in sst4^{+/+} mice, yet it was ineffective in the knockout group. The 45% hyperalgesia measured following the nerve ligation did not change significantly in the absence of the sst4 receptor, but J-2156 inhibited hyperalgesia in sst4^{+/+} mice. Both groups developed a 70% hyperalgesia after the meniscectomy, which decreased to 40% during the experiment. J-2156 was ineffective in this model.

CONCLUSIONS: The endogenous activation of the sst4 receptor is analgesic in acute inflammation, however, it does not have a protective role in chronic neuropathic and postoperative pain. The exogenous activation of the receptor effectively decreases hyperalgesia both in acute inflammation and chronic neuropathy.

B/5. DISPARATE AGE-RELATED ALTERATIONS IN CHOLECYSTOKININ (CCK) EFFECTS ON ENERGY HOMEOSTASIS

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Keywords: cholecystokinin, energy homeostasis

Obesity of the middle-aged is followed at old age by anorexia and cachexia. Complex age- and body composition-related alterations in the regulation of energy homeostasis may be assumed in the background. Energy homeostasis involves both body weight- and thermoregulation. Age-related changes in the responsiveness to catabolic brain-gut axis peptide cholecystokinin (CCK) possibly contribute to variations in energy balance during aging.

Male Wistar rats of different age-groups (2-, 3-, 6- or 12- and 18-24 months corresponding to juvenile, young adult, early or late middle-aged and old) were injected intraperitoneally (5 ug, to test anorexigenic effects on 48-h fasting-induced re-feeding) or intracerebroventricularly (500 ng, to test thermoregulatory actions) with CCK. Calorie-restricted 12-month (40% reduction) and high-fat diet-induced obese (60% fat calories) 6-month old groups were also established. Food intake was recorded in a FeedScale system, thermoregulatory analysis was performed using thermocouples (recording core- and tail skin temperatures) and measuring oxygen consumption in an indirect calorimeter (Oxymax).

CCK suppressed re-feeding in young adult, early middle-aged and old, but not in juvenile and late middle-aged animals. CCK-resistance of late middle-aged rats was prevented by life-long calorie-restriction. Conversely, in the obese early middle-aged rats anorexigenic CCK effects were diminished. Disparate age-related alterations were found in thermoregulatory responsiveness: strong hyperthermic effects in young rats diminished with aging.

Thus, age-related changes in responsiveness to CCK may contribute to the explanation of age-related obesity as well as aging anorexia. CCK-responsiveness is also influenced by body composition: calorie-restriction prevents the development of resistance to CCK.

B/6. MODULATION OF VASCULAR SMOOTH MUSCLE CONTRACTION BY TRANSIENT RECEPTOR POTENTIAL MELASTATIN-4 (TRPM4)

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Keywords: TRPM4, 9-phenanthrol, vasoconstriction, vascular biology, hypertension

INTRODUCTION: The transient receptor potential melastatin-4 (TRPM4) is a calcium-activated monovalent cation channel. TRPM4 has a major role in pressure-induced depolarization and vasoconstriction in intracranial arteries. Our aim was to study the regulatory function of TRPM4 in basilar and mesenteric arteries.

METHODS: Arteries were isolated from Wistar-Kyoto (WKY) rats and experiments were performed in oxygenated Krebs buffer, under isobaric conditions (at 80mmHg) on mesenteric arteries and isometric conditions (preconstriction by about 5mN) on basilar arteries.

RESULTS: Initial diameter of the mesenteric arteries was $325 \pm 18 \mu\text{m}$ ($n=9$). Extracellular K^+ (120 mM) evoked a vasoconstriction (decrease in diameter from $316 \pm 30 \mu\text{m}$ to $155 \pm 40 \mu\text{m}$, $n=4$, $p=0.03$), similarly to norepinephrine (10 μM , decrease from $387 \pm 17 \mu\text{m}$ to $127 \pm 18 \mu\text{m}$, $n=5$, $p<0.01$). Arteries were pre-constricted with norepinephrine and treated with the TRPM4 channel inhibitor 9-phenanthrol (1 μM -300 mM), which evoked a dilation (increase of diameter from $206 \pm 22 \mu\text{m}$ to $390 \pm 10 \mu\text{m}$, $n=5$, $p<0.01$). Extracellular K^+ mediated constriction was also inhibited by 9-phenanthrol. Extracellular K^+ (60 mM) evoked an increase in contractile force in the basilar arteries of the rat (contractile force from $2.6 \pm 0.9 \text{ mN}$ to $9.3 \pm 1.3 \text{ mN}$, $n=4$, $p<0.01$). This extracellular K^+ mediated constriction was also inhibited by 9-phenanthrol (contractile force from $8.3 \pm 1.4 \text{ mN}$ to $2.9 \pm 0.9 \text{ mN}$, $n=4$, $p=0.02$).

CONCLUSION: Our data suggest that TRPM4

has a major role in the modulation of contraction followed by various agonist stimuli in different arteriolar beds of the rat. TRPM4 may participate in pathological conditions characterized by increased arteriolar tone, such as hypertension.

B/7. EX-VIVO MODELLING OF VASOACTIVE EFFECTS OF SUBARACHNOIDAL HEMORRHAGE ON ISOLATED CEREBRAL ARTERIES

Istvan Zoárd Batai¹, Peter Cseplo¹, Orsolya Torok¹, Zsolt Springo¹, Zoltan Vámos¹, Dalma Kosa¹, Janos Hamar¹, Akos Koller^{1,2}

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Keywords: hemorrhagic stroke, subarachnoid hemorrhage, vasomotor, basilaris, isolated artery

PURPOSE: Previous studies reported that acute hemorrhage (stroke, trauma) is followed by an early and delayed vasospasm which inflicts severe damage to the cerebral blood flow. However, the vasoconstrictor effects of the hemolyzed blood (HB) have not yet been characterized. We hypothesized that the tone of the isolated cerebral arteries are substantially increased by HB.

METHODS: Basilar artery (BA) from male rats was isolated and placed in a pressure-myograph chamber. The diameters of vessels were measured by videomicroscopy. During incubation (80 mmHg) a substantial active vasomotor tone (AD) developed. The effect of extravasated blood was modeled by adding HB directly to the chamber. The vasoactive function of vessels was studied by the responses to acetylcholine (ACh 10-4 M), sodium-nitroprusside (SNP 10-4M), nifedipine (10-6M) and CO₂.

RESULTS: The active diameters of BA were $277.5 \pm 11.5 \mu\text{m}$ ($n=9$). HB (200 μl /chamber) significantly decreased the diameter compared to the control (to $187 \pm 7 \mu\text{m}$; $46.3 \pm 3\%$ of AD) In control conditions significant dilatation was induced by ACh, SNP, nifedipine and CO₂ (+19 $\pm$ 4%, + 26 $\pm$ 2%,

+32±4% and +28±3%). In contrast, HB induced a greater decrease of dilations to ACh, SNP, whereas there was no significant changes in response to nifedipine and CO₂ (+7±1%, +11±1%, +28±3% and +31±4%).
CONCLUSION: Thus that HB elicits a significant vasoconstriction and inhibits the endothelium- and smooth muscle-dependent NO related vasodilator mechanisms. Further elucidation of the underlying mechanisms of hemolyzed blood-induced vasomotor dysfunction could contribute to a better understanding and treatment of intracranial hemorrhage.

B/8. NEBIVOLOL INDUCES DILATATION IN ISOLATED RAT BASILAR ARTERY

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Keywords: nebigivolol, cerebral artery, vasomotor, basilar artery, isolated artery

Experimental and clinical studies have demonstrated that nebigivolol has antiarrhythmic, antihypertensive effects, and in peripheral arteries nebigivolol elicits release of nitric oxide. However, its effect on the regulation of cerebrovascular tone has not been investigated. We hypothesized that nebigivolol increases the diameter of isolated cerebral arteries.

Basilar arteries (BA) were isolated from male Wistar rats and were mounted into a pressure-flow myograph chamber and cannulated at both ends. Vessels were incubated until a spontaneous myogenic tone (active diameter, AD) developed. Diameters of vessels were measured with video-microscopy. Vasomotor function of vessels was studied in response to acetylcholine (ACh) and nebigivolol. Nitric

oxide synthase was inhibited by L-NAME.

The active diameter (AD) of BA was 215±11 µm and passive diameter was 378±15 µm (n=9). Nebigivolol caused significant vasodilation (10-5 M: to 289±15 µm, a 30±7% increase in AD; p<0.05). Incubation of BA with L-NAME significantly reduced the active diameter (to 162±11 µm), which was maintained until the end of the experiment. In the presence of L-NAME nebigivolol caused significant vasodilation as well (at 10-5 M: to 211±12 µm, a 25±5% increase in AD; p<0.05), while ACh-induced vasodilatation decreased significantly (control: 38±3 AD%; after L-NAME: 3.1±1 AD%; p<0.05).

The results demonstrate that in isolated cerebral arteries 1) nebigivolol elicits significant dilation, 2) NO contributes to the development of basal tone and mediation of ACh-induced dilation, but do not contribute significantly to the nebigivolol-induced dilation. Elucidating the underlying mechanisms could contribute to a better understanding of the effects of nebigivolol on cerebral circulation.

B/9. INCREASES IN INTRALUMINAL FLOW ELICIT BIPHASIC RESPONSES IN ISOLATED RAT BASILAR ARTERIES

Gabor Szijjarto¹, Peter Cseplo¹, Zsolt Springo¹, Peter Tóth^{1,2}, Orsolya Torok¹, Istvan Batai¹, Zoltan Vamos¹, Zoltan Nemeth¹, Janos Hamar¹, Akos Koller^{1,2}

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Keywords: pressure-diameter, flow-diameter, wall shear stress, Monroe-Kelly doctrine

Background: The increases in flow elicit dilations in small arteries and arterioles of most tissues. However, vasomotor responses of cerebral vessels to increases in flow have not yet been clarified. It is also known that intracranial volume (brain, blood, liquor) is tightly regulated. Thus we hypothesized that vasomotor responses of cerebral arteries of different locations will be different to increases in intraluminal flow. In our previous studies we have found

that increases in flow elicit constrictions in middle cerebral artery (MCA).

Methods: Changes in diameter of isolated basilar arteries (BA) were measured by a microangiometer to stepwise increases in intraluminal flow (at a constant intraluminal pressure of 80 mmHg). Intraluminal flow was established by increasing the pressure difference throughout the vessels. Finally, the passive diameters of vessels (in Ca²⁺ free solution) were measured.

Results: The 80 mmHg intraluminal pressure elicited pregnant vasomotor tone in the BA. As the cause of the increasing flow the diameter decreased from the starting 272±11 µm active diameter to 228±9 µm (Q=60µl/min), then it increased to 254±9 µm (Q=60µl/min).

Conclusion: We propose that the opposite responses of cerebral arteries to increases in flow have important physiological roles: biphasic response of basilar arteries could be important to amplify the increase in blood flow to brain tissues, whereas constrictions of middle cerebral arteries could be important to maintain constant cerebral volume.

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C-D-E Multidisciplinary session II.

C. Immunology-cell biology-genetics Session

C/1. RESEARCH OF SPLENIC LYMPHOCYTE HOMING USING IN VIVO CELL COMPETITION METHOD

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Keywords: spleen, lymphocyte, homing, lectin, cell competition

Introduction: The spleen is the largest peripheral lymphoid organ with major lymphocyte homing activity. In contrast to lymph nodes, the exact details of splenic

lymphocyte recirculation are not yet known. According to literature, carbohydrate components presumably play key role in the adhesion of lymphocytes to vascular endothelium. Our goal was to develop a method in which adhesion and migratory behavior of two sets of lymphocytes (treated and control groups) can be compared within one organism, to investigate splenic homing on a cellular level.

Methods: Lymphocytes were obtained from donor mice, and were made distinguishable with two different labeling methods: intracellular dye carboxy-fluorescein diacetate succinimidyl ester (CFSE), and non-specific biotinylation of cell surface proteins. The cells were injected into recipient mice and the spleen was removed for investigation. To justify the method's concept, we have studied the effect of cell modifying substances: ConA lectin, binding to cell surface carbohydrate chains and colcemid (similar to colchicin) inhibiting microtubule polymerization and immobilizing cells.

Results: Flow cytometry and fluorescent microscopy studies have verified that the labeling procedures have not influenced the adhesion and tissue specific localization of the cells significantly. ConA lectin inhibited CFSE-labeled lymphocyte entry into the spleen and almost completely prevented their migration to the white pulp compared to untreated competitor cells. Colcemid treatment did not alter the number of CFSE-labeled lymphocytes entering the spleen significantly; however their migration in splenic tissues was greatly inhibited.

Conclusion: According to our results, this method will be suitable for further research of splenic lymphocyte homing.

C/2. EXAMINATION OF SUBCUTANEOUS B16 MELANOMA CELL-DERIVED TUMOR GROWTH IN STAT6 DEFICIENT MICE

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Keywords: STAT6, melanoma, tumor, IL4, Th2

Introduction: STAT6 transcription factor has a central role in the development of Th2 cells and M2 macrophages activating transcription in response to Th2-type cytokines (IL-4, IL-13) produced by tumor-infiltrating immune cells and, in some cases, also by tumor cells. Th2 cells and M2 macrophages are known to inhibit anti-tumor immunity and promote tumor progression. According to previous results in other murine tumor models, an increased Th1 response and M1 macrophage differentiation can be observed in STAT6 knock-out animals. The main goal of our work was to determine the role of STAT6 transcription factor in tumor development using subcutaneous B16 mouse melanoma tumor model in STAT6 knock-out and wild type mice.

Methods: Subcutaneous tumors were removed 14 days after inoculation and individual tumor weights were measured. We also examined the basal structure and macrophage content of tumors using immunohistochemistry, and characterized the tumors' immunological status with measurement of different immune cell markers by qPCR.

Results: Our results show a significantly increased subcutaneous tumor growth in STAT6 deficient mice compared to the wild type animals. Basal structure of the tumor tissue was similar in both groups, but peripheral tumor cell infiltration to the neighboring tissues was enhanced in STAT6 KO mice. Gene expression analysis revealed significant down-regulation of M2 macrophage marker arginase 1 and anti-inflammatory cytokine IL-10 in STAT6 knock-out mice-derived tumors.

Conclusion: STAT6 may have a role in controlling the phenotypic switch of tumor-infiltrating immune cells, thus influences tumor development in murine melanoma model.

C/3. CHANGES OF HAEMATOLOGICAL PARAMETERS AFTER DANAZOL TREATMENT IN PATIENTS SUFFERING IN HANO

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Keywords: Hereditary Angioedema – HAE, Complement system, Haematology

No English abstract arrived.

D. Neurology-ortopedics-pulmonology session

D/1. NEUROPROTECTIVE EFFECT OF FREE RADICAL SCAVENGER EDARAVONE AFTER TISSUE PLASMINOGEN ACTIVATOR DAMAGE TO RAT'S BRAIN

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Keywords: edaravone, neurovascular unit, oxidative stress, plasmin, tissue plasminogen activator

Introduction: One of the therapeutics for acute cerebral ischemia is tissue plasminogen activator (t-PA). Using t-PA after 3 hour time window increases the chances of hemorrhage, involving multiple mechanisms.

Methods: In order to show possible mechanisms of t-PA toxicity and the effect of the free radical scavenger edaravone, we administered vehicle, plasmin, and t-PA into intact rat cortex, and edaravone intravenously. In vitro experiment was also performed.

Results: Plasmin and t-PA damaged rat brain with the most prominent injury in t-PA group on 4-HNE, HEL, and 8-OHdG

immunostainings. Such brain damage was strongly decreased in t-PA plus edaravone group. For the neurovascular unit immunostainings, occludin and collagen IV expression was decreased in single plasmin or t-PA group, which was recovered in t-PA plus edaravone group. In contrast, matrix metalloproteinase-9 intensity was the strongest in t-PA group, less in plasmin, and was the least prominent in t-PA plus edaravone group. In vitro data showed a strong damage to tight junctions for occludin and claudin 5 in both administration groups, while there were no changes for endothelial (NAGO) and perivascular (GFAP) stainings. Such damage to tight junctions was recovered in t-PA plus edaravone group with similar recovery in Sodium-Fluorescein permeability assay. Conclusions: Administration of t-PA caused oxidative stress damage to lipids, proteins and DNA, and led to disruption of outer parts of neurovascular unit, greater than the effect in plasmin administration. Additive edaravone ameliorated oxidative damage by t-PA with protecting outer layers of blood-brain barrier (in vivo) and tight junctions (in vitro).

D/2. INNOVATION IN THE REPAIR OF FOCAL CHONDRAL DEFECTS

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Keywords: focal chondral defects, patent, human trial

Introduction: Cartilage has very little potential to heal therefore several distinct methods have been developed for cartilage repair. Thus far no universal method has been established. In our previous animal experiments we repaired focal chondral lesions of porcine femoral condyles using pure cartilage allograft with a unique surface augmentation method. This basically new treatment worked excellently in porcine model but before the human clinical trial we had to develop/convert it. **Methods:** To obtain a perfect pure cartilage graft we used high speed drill with water-cooling for cleaning the hyaline graft from the osseal and calcified areas. The

successfully isolated graft was stored in DMEM (+4c°) and directly before the operation we incised the grafts on the deep side (femoral osseal surface) converting the specimen into an easily pliable tissue. We used our novel technique to prepare the grafts utilising a specially designed device (incisor – a patented technique for multiple parallel incomplete surface incisions). The appropriately sized, implanted processed allograft was fixed in the chondral defect site with 6/0 absorbable sutures and fibrin glue around the graft.

Results: In our experiments we found that this novel cartilage repair method was successful, the grafts integrated to the defect site well.

Conclusion: We converted this cartilage transplantation to a safe and feasible technique, therefore this method has been used for a human clinical trial.

D/3. THE CHILDHOOD EXAMINATION OF THE FEMURAL BONE- AND HIP JOINT'S ANATOMICAL PARAMETERS WITH EOS IN 2D AND 3D

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PTE KK Mozgásszervi Sebészeti Intézet Ortopédiai Klinikai Tanszék

Keywords: Lower limb, 3D, EOS, geometrical parameters, child

GOAL: Low-dose X-ray devices are a new method in the field of radiology. They produce, 3D reconstructionable stereo images of the skeleton of a standing patient with low dose radiation. Using this technology we can define geometrical parameters, which has not been done before, using these conditions, in a large population. We examined geometrical characteristic and development of the femur and hip joint by images created in the Regional Screening and Diagnostic Centre of our University.

METHODS: We recreated the 3D reconstruction of 506 child (187 boys, 319 girls, age: 4-16). The indication of the examinations were not lower limb pathology. The modelling was made by SterEOS 3D reconstruction software. We performed statistical analysis with Welch-test, two-sample t-test and linear regression. The

important measured parameters: neck shaft angle, HKS, femoral torsion, femoral mechanical length.

RESULTS: We found a fluent, significant decrease in the neck shaft angle and femoral torsion, increase in the HKS and femur mechanical length in correlation with the age. The neck-shaft angle is increased in girls in the 7-8 year age-group, but the femoral mechanical length is longer in boys in the 11-12 year age-group.

SUMMARY: We were able to confirm, that the method is useable in this age-group to examine anatomical parameters. We defined the normal standards of the femur's anatomical parameters by sex and age-groups, to be underlined by the femoral torsion, which has not been done before in a large population. We could confirm the femur development's age and gender related characteristics.

D/4. RESULTS OF A NEW QUESTIONNAIRE TO ASSESS CHILDREN AND ADOLESCENT SLEEP PROBLEMS

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Keywords: sleep disorders, children, questionnaire, polysomnography

Introduction: Screening of sleep disorders in children is of high importance. In Hungary there is no standardized questionnaire for assessing sleep problems in children. We evaluated the results of sleep quality scales of our questionnaire and compared the data of healthy and clinical population. We analyzed the correlation between our questionnaire and validated tests and the severity of obstructive sleep apnea (OSA).

Methods: Our questionnaire is designed to estimate sleep hygiene and quality in two age groups (8-14 and 15-18 ys.) by nighttime and daytime symptoms score. Two groups of children were analyzed: 1. healthy group (n=2020), 2. children with sleep problems (n=66). The second group filled out two validated tests, Modified Pediatric Epworth Sleepiness Scale (MP-ESS), Conner's Rating Scales-Revised (CRS-

R) and underwent polysomnography. Severity of OSAS was characterized by Apnea-Hypopnea Index (AHI) and Oxygen-Desaturation Index (ODI).

Results: Children underwent polysomnography had significantly higher score both on nighttime and daytime symptoms scale than healthy children. Correlations were: score of nighttime symptoms scale and CRS-R score ($r=0.441$; $p=0.001$), score of daytime symptoms scale and MP-ESS score ($r=0.389$; $p=0.001$). Children in the highest quartile of nighttime symptoms scale had significantly higher AHI (mean $\pm$ SD: 0.62 ± 1.07 vs. 5.97 ± 11.39 ; $p=0.04$) and ODI (mean $\pm$ SD: 0.49 ± 0.53 vs. 6.23 ± 12.07 ; $p=0.02$) than children in the lowest quartile. The nighttime and daytime score index had higher sensitivity to predict OSA than other tests.

Conclusions: Our questionnaire can be potentially useful in evaluating sleep problems in children. However validation of the questionnaire is still needed.

D/5. ASSESSING CONSCIOUSNESS AFTER TRAUMATIC BRAIN INJURY: A BEHAVIOR-BASED AND A PSYCHOPHYSIOLOGIC APPROACH

Andras Szeles

Moss Rehabilitation Research Institute, Albert Einstein Healthcare Network

Keywords: TBI, psychophysiology

Introduction: The presentation will serve as a brief introduction to the challenges encountered, both clinically and in the lab, during assessment of consciousness after severe TBI. Preliminary work in exploring the utility of 'event-related potentials' (ERP) with such a population and the challenges encountered in implementing such tasks as part of a large scale, double-blind placebo controlled study therein will be discussed.

Methods: single subject design

Results: Patients previously diagnosed with varying degrees of consciousness after TBI show variable tolerance (pain, fatigue, positioning) and equivocal outcome during psychophysiological testing with ERP.

Conclusions: ERP may hold value in supplementing traditional, behavior based assessments of consciousness in clinical

diagnosis and research, pending further investigation and adjustments that tailor to the complex needs of the TBI patient population.

E. Pediatrics Session

E/1. THE ROLE OF MANNOSE-BINDING LECTIN IN THE FEVER OF ONCOLOGICAL PAEDIATRIC PATIENTS

Marianna Dobi

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Keywords: complement system, mannose-binding lectin, polymorphisms, neutropenic fever, MBL substitution therapy

Background: The appropriate function of the complement system is essential for leukemic children; partly the developing neutropenia due to the malignant disease, partly the chemotherapy caused immunosuppression. The key element in lectin pathway of the complement system is the mannose-binding lectin (MBL). 3 polymorphisms of MBL gene are known, resulting in lower serum MBL concentration. The aim of our study was to find correlation between the polymorphism with low MBL level and the frequency and severity of the feverish episodes in leukemic children.

Methods: We followed 81 patients for 7 months and recorded the number of the feverish period, the specific laboratory data (C-reactive protein, white blood cell and absolute neutrophil count) and the applied therapy. We isolated DNA via 'salting technique' and the alleles were determined by real-time PCR. For the statistical analysis, we used SPSS program.

Results: In the follow-up period 11 patients died. The numbers of the periods of neutropenic fever were lower in patients with normal MBL levels and wild genotypes than in patients carrying variant alleles (median 2 vs. 3 Mann-Whitney U test $p=0.05$). Underlying disease, age and sex-adjusted logistic regression analysis showed that patients with MBL deficiency have four times higher risk ($OR=4.1$, $p=0.03$) for

frequent infections (>3).

Conclusion: MBL genotypes have an important role in the immunosuppression associated infections. In the future, MBL may contribute to the estimation of the risk for infection and modifying therapeutic options for individuals.

E/2. GENETIC POLYMORPHISMS IN ANTHRACYCLINE-INDUCED CARDIOTOXICITY IN PAEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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3: Heim Pal Children's Hospital

Keywords: pharmacogenetics, anthracyclines, cardiotoxicity, left ventricular function, paediatric

Introduction: Cure rates of paediatric acute lymphoblastic leukemia exceed 80% by using modern treatment protocols. However, survivors may face a range of late effects such as cardiotoxicity the main dose-limiting side-effect of anthracyclines. Our objective was to find associations between the left ventricular function and single nucleotide polymorphisms (SNPs) in the genes CBR1, CBR3 and AKR1A1 coding enzymes involved in anthracycline metabolism.

Methods: We performed our analyses on data from 254 paediatric acute lymphoblastic leukemia patients who had been treated with ALL BFM protocols. Left ventricular function was assessed as fractional shortening (LVFS) obtained by echocardiography. Genotyping a total of 7 SNPs was conducted using Sequenom® iPLEX® Gold Genotyping Technology. General linear model statistics were performed to test for associations.

Results: Patients under the age of 10 with AKR1A1 rs2088102TT/TC genotype had lower LVFS at the final examination compared to CC patients (38.6%, $SD=5.7\%$ and 41.8%, $SD=6.7\%$ respectively, $p=0.0056$). Creating subgroups by sex we

found that boys with AKR1A1 rs2088102TT/TC genotype had reduced LVFS at the final examination compared to CC patients (37.6%, SD=5.7% and 42.2%, SD=8.1% respectively, $p=0.0120$). However, we found no genotype-dependent differences among girls.

Conclusion: Our results suggest that AKR1A1 rs2088102 variations are associated with altered left ventricular function in late survivors of paediatric acute lymphoblastic leukemia.

E/3. PREVENTION OF MEDICAL FEARS IN PRESCHOOL AGE

Reka Siklosi, David Pocs

Department of Children and Youth Psychiatry, University of Szeged

Keywords: medical fears, prevention, preschool age, health education, medical students, Teddy Bear Hospital

Introduction: The anxiety (includes medical fears) is the most common psychological problem in childhood. Our study aims to show that we can prevent medical fears in preschool age within an organized program, called "Teddy Bear Hospital" (TBH). The TBH is a project of IFMSA (International Federation of Medical Students' Associations) in 36 countries with nearly 200 medical universities around the world.

Methods: The study group comprised 129 preschool children (average age: 5.5 years, 45% girl, 55% boy), and 119 preschool children, age and sex matched, from a similar residential area, served as the control group. Assessment included Visual Analog Scale (VAS), Picture Test (PT) Drawing Investigation (DI) about medical fears. This was assessed individually, one day prior to the intervention and again 3 week after the intervention in both groups. We analyzed the results using SPSS statistical software.

Results: Children in the "Teddy Bear Hospital" group reported significantly lower levels of medical anxiety than the control group at follow-up, measured by PT ($p<0.001$) and DI ($p<0.001$). But there is no significant decrease, measured by VAS. During the analysis we realised, that children in the study group drawn

significantly more new informations about the health care than the control group ($p=0,008$).

Conclusions: The "Teddy Bear Hospital" is effective in reducing children's medical fear. Also we realised, that this pain-free encounter with the medical environment is a good opportunity to teach them about the health care.

F. Lunch Symposium

F/1. UPDATE IN IVF: PREIMPLANTATION GENETIC DIAGNOSIS

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**Temple University School of Medicine
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Keywords: IVF, PGD, Genetic diseases

Preimplantation geneticic Diagnosis (PGD) represents the cutting edge of reproductive technology. It provides the ability to prediagnose many common chromosomal aneuploidies as well as some genetically based diseases. PGD has been developed as a method to help couples who choose IVF to identify chromosomal abnormalities prior to embryo implantation. Recent advances now allow all 23 sets of chromosomes to be analyzed using comparative genomic hybridization (CGH).

PGD may also be used in couples who have a family history of a specific genetic disease that is based on a sinle gene mutation.

In IVF pregnancies in women 35 years or older, research has shown that aneuploidies (refers to blastomeres in an embryo having one less or one extra chromosome) and other genetic abnormalities of the embryo will increase the risk of spontaneous miscarriage or the development of an abnormal fetus. Thus, performing genetic analysis prior to embryo implantation could prevent the initiation of abnormal pregnancies. PGD may increase the chance for a successful pregnancy and the delivery of a healthy and disease free newborn. This technique may very well revolutionize the way reproductive medicine is practiced.

F/2. Treatments of hypertensive urgency in children and in elderly

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Hypertensive emergencies encompass a spectrum of clinical symptoms in which the uncontrolled blood pressure (BP) leads to progressive end-organ dysfunction (EOD). The most common clinical presentations of hypertensive emergencies are cerebral infarction (24.5%), pulmonary edema (22.5%), hypertensive encephalopathy (16.3%), and congestive heart failure (12%). Other clinical symptoms are associated with hypertensive emergencies include intracranial hemorrhage, aortic dissection, and eclampsia, as well as acute myocardial infarction. Malignant hypertension and accelerated hypertension are both hypertensive emergencies, with similar outcomes and therapies in all age groups. In children hypertensive emergencies appear rarely and often associated with specific organ dysfunctions and endocrine disorders. Essential hypertension starts early in overweight teenage. This population have higher risk for severe hypertension in adulthood, especially when hypertension is combined with diabetes mellitus, hyperlipidaemia and metabolic dysfunction. The treatment of hypertensive urgency/crisis is similar in children and in elderly. The α_1 -adrenoceptor antagonist and 5HT_{1A} receptor agonist Urapidil is safely used in both population, as well as in pregnant patients. In adults nitrate, angiotensin receptor blockers are widely used in urgency. It is worth considering, that experimental studies proved that angiotensin receptor blockers have poor therapeutic effect in the old population. In this short presentation we will review some of the important aspects of pediatric and old age hypertensive emergencies, including diagnosis, emergency department investigations, and

pharmacologic management. (Supported by Grants by Hungarian Nat. Sci. Res. Fund-OTKA F- 048837, T-048376, K71591, AHA Founders Aff., 0555897D, MHT Grant – 36674-, NTP – OKA –VIII – B – 065, Hungarian Society of Hypertension 2011/2012).

G. Plenary Session, Part I.

G/1. GENETIC SCREENING: EVOLVING SCIENCE, EVOLVING ETHICS

Maria Judit Molnar

Clinical and Research Centre for Molecular Neurology, Semmelweis University, Budapest, Hungary

The new molecular technologies opened a new era in genomics and medicine. The story started with the Human Genome Project, which made possible to decode the human genome sequence. Since the costs of the whole genome sequencing is less than 10.000 USD the number of public whole genome data are increasing. Many people shows a big interest to their genetic risk factor for different disorders, curiosity for traits of different phenotypic features, which resulted in a new service, the so called „direct to customer” genetic testing. In the Personal Genome Project researchers are collecting whole genome sequences and related phenotypic data from individuals who agree to make this information public. They are volunteers, who are willing to share their genome sequence, many type of personal information with the research community and the general public, so we will be able to better understand the genetic and environmental contributions to human traits. Many people have fears from the past and associate these initiatives with: eugenics, and genetic determinism. Presently these fears seems to be reseeded, asking that genetic information is different than a family history, psychiatric history, the meds in the medicine cabinet, or the records of somebody's web searches. A new question is coming up: who should have access to the personal genomics data. Can laws, rules and morals be imported from other domains to „cover” genomics? The talk will give an overview about the present

state of “direct to customer” genetic testing, the Personal Genome Project and its impact on the clinical practice and in our everyday.

G/2. THE PUZZLE OF TELOMERASE ACTION, FRIEND OR FOE?

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Keywords: epigenetics, psychosomatic, telomer, telomerase, cellular aging

Telomeres are “cap-like” regions at the ends of chromosomes, which play a vitally important part in preserving the integrity and stability of chromosomes during DNA replication. The human telomere contains a few kilobases of TTAGGG sequence. The length of the sequence may differ in different species or within the same species. Sequence length also depends on cell type, and may change with time in a given cell type.

There is an increasing number of proofs, that exogenous environmental effects influence the intracellular telomerase activity and telomere length. These effects as epigenetic inputs increase in telomerase activity and the protective effect of the immune system may be connected at the level of long-term cell viability and/or genome stability (e.g. DNA repair). Moreover, bibliographic data prove, that telomerase activity and telomere shortening in mothers of chronically ill and healthy children demonstrates how stress gets “under the skin”. The study found that the mothers of sick children showed significantly lower telomerase activity and significant telomere shortening, which corresponded to a cellular aging of 9-17 years compared to the mothers of healthy children. Significant telomere shortening was also observed among caregivers of Alzheimer’s disease patients compared to the control group matched for age and gender. In caregivers of Alzheimer’s disease patients – telomere shortening showed a close connection with depression symptoms. Based on these trials, telomere shortening seems to serve as a biological marker of experiencing a chronic stress condition.

The various aspects of telomerase activities in normal and tumor cell functions will be discussed, as well.

G/3. THE ASSOCIATIONS OF CELLULAR AGING AND PSYCHOSOCIAL FACTORS: AN EPIGENETIC LINK

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Keywords: epigenetics, cellular aging, telomere length, psychosocial factors, religiosity/spirituality

Background: Telomere length and rate of telomere shortening are indicators of mitotic cell age. Telomere shortness in humans is a prognostic marker of disease risk, progression, and premature mortality.

Aim of the study: We conducted a pilot study to investigate the psychosocial determinants of cellular aging. In this study we focused on religiousness, spirituality and life meaning.

Sample: 40 full time working women (n=20) and men (n=20) participated in our study. The age range was between 40 and 70.

Methods: Telomere length was determined in peripheral blood mononuclear cells (PBMCs). Telomere PNA Kit/FITC for Flow Cytometry was used for detection of the telomeric sequences which allows the estimation of the telomere length. Religiousness and spirituality dimensions were assessed by four items derived from the Brief Multidimensional Measure of Religiousness/Spirituality (BMMRS). We used the eight-item version of the Brief Stress and Coping Inventory’s Life Meaning Subscale (BSCI-LM) to measure person’s sense that life is meaningful. Organizational religiousness was assessed by two separate items measured by the frequency of religious service attendance and the form of religious practice. We used partial correlation analyses to determine the association of psychosocial variables and telomere length. Age and gender was used as covariates.

Results: Religiousness and spirituality assessed by BMMRS positively associated with telomere length ($r=0.34$; $p=0.03$). A moderate positive relationship was found between meaning in life measured by BSCI-LM and the indicator of cellular age ($r=0.42$; $p=0.01$). Those who attended religious services more frequently, had longer telomere ($r=0.37$; $p=0.02$). The form of the religious practice also significantly associated with telomere length ($r=0.41$; $p=0.01$).

Conclusions: This pilot study showed that there were associations between cellular age and religiousness, spirituality and meaning in life, independently from age and gender. The results suggest that these psychosocial factors have protective role to avoid early health deterioration and premature mortality. Since the sample was small, further investigations on larger representative samples are needed to confirm the findings of this study.

G/4. PERSONALIZED MEDICINE AS THE CHALLENGE TO TRADITIONAL THERAPEUTICS

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Keywords: personalized medicine, stratification, treatment options, nichbuster,

Today, it is common for a medical product to be fully effective for only about 60 percent of those who use it. As the medical community is now learning, this in part reflects biological variation among individuals that affects the clinical response. In the past, they have not had the tools or knowledge to understand those differences. „Personalized medicine” refers to the tailoring of medical treatment to the individual characteristics of each patient. It does not liberally mean the creation of drugs of medical devices that are unique to a patient but rather the ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment. Personalized medicine may be considered an extension of traditional approaches to

understanding and treating disease. Physicians have always used observable evidence to make a diagnosis or prescribe a treatment tailored to each individual. In the modern conception of personalized medicine, the tools provided to the physician are more precise, probing not just the visually obvious, but the very molecular makeup of each patient. It is an approach that is well suited to the medical challenges faced in the 21st century. Although we have prevailed over many of the diseases that have plagued humanity throughout the ages, what remains are diseases of greater complexity: diabetes, cancer, heart disease, and Alzheimer’s disease. They are not caused by a single gene or a single event but by a combination of genetic and environmental factors, and they tend to be chronic, placing a heavy burden on the healthcare system. Personalized medicine provides the tools needed to better manage chronic diseases and treat them more effectively. As evidence of the benefits continues to grow, an infrastructure of laws, policy, education, and clinical practice is building around personalized medicine to support its use. Ultimately, the success of personalized medicine will rise or fall on its ability to demonstrate its value– to the healthcare system, to the industries that develop its products, and to patients.

G/5. TWIN RESEARCH UPDATE IN 2012- GENETICS AND EPIGENETICS

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Keywords: heritability, methylation, twin

Twin research is a powerful approach for investigating the role of genetic and environmental influences on a phenotype by the traditional ACE model. The twin design compares the similarity of a phenotype within identical or monozygotic (MZ) twin pairs who share 100% of their genes, to that within fraternal or dizygotic (DZ) twin pairs, who share on average 50% of their genes, assuming that relevant environmental exposure are equally shared by MZ and DZ

twins. Compared to family studies, twin studies are useful in the differentiation of common (shared) and unique (unshared) environmental variances. Furthermore, for a given pair of phenotypes, a higher cross-twin/cross-trait correlation in MZ than in DZ twins points to genetic influences common to the two phenotypes (genetic covariance) which can be assessed by Cholesky decomposition model. Disturbance of DNA methylation leading to aberrant gene expression has been implicated in the etiology of many diseases. Since MZ twins share a common DNA sequence, their study represents an ideal design for investigating the contribution of epigenetic factors to a disease etiology. In the recent years, therefore, twin researchers have been started to focus on MZ twin pairs discordant for a phenotype (eg., obesity) in order to assess the epigenetic factors (associated with DNA methylation) which are responsible for discordance. Genome-wide analysis of DNA methylation on peripheral blood DNA samples are obtained on these samples of MZ twin pairs discordant for a certain disease. Some genetic influences on DNA methylation variation was reported by recent studies. Longitudinal twin studies are useful for investigating the longitudinal contribution of genes on a phenotype.

H. Multidisciplinary Session III.

H. Ophthalmology Session

H/1. EFFECT OF ANTI-VEGF INJECTIONS (LUCENTIS) ON READING SPEED IN WET-AMD PATIENTS

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Keywords: Wet-AMD, Lucentis, Radner Reading Chart

Background: Patients suffering from Age-related Macular Degeneration (AMD) are losing their reading capability. The objective of this study is to investigate the effectiveness of a new method, measuring the reading speed in wet-AMD patients treated with anti-VEGF injections.

Patients and method: Routinely, anti-VEGF treated wet-AMD patients are evaluated by measuring the best corrected distant visual acuity (BCVA) via ETDRS chart and macular thickness via Optical Coherence Tomography (OCT). In addition to a full ophthalmological examination we measured the reading speed via Radner chart on 30 patients before and 3 months after treatment. The collected data were analyzed using a Paired T-test.

Results: After the anti-VEGF treatment, BCVA increased from 59 to 67 letters, retinal thickness decreased from 362 μm to 225 μm . The reading speed (sentences/sec) improved from 16 seconds to 10 seconds per sentence, and the amount of words read per minute increased from 65 words/min to 101 w/min. The results were statistically significant ($p < 0.01$).

Conclusions: Significant improvement of reading speed was observed after Lucentis treatment in wet-AMD patients. Radner reading chart is an effective tool to follow the evolution, and the treatment-effect of wet-AMD patients.

H/2. RETINAL BLOOD VESSEL BASED DIABETIC RETINOPATHY CLASSIFICATION

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Keywords: Diabetic Retinopathy, automated diagnostics, retinal blood vessels, color fundus photography, image segmentation

Introduction: Diabetes mellitus is the leading cause of blindness amongst working-age adults in Western countries. We propose a method to observe Diabetic Retinopathy (DR) based retinal vascular changes and to find the most accurate features to distinguish between fundus images of DR and healthy patients (C).

Methods: 15 eyes of 15 diabetic patients with mild or severe DR underwent ophthalmic examination then color fundus images were acquired by a CANON CF-60UVi camera (3504x2336pixels). Two set

of segmentation results are used for evaluation: manual and automatic. Using binary vessel images density and distance maps were generated and vessel thickness data was calculated. We enrolled 15 control subjects (C) in the study. Statistical evaluation were implemented by two sample t-test and ROC analysis (SPSS Statistics 15.0).

Results: The vessel density showed significant decrease in eyes with DR (DR: 32.463 ± 952 pixels, K: $33,163 \pm 383$ pixels $p=0,013$) whilst the vessel distance values increased significantly in group DR (DR: $35,732 \pm 355$ pixels, K: $34,859 \pm 277$ pixels, $p<0.001$). There were no significant difference in the vessel thickness values of groups DR and C.

The ROC analysis showed the vessel density feature to be the most accurate (AUC=0.973).

Conclusion: We observed DR related retinal vascular changes which could henceforth be used by differentiation of diabetic and healthy eyes. Our results showed especially significant differences in vessel distance parameter, supporting the possible use of it when composing novel, automated DR diagnosing or classification methods. An affirmative study is planned with pregnant expansion of the number of participants.

I-J. Multidisciplinary Session IV.

I. Behavioural sciences Session

I/1. FACTORS INFLUENCING STUDENTS' SATISFACTION: A FOLLOW UP STUDY

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Keywords: student's satisfaction, predictive model, descriptive model, educational management, inventory

GOAL: The main goal of this study is a data-mining approach of the students satisfaction based on an educational inventory and to provide educational management with an adequate tool as well.

METHODS: An in-house 16-items inventory was created to evaluate students'

satisfaction. 11.294 anonymous records were processed by a multi-language questionnaire at the Medical Faculty. First, a statistical validity analysis was used by Confirmatory Factor Analysis. Secondly, an Item-Response Theory (IRT) and CHAID decision tree models were created.

RESULTS: Significant differences were found between the preferences of the first-year and the second-year students. In the first year, quality of the lectures and motivation for independent thinking were the most important influencing factors compared with that of the second year students who preferred the general quality of subject. This tendency remains unchanged in the third year. In the clinical modul of education, the quality of the practices is the predominant factor.

CONCLUSION: It is feasible to develop statistical models that can help us to find optimal modifications in education to increase the students' satisfaction. Based on the results, our inventory is a valid predictive and descriptive tool for measuring students' satisfaction concerning education.

I/2. GENDER DIFFERENCES IN ADOLESCENTS' SMOKING

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Keywords: smoking, adolescents, problem behaviour, risk factors, gender

Smoking is one of the most important social and public health problems all over the world. The youth smoking is especially a key problem in terms of prevention and health promotion. The presence of smoking in young ages can determine the smoking in adulthood. The gender differences are not always so characteristics, in our study we try to identify some fields where significant differences can be assumed.

Our sample is consisted of 2072 students from elementary and secondary schools. The study was performed in Mako and the

villages in its area in Hungary. The survey included sociodemographic variables, lifetime and monthly prevalence of smoking, beliefs and attitudes related to substance use. Cross-tabulations and chi-square tests were used to test these relationships with SPSS MS 19.0 statistical program.

According to our results we did not find any strong relationships in life prevalence, but significant connection was revealed in case of the age of first cigarette smoking, daily amount of smoking. The smoking attitudes were not associated with genders. However, the different social beliefs and motivations had strong relationships with gender.

The high prevalence of smoking is the same in different gender groups, however we can identify some fields where there are differences between girls and boys, therefore we should pay attention to these relationships during planning prevention and health promotion programs, to reduce more effectively the high level of smoking among adolescents.

I/3. COMPARATIVE STUDY OF FAMILY STRUCTURE OF ASTHMATIC AND PANIC DISORDER YOUNG PEOPLE

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Keywords: Asthma, panic disorder, psychosomatics, Family Structure Test (FAST), Lazarus's Coping Modes Questionnaire

Introduction: Asthma history can often be detected in panic disorder. In this research I sought to reveal family structure and dynamics of asthmatic and panic disorder young people. I wanted to identify the differences which may help to provide more efficient therapy for these individuals. My hypothesis is that lower cohesion and higher hierarchy lie in the background as the sources of anxiety problems. I thought that different kinds of coping strategies are used in asthma and panic disorder.

Methods: Family Structure Test (FAST) and Lazarus's Coping Modes Questionnaire were used in my investigation.

Results: Based on the results, a more inflexible family structure was revealed in

both illness groups. Although I found a nearly stable family structure in the asthmatic group, this was not true for patients with panic. Members of the latter group more often used projective strategies by coping and wished to change their lifestyle from the present one. Problem focused coping rather characterized healthy individuals. Patients with panic used more action motivated by emotion than other groups ($p=0.045$). The adaptation factor of emotional coping was high in panic disorder compared with healthy people ($p=0.024$) and the distancing factor showed the same image in the latter group compared to asthmatic persons.

Conclusion: In summary, it appears that cognition was changed in panic disorder and these people preferred suppression rather than projection and the dynamics of their breathing was synchronized with this emotional movement. Some factors of emotional coping also seem to be significant to predict the epidemiology of diseases.

I/4. OBJECT USE IN AUTISM SPECTRUM DISORDER

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Keywords: object use, play activities, sensory profil, autism, cognitive capacity

Introduction: Organism and its environment make inseparable pair. Autism is a pervasive developmental disorder. There are more difficulties in the next three areas: (1) frequency of spontaneous play (2) frequency of imaginative play (3) frequency and complexity of symbolic sequences (Volkmar, Paul, Klin, & Cohen, 2005). In our research our goal was to know how children select the right informations for learning and use objects during their movements. Piaget already demonstrated that play is obviously related to the development of cognitive capacity. In our investigation we focused primarily on similarities and differences in object use and play performance in autism and typical development.

Methods: We used Sensory Status Questionnaire and head cameras in our

research to explore sensory profil and cognitive processes in autism and typical development.

Results: Our results support that sensory environment is very important for autistic people (Bogdashina, 2003). Children choose objects based on their sensory profil, needs, motivations and abilities. Using dynamic representations seems to be more difficult for autistic people than children with typical development.

Conclusion: Effect of atypical perception seems to be very important in terms of object use and play activities. In our further investigations we would also like to explore the development of dynamic representational skills in autism and typical development. In this case results would have a significant impact both on early treatment and intervention.

I/5. RATES OF MEDICAL FEARS IN PRESCHOOL AGES

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Keywords: medical fears, medical anxiety, preschool, pediatrics, Teddy Bear Hospital

Introduction: Almost every 10th adult has fear of needles or dentists. These adults typically avoid vaccination, blood donation, and visiting doctors. Generally this kind of medical anxiety begins in preschool ages, since children under 6 meet GPs most frequently. The aim of our study is assessing the rates of medical fears among preschool children. Our study was performed in Szeged.

Methods: The study population is comprised of 248 preschool children (average age: 5.5 years, 45% girl, 55% boy). Assessment included Visual Analog Scale (VAS), Picture Test (PT), and Drawing Investigation (DI) about medical fears. Children were investigated individually in their kindergarten.

Results: The performed VAS and PT showed that 10-34% of the participants fear from doctors, and 57-60 % from needles. During the drawing analysis, we found that 11-21%

of participants have fear of doctors, 31-34% of medical environment, 25-28% have fear because the lack of information, and 14-15% of them have severe fears of pain.

Conclusions: Medical anxiety presents in preschool ages frequently. Based on our findings reduction of medical fears is essential in kindergartens of Szeged. Therefore, medical students run a program which helps to reduce medical fears of children. The name of this program is "Teddy Bear Hospital".

J. Internal medicine and Family medicine session

J/1. THE EFFECTS OF THE OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS) ON BONE METABOLIC PARAMETERS

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Keywords: OSAS, BMD, bone fractures, metabolic disease

Introduction: The prevalence of the OSAS among Hungarians is between 2-4% and it has been associated with metabolic diseases, hypertension, type 2 diabetes mellitus and hyperlipidaemia. The aim of our study was to compare the bone metabolic parameters of male patients suffering from metabolic diseases with or without OSAS in order to answer the question whether the presence of OSAS has an effect on bone mineral density (BMD) and bone fragility.

Methods: Age-matched 68 male patients with metabolic diseases with OSAS and without OSAS (mean age: 54.9 vs. 56.2 years) were evaluated. To evaluate OSAS we used "Berlin Sleepiness Scale" and "Epworth Sleepiness Scale". Patients identified by these tests were sent to sleep laboratory for further examination and confirmation of diagnosis. BMD and prevalence of bone fractures were measured.

Results: The BMD, measured at the left femoral neck and lumbar spine was lower in patients with OSAS than in patients without OSAS (femoral neck: Z-sc: -1.07 ± 0.11 vs. -0.61 ± 0.1 $p < 0.05$ and T-sc: -2.45 ± 0.16 vs. -1.98 ± 0.15 , lumbar spine: Z-sc: -1.11 ± 0.15 vs. -0.48 ± 0.15 , $p < 0.05$ and T-sc: -2.53 ± 0.20 vs. -1.91 ± 0.20 , $p < 0.05$). Also the prevalence of the bone fractures was higher among patients with OSAS than in patients without it (35% vs. 20%).

Conclusion: Screening OSAS and starting its treatment in time not only lowers the frequency and severity of the metabolic diseases and bone fractures but it also increases the quality of life.

J/2. GENETIC DEFICIENCY OF THE LEUKOCYTE INTEGRIN MAC-1 AGGRAVATES ADIPOSE TISSUE INFLAMMATION, OBESITY AND INSULIN RESISTANCE IN MICE

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Keywords: Mac-1, Metabolic Syndrome, Inflammation, Diet-induced Obesity, Insulin Resistance

Background: The metabolic syndrome is driven by the continuous infiltration of inflammatory cells in adipose tissue. The leukocyte integrin Mac-1 ($\alpha M\beta 2$) is a classical adhesion factor critically regulating leukocyte recruitment. Here, we test the hypothesis that genetic deficiency for Mac-1 modulates the metabolic syndrome in mice. **Methods and Results:** To induce the metabolic syndrome, C57Bl6/J mice

genetically deficient (Mac-/-) or competent for Mac-1 (WT) were fed a high fat diet for 20 weeks ($n > 20$ per group). Surprisingly, Mac-1 deficiency did not protect from diet-induced obesity (DIO), but did significantly increase diet-induced weight gain during the late stages of the feeding period. Accordingly, fasting blood glucose levels were elevated in Mac-1-/- mice at the end of the studies. Also, intraperitoneal insulin tolerance (ITT) and hyperinsulinemic-euglycemic clamp analysis revealed worsened muscle insulin sensitivity in these mice. While Mac-1 deficient mice showed decreased peripheral leukocyte counts, circulating inflammatory monocytes as marker for systemic inflammation were highly elevated. Correspondingly, accumulation of pro-inflammatory CD8+ T-cells and inflammatory CD11c+ M1-macrophages as quantified by flow cytometry were increased in adipose tissue, while circulating pro-inflammatory cytokine levels were not affected.

Conclusions: We present the surprising finding that genetic abrogation of the pro-inflammatory leukocyte integrin Mac-1 aggravates adipose tissue inflammation, diet-induced obesity and insulin resistance in a mouse model of the metabolic syndrome. These findings point towards a differential role for Mac-1 in specific inflammatory pathologies.

J/3. ASSESSMENT OF VENTRICULAR REPOLARIZATION IN PATIENTS WITH POLYCYSTIC OVARIAN SYNDROME

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Keywords: ventricular repolarization, polycystic ovarian syndrome

Introduction: The aim of the present study was to evaluate the possible alterations of repolarization characterized by conventional ECG parameters in PCOS.

Methods: 25 PCOS patients (age: 30.8 ± 1.0 years, BMI: 32.3 ± 1.8 kg/m², blood glucose: 4.7 ± 0.1 mmol/l, HbA1c: $5.6 \pm 0.1\%$, serum insulin: 15.4 ± 2.8 mU/l, HOMA-IR: 3.3 ± 0.6 ;

mean $\pm$ SEM) and 25 healthy controls (age: 30.8 $\pm$ 2.0 years, BMI: 22.9 $\pm$ 0.7 kg/m², blood glucose: 4.6 $\pm$ 0.1 mmol/l, HbA1c: 5.4 $\pm$ 0.1%, serum insulin: 8.2 $\pm$ 1.2 mU/l, HOMA-IR: 1.7 $\pm$ 0.3; mean $\pm$ SEM) were enrolled into the study. ECGs were recorded, then analyzed off-line using SPEL Advanced Haemosys system (Experimetria Ltd.). The ventricular repolarization was characterized by uncorrected QT-interval and QT intervals corrected by Bazett, Fridericia and Hodges formulas. The spatial repolarization inhomogeneity was specified by QT dispersion (QTd). Short-term temporal QT-interval variability (QTV) was also determined. Autonomic function was assessed by means of five standard cardiovascular reflex tests.

Results: QT interval and in the different manner corrected QTc intervals revealed significant shortening in PCOS compared to the control group. Comparison of the two groups shown no difference in the QTd. The QTV, however, was enhanced in the PCOS patients relative to those for the control group. The results of the autonomic reflex tests were similar in the both groups.

Conclusion: In polycystic ovarian syndrome the homogenous shortening of QT interval was detected. This shortening was not associated with any alterations in the QT dispersion. The change of repolarization time may reflect the effect of the higher testosterone level characteristic in PCOS. The increased short-term QT-variability may be indicative of attenuated repolarization reserve.

J/4. NEUTROPHIL ACTIVATION IN THROMBOTIC THROMBOCYTOPENIC PURPURA

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Keywords: neutrophil activation; neutrophil elastase; thrombotic thrombocytopenic purpura; complement activation; haemolysis

Introduction: Previously, the role of neutrophil elastase (PMNE) was examined in the animal model of thrombotic microangiopathy (TMA). The data indicated that PMNE was essential for the development of thrombosis in the vessels of the kidney. Moreover, the connection between inflammation and thrombosis was also shown in the above mentioned model.

Earlier our group described that complement activation is present in acute thrombotic thrombocytopenic purpura (TTP). The aim of our research was to investigate neutrophil activation (we choose elastase as biomarker) and relation to complement activation in the pathomechanism of TTP.

Methods: 37 TTP patients (mean age: 41 $\pm$ 13, 30 woman) and 19 healthy controls (mean age: 35 $\pm$ 18, 13 woman) were involved in our study. TTP was diagnosed in case of low platelet number, intravascular haemolysis and presence of fragmentocytes. ELISA was used to measure the PMNe/ α -1 proteinase inhibitor complex and complement activation product Bb. For the statistical analysis non parametric tests were applied.

Results: We observed that PMNe levels were significantly higher in acute TTP (1.1 ng/mL, interquartile range 0.67-2.59) than in remission (0.56, 0.48-0.84) or in controls (0.50, 0.35-0.56; p<0.0001). We observed positive correlation between activation of neutrophils (PMNe/absolute neutrophil number) and complement activation (Bb, r=0.7, p=0.008), and inverse correlation between neutrophil activation and haemolysis.

Conclusion: Neutrophil activation is increased in acute TTP and shows correlation with haemolysis and complement activation. Our results suggests that neutrophil activation may play an important role in the pathogenesis of TTP.

J/5. COLLATERAL CIRCULATION OF THE RAT LOWER LIMB AND ITS SIGNIFICANCE IN ISCHEMIA-REPERFUSION STUDIES

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Keywords: ischemia, reperfusion, injury, rat, collateral

Introduction: Rats are the most commonly used experimental animal models for studies of human lower limb ischemia-reperfusion injuries. Ischemia performed by artery clamping causes a milder injury than the application of tourniquet. The explanation lies within the collateral circulation. The aim of this study was the examination of the collateral system and its physiological significance.

Methods: Male Wistar rats (n=20) were randomized into two groups: ischemia induced by clamping the infrarenal aorta (A1) and by the placement of a rubber tourniquet around the lower limbs at the level of the common femoral artery (A2). Following 3 hours of ischemia and 4 hours of reperfusion, blood and muscle histological samples were taken. Measurement of necroenzymes (CK, LDH) and serum potassium levels, muscle fiber viability and histological examinations were performed. Ten additional animals were injected with a resin mixture. The soft tissues were corroded with concentrated KOH solution, the corrosion casts were examined macroscopically.

Results: The differences between the CK levels measured in both examined groups (A1: 822±140; A2: 3567±318) are significant (p<0.01), as well as the LDH levels (A1: 1075±144; A2: 2213±928) (p<0.05). The viability assay confirms the results mentioned above. The corrosion casts showed anastomoses between 8 different arterial systems capable of supplying the lower limb.

Conclusions: The rats' lower limbs have a rich collateral system, through which the residual perfusion is ensured in case of iliac

artery/infrarenal aorta ligation. The results obtained using artery ligation do not refer to a real anoxic, but rather to a hypoperfused condition. We emphasise the importance of these collaterals, therefore we recommend the application of tourniquet to perform absolute lower limb ischemia in rat experimental model.

K. Poster Session I.: Basic sciences

K/1. SYNTHESIS AND CHARACTERIZATION OF ORGAN SPECIFIC KINASE INHIBITORS

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Keywords: kinase inhibitor, Orantinib, targeting, lysozyme, kidney

Introduction: Our goal is to develop organ specific, Sunitinib analogue kinase inhibitor bioconjugates. We use proteins as carriers to which the active agent is coupled covalently, thus obtaining conjugates that follow the pharmacokinetics of the carrier proteins. Orantinib, is an excellent choice for this kind of targeting strategy due to it's carboxyl group which can be used for conjugation to lysine residues. We assume that after lysosomal degradation –the common degradation pathway for this type of drug-protein conjugates– the amino acid directly coupled to the active agent will remain attached, but the metabolite still can be active against kinases.

Methods: We determined the structure-activity relationships of Orantinib- ϵ -lysine against four different target kinases. We used local cross docking method performed by YASARA. We have determined the K_i value of Orantinib against Aurora A using IMAP-TAMRA technology. We synthesised the assumed metabolite Orantinib- ϵ -lysine, using liquid and solid phase synthesis methods.

Results: In the case of tyrosine kinases, the RMSD (Route Mean Square Deviation) analysis showed that Orantinib- ϵ -lysine was able to dock into the kinases' ATP pockets in a similar manner as Orantinib. In the case of Aurora A Orantinib- ϵ -lysine binds differently, which can be an explanation to the low binding affinity.

During the synthesis we could obtain high purity intermediates and final product.

Conclusion: We synthesised the assumed metabolite of an Orantinib-protein bioconjugate, Orantinib- ϵ -lysine. We proved in silico that Orantinib- ϵ -lysine can be an active metabolite. We are planning to use the synthesised molecule in a series of biochemical experiments to verify the in silico results.

K/2. REAL-TIME FRACTAL ANALYSIS: APPLICATION FOR CHARACTERIZING COMPLEXITY OF CEREBRAL HEMODYNAMICS DURING CARDIOPULMONARY BYPASS

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Keywords: fractal analysis, real-time, near-infrared spectroscopy, cardiopulmonary bypass

Introduction: Fractal analysis has become a standard tool in quantitative characterization of complex time series. The analysis has commonly been done offline with the signal being resident in memory in full length. Fractal analysis can be especially useful in clinical situations when a

measured physiological signal's complexity (autocorrelation) may shift to a pathological range calling for immediate attention. Our aim was to develop and test real-time algorithms which are capable of monitoring the autocorrelation of physiological processes obtained in vivo.

Methods: Fractal algorithms (Detrended Fluctuation Analysis and Signal Summation Conversion) were rendered real-time, both yielding Hurst-exponent (H), as a measure of scale-free autocorrelation. Precision, signal classification, numerical stability, memory usage and execution time were assessed in numerical experiments. Applicability of these algorithms were demonstrated on near-infrared spectroscopy (NIRS) signals obtained during open-heart surgery.

Results: Real-time analysis is more precise with a decreased need for memory and CPU. Signal classification has >95% precision with the exception of a narrow range around the 1/f boundary separating signal classes. Algorithms become numerically unstable on signals with low coefficient of variation or non-stationarity. Reliable in vivo monitoring of H requires a 5 minute update time. H increased significantly during extracorporeal circulation.

Conclusion: According to numerical tests, real-time algorithms use computational resources very efficiently. Numerical instability can be prevented by alternating signal class or subtracting moving average. Sampling frequency of NIRS, computing speed may limit the rate of H assessment. In summary, real-time fractal analysis may well prove a useful tool for clinical monitoring.

K/3. DISPARATE AGE-ASSOCIATED ALTERATIONS IN CORTICOTROPIN EFFECTS ON ENERGY HOMEOSTASIS

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Keywords: corticotropin-releasing factor, catabolic, energy metabolism, aging, rat

INTRODUCTION: In the background of obesity of the middle-aged and later

appearing anorexia, cachexia, complex age-related alterations in the anabolic and catabolic peptide systems are assumed. Our previous studies revealed well-defined age-related shifts in the responsiveness to a centrally applied melanocortin (MC) agonist. Catabolic mediators downstream of MCs include the corticotropin system. Coordinated catabolic actions of corticotropin-releasing factor (CRF) include anorexigenic and hypermetabolic components. In the present study age-related alterations in the responsiveness to centrally applied CRF were analyzed.

METHODS: The effects of a 7-day intracerebroventricular CRF infusion (0.3 µg/µl/h) were measured in various age-groups of male Wistar rats (3 months - young adult, 12 months - middle-aged, 18- and 24 months, aging and old). Core temperature (Tc), heart rate (HR) and spontaneous locomotor activity of freely moving animals were recorded in a biotelemetric system (MiniMitter). Food intake and body weight (BW) were measured daily.

RESULTS: CRF infusion suppressed BW in the young, aging and old rats, but failed to reduced it in middle-aged animals. Anorexigenic responses were especially pronounced in the oldest group. Hyperthermic effects (Tc) were detected in the youngest and oldest, HR increased in the middle-aged and older animals. Altogether, middle-aged rats exhibit the weakest, the oldest age-groups the strongest catabolic responsiveness to CRF.

CONCLUSION: Anorexigenic and hypermetabolic responses to CRF show non-parallel changes with aging. Thus, similarly to observations concerning the MC system, age-dependent and disparate shifts were demonstrated in the effects of corticotropins on energy metabolism. (Supported by OTKA PD-84241, PTE AOKKA-34039-02/2010), 34039/KA-OTKA/11-01.)

K/4. HYPERCHOLESTEROLEMIA-INDUCED OXIDATIVE/NITROSATIVE STRESS IN THE HEART: THE ROLE OF MICRORNA-25

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Keywords: microRNA-25, NADPH-oxidase 4, hypercholesterolemia, oxidative stress, nitrosative stress

Introduction: Hypercholesterolemia, an important risk factor of ischemic heart diseases, is associated with oxidative/nitrosative stress and consequent myocardial dysfunction in the heart. It has been shown recently that microRNAs played an essential role in various pathological conditions; however, their role in hypercholesterolemia remains unclear. We have shown previously that microRNA-25 is downregulated in the heart due to hypercholesterolemia. Our present aim was to investigate the role of microRNA-25 in hypercholesterolemia-induced myocardial oxidative/nitrosative stress.

Methods and Results: To induce hypercholesterolemia, male Wistar rats were fed with 2 w/w% cholesterol and 0.25 w/w% cholic acid for 12 weeks. Serum cholesterol level was significantly elevated (4.1 ± 0.6 vs. 2.9 ± 0.2 mM; $p < 0.05$) due to the cholesterol enriched diet as compared to the standard chow fed control group. Oxidative/nitrosative stress was significantly increased in the heart of hypercholesterolemic rats as assessed by dihydroethidium staining and nitrotyrosine ELISA (2.3 ± 0.3 vs. 1.3 ± 0.2 ng/mg; $p < 0.05$). NADPH-oxidase 4 (NOX4) was defined as a potential target of microRNA-25 by using microRNA target scan software. The expression of NOX4 was significantly increased in the heart of hypercholesterolemic rats as assessed by Western-blot analysis. To determine the causal role of microRNA-25 in hypercholesterolemia induced oxidative/nitrosative stress, neonatal primary rat cardiomyocyte cultures were transfected with a microRNA-25 antagonist. Oxidative stress was significantly increased by transfection with the microRNA-25 antagonist; however, the microRNA-25

antagonist-induced oxidative stress was attenuated by the non-selective NOX-inhibitor, diphenyleneiodonium.

Conclusion: Downregulation of microRNA-25 contributes to hypercholesterolemia-induced increase in oxidative/nitrosative stress by upregulating NOX4 in the heart.

K/5. THE ROLE OF MICROGLIAL FRACTALKINE SIGNALING IN MEDIATION OF STRESS RESPONSES

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Keywords: fractalkine, mice, microglia, hypoglycaemia, CRH

The chemokine fractalkine plays an important role in the migration of the immune cells and in cell-cell communication. Within the central nervous system neurons express fractalkine (CX3CL1) that activate specific receptor (CX3CR1) on the brain resident macrophages, microglia. CX3CR1 plays an important role in the communication between neurons and microglia. Microglia involved in the pathogenesis of several neuroinflammatory diseases, such as Alzheimer -, Parkinson diseases or macula degeneration, however their role in homeostatic regulation is just emerging.

The aim of our work was to address the role of neuron-microglia communication and especially the role of fractalkine signalling in central metabolic and stress regulation by using CX3CR1 receptor deficient transgenic mice. After 16 hours fasting insulin induced hypoglycaemia was used, as metabolic stressor to determine the differences between stress responses. The weight of the animals were monitored. Throughout the time course the blood glucose levels were measured. Insulin resulted hypoglycaemia only in the wild type mice, the receptor deficient mice had higher blood glucose values at every time point. Changes in the IL-1 mRNA level in the hypothalamus were followed by real time PCR. In the CX3CR1 deficient mice did not display elevated IL-1 mRNA levels as it was found in wild type

mice. Hypoglycaemia is a strong metabolic stressor, so corticotropin-releasing hormone (CRH) mRNA expression was measured in the hypothalamus samples by rtPCR. Fasting resulted decrease in the CRH mRNA level in the receptor deficient mice, while the level increased in both phenotype after hypoglycaemia.

Our results show that the fractalkine signalling and neuron-microglia crosstalk plays an important role in the neuroendocrine and metabolic regulation.

K/6. THE EFFECTS OF KV1.3 AND IKCA1 POTASSIUM CHANNEL INHIBITION ON CALCIUM INFLUX OF HUMAN PERIPHERAL T LYMPHOCYTES IN RHEUMATOID ARTHRITIS

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Keywords: rheumatoid arthritis, T-lymphocyte activation kinetics, novel immunomodulation, potassium channels, calcium influx

The transient increase of the cytoplasmic free calcium level plays a key role in the process of lymphocyte activation. Kv1.3 and IKCa1 potassium channels are important regulators of the maintenance of calcium influx and present a possible target for selective immunomodulation.

We took peripheral blood samples from 10 healthy individuals and 9 recently diagnosed RA patients. We registered the calcium influx kinetics of CD4, Th1, Th2 and CD8 cells, applying a novel flow cytometry approach. We also assessed the sensitivity of the above subsets to specific inhibition of the Kv1.3 and IKCa1 potassium channels. We measured the expression of Kv1.3 channel.

The peak of calcium influx in lymphocytes isolated from RA patients is reached more rapidly, indicating that they respond more quickly to stimulation than controls. In healthy individuals, the inhibition of the IKCa1 channel decreased calcium influx in Th2 and CD4 cells to a lower extent than in Th1 and CD8 cells. On the contrary, the

inhibition of Kv1.3 channels resulted in a larger decrease of calcium entry in Th2 and CD4 than in Th1 and CD8 cells. No difference was detected between the subsets in the sensitivity to IKCa1 channel inhibition among RA patients. However, during the specific inhibition of the Kv1.3 channels in RA, CD8 cells are inhibited the most dominantly.

The changes to the sensitivity of Kv1.3 channel inhibition seem to be unrelated to its altered expression.

The specific inhibitors of Kv1.3 channels seemed to be promising novel immunomodulators with improved specificity for autoreactive T cells.

L. Poster Session II.: Clinical sciences

L/1. THE USE OF ANTIFIBRINOLYTICS IN REDUCING POSTOPERATIVE BLOOD LOSS: APROTININ AND TRANEXAMIC ACID

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Keywords: aprotinin, tranexamic acid, antifibrinolytics, cardiopulmonary bypass (CPB), haemorrhagic complications

Introduction: Anti-haemorrhagic drugs are being used to prevent and treat surgical haemorrhagic complications or hemostaseologic disturbances. The serine-protease-inhibitor aprotinin, an antifibrinolytic agent, was used for decades until the BART-study revealed its unfavourable effects on mortality that led to its withdrawal from the market. Today, the lysine-analogue tranexamic acid (TA) is available for the clinical routine.

We compared the effects of aprotinin and TA on postoperative blood loss, hemodynamic, hemostaseologic and inflammatory parameters, using a canine model of cardiopulmonary bypass (CPB).

Methods: Control dogs received placebo, treated groups were given aprotinin or TA.

All animals received heparin and underwent 90min of CPB. After weaning from the heart-lung-machine, protamine was administered followed by 130min observation. Blood loss and coagulation parameters were determined regularly, hemodynamic parameters were monitored continuously. To assess the systemic inflammatory response induced by CPB, plasma levels of IL-6, IL-8 and TNF- α were determined by ELISA.

Results: Compared to controls, aprotinin significantly reduced blood loss (105 ± 22 ml vs. 41 ± 8 ml), while TA proved to be less effective (65 ± 16 ml). Examining hemodynamic and coagulation parameters, no significant difference was detected among the groups. The rise of proinflammatory cytokines during CPB was tendentially decreased by aprotinin, while a significant anti-inflammatory effect was observed in the TA group (TNF α 90min after starting CPB: 5.2 ± 1.2 ng/ml control vs. 3.7 ± 0.9 ng/ml aprotinin vs. 0.8 ± 0.3 ng/ml TA).

Conclusions: Compared to aprotinin, the clinically used TA exerts lower anti-haemorrhagic but stronger anti-inflammatory efficacy. Our work points out the need for development of novel pharmacological tools for effective and safe postoperative blood loss reduction.

L/2. EFFECTS OF PHARMACOLOGICAL ACTIVATION OF THE SOLUBLE GUANYLATE CYCLASE IN DIABETIC CARDIOMYOPATHY

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Keywords: cardiology, haemodynamics, diabetes, cGMP, cinaciguat

Introduction: Endothelial and cardiac dysfunction are major cardiovascular consequences of diabetes mellitus (DM), which are accompanied by altered nitric oxide (NO) - soluble guanylate cyclase (sGC) - cyclic guanosine monophosphate (cGMP) signaling. Cinaciguat, an activator of sGC has been developed and reported to effectively increase intracellular cGMP levels resulting in cardioprotective effects. We investigated

the effects of sGC-activation by cinaciguat in a rat model diabetic cardiomyopathy.

Methods: We induced type-1 DM in rats with intraperitoneal injection of streptozotocin. Rats were treated with placebo or 10mg/kg/day cinaciguat for 8 weeks. To assess cardiac function, we performed left ventricular (LV) pressure-volume analysis with a conductance microcatheter, and sensitive contractility parameters such as preload recruitable stroke work (PRSW) were calculated. In addition, immunohistochemical measurements were performed, and myocardial gene expressions were investigated by qRT-PCR

Results: Compared to healthy controls, we found significantly changed myocardial expression of atrial natriuretic factor (ANF), endothelial NO synthase and matrix metalloproteinases, and also observed elevated myocardial transforming growth factor- β (TGF- β) immunoreactivity in our diabetic rats. We also found decreased LV contractility (PRSW: 49.5 ± 3.3 vs. 83.0 ± 5.5 mmHg) and diastolic function (time constant of LV pressure decay, τ : 17.3 ± 0.8 vs. 10.3 ± 0.3 ms) in DM. Cinaciguat-treated diabetic rats showed significantly better systolic (PRSW: 66.8 ± 3.6 vs. 49.5 ± 3.3 mmHg) and diastolic (τ : 14.9 ± 0.6 vs. 17.3 ± 0.8 ms) function, and improved expression of ANF, matrix metalloproteinase-9 and TGF- β compared to untreated diabetic animals.

Conclusions: Cinaciguat prevents diabetes-associated deleterious myocardial changes and improves diabetic cardiac dysfunction in our rat model. Pharmacological sGC-activation might represent a novel therapy approach for diabetic cardiomyopathy.

L/3. NETWORK REMODELING OF INTRAMURAL CORONARY RESISTANCE ARTERIES IN THE AGED RAT

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Keywords: coronary, resistance arteries, network, aging, remodelling

INTRODUCTION: We wanted to analyse the statistical geometry of age induced remodeling of the left anterior descendent coronary resistance artery network in the rat.

METHODS: Eight rats, aging 3 months and 7 aged rats, 18 months old were included in this study. The animals were anesthetized, and the heart removed. Preparation of the whole left anterior descendent coronary artery network was made under the preparation microscope. The preparation process isolated the surface of all arterial segments down to about 80 μ m. Then the orifice was cannulated and the whole network was perfused. After equilibration while perfused and superfused with oxygenated saline, the videomicroscopic image of the network was recorded. Small and large magnification digitized photos (pixel sizes from 5.21 to 31.04 μ m) were selected for further analysis.

RESULTS: New population of vessel segments with larger diameter (>500 μ m) appeared in the older hearts. While 200-250 μ m segments are the most frequent in young networks that peak has been dislocated toward larger diameters (300-350 μ m) in the old ones. There was a characteristic reduction in the 200 μ m ring population (rarefaction) in the older hearts. The older small arteries were more tortuous. Both young and old networks have the tendency to keep the Murray law.

CONCLUSION: Significant alterations in the left anterior descendent coronary resistance artery network of the rat occurred during the process of aging as they could be revealed by us on in situ perfused whole networks.

L/4. EARLY-ONSET DYSTONIAS. DIAGNOSTIC AND THERAPEUTIC ASPECTS

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Keywords: neurodegeneration with brain iron accumulation, early dystonia, eye-of-the-tiger sign, deep brain stimulation

Background: Neurodegeneration with brain iron accumulation (NBIA) is a group of rare, progressive neurodegenerative disorders characterized by iron accumulation predominantly in the globus pallidus. To date, advances in radiologic and molecular genetic testing have allowed in vivo diagnosis based on the clinical presentation, radiological features on brain MRI and the underlying disease-causing gene. Early diagnosis will hopefully lead to the development of novel therapeutic strategies in the future to improve clinical treatment and quality of life of children with NBIA.

Methods: Clinical, neuroradiological and molecular investigations have been performed.

Results: We report a case of 5-year old girl who presented with severe dytonia. Her clinical history and actual status was suggestive of progressive neurodegeneration with brain iron accumulation. Brain MRI one year before showed isolated T2 hyperintensity within the globi pallidi. Presently, MRI revealed the typical eye-of-the-tiger sign that supported the clinical diagnosis of NBIA. Molecular genetic tests were carried out to confirm mutation of the panthotenate-kinase gene.

Conclusions: Prompt and accurate diagnosis of NBIA phenotypes requires recognition of key clinical phenotypic features, radiological diagnosis of high brain iron, and subsequent molecular genetic confirmation of the causative gene. The limited benefits of medical treatments have prompted early attempts with neurosurgical therapy. Deep brain stimulation seems to be effective in the treatment of early-onset dystonias.

L/5. ALCOHOL AND ADOLESCENTS – THE ROLE OF RURAL-URBAN DIFFERENCES AND THE COMMUTING STATUS

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Keywords: alcohol, adolescents, commuting status, rural-urban differences

The alcohol consumption and alcohol related health problems are serious public health concerns all over the world. Adolescence is a critical period from the viewpoints of problem behaviours, such as alcohol abuse. Alcohol consumption can be influenced by several risk factors, such as social factors, the environment, and the place where the adolescent lives. Therefore the purpose of the present study was to obtain different effects of rural-urban differences and the commuting status.

Our sample is consisted of 2072 students from elementary and secondary schools. The study was performed in Mako and the villages in its area in Hungary. The survey included sociodemographic variables, lifetime and monthly prevalence of drinking, beliefs and attitudes related to substance use. Cross-tabulations and chi-square tests were used to test these relationships with SPSS MS 19.0 statistical program.

We found strong relationship between alcohol drinking and the commuting status and type of residency both in case of monthly prevalence, daily amount of alcohol and other factors of alcohol consumption.

The place where the target population live is an essential factor which should be paid attention during planning interventions. The lower parental control maybe a major risk factor, therefore in terms of it we could identify some highly risked subpopulations among adolescents, such as dormitory pupils. Mapping of risk factors can provide a better chance to reduce the high level of alcohol consumption among youth.

L/6. THE IMPORTANCE OF TRANSMETHYLATION IN ALCOHOL CONSUMPTION

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Keywords: transmethylation, wine, resveratrol, alcohol, redox homeostasis

Studies all around the world prove that a glass of wine is cardioprotective. On the other hand, red wine consumption can disturb metal ion composition and the growth factor pattern in blood.

The aim was to study the reason of altered effect of excessive red wine consumption, and therefore transmethylation processes were examined in vitro and in vivo in rats.

In the in vitro study the concentration dependence was carried out between trans-resveratrol and formaldehyde, and after incubation time dimedone was given to the system, and formaldemeton was detected by OPLC.

In the animal-study male Wistar rats were treated partly Egri Cuvée (N=5) (10.5 % V/V ethanol) partly equivalent alcohol (N=5) for 10 days with appropriate control animals (N=5).

Routine laboratory parameters (ALP, ALT, TBIL, CHOL) were measured by Hitachi modular Equipment. The redox parameters were determined by chemiluminescent and spectrophotometric methods and transmethylation was measured by OPTLC.

Transmethylation is an intracellular modifier and regulator mechanism that is carried out by bound formaldehyde.

Studies showed a linkage between transmethylation ability and antioxidant defense mechanism, in which resveratrol had a significant role.

M. Good morning and breakfast Session:

State-of-the-Art Session

M/1 RISK ASSESSMENT IN NONALCOHOLIC FATTY LIVER DISEASE

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Keywords: nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, fibrosis, cirrhosis, hepatocellular carcinoma

Nonalcoholic fatty liver disease (NAFLD) is the hepatic manifestation of the metabolic syndrome, a constellation of medical disorders characterized by visceral obesity, insulin resistance, hyperlipidemia, and endothelial dysfunction. Mirroring the recent and dramatic growth in the prevalence of obesity and associated adverse health effects, NAFLD has become exceedingly common, affecting up to one-third of the general adult population in industrialized countries and becoming increasingly diagnosed in other parts of the world.

NAFLD is identified as non-progressive hepatic fat accumulation (steatosis) in about 80% of the cases, but it presents as steatohepatitis in the remaining 20% with evidence of cell injury, inflammation, and variable degree of fibrosis with considerable propensity (~20%) to advance into cirrhosis. NAFLD has also been linked to increased cardiovascular morbidity. In addition, NAFLD may also evolve into hepatocellular carcinoma (HCC), a malignancy with poor overall outcomes. NAFLD often coexists and may synergize with other risk factors of HCC such as chronic hepatitis C and alcoholic liver injury. Importantly, over one-third of HCC cases reported in NAFLD have been diagnosed in noncirrhotic livers, greatly expanding the pool of individuals potentially at increased risk for cancer and indicating the need for improved risk assessment.

The role of noninvasive panels based on

clinical, laboratory, and imaging biomarkers in distinguishing steatosis and steatohepatitis in the absence and presence of liver fibrosis and the prediction of risk for HCC by these and other emerging methodologies will be discussed.

Multidisciplinary Session V.:

N. Cardiology Session

M/1 CHARACTERISATION OF HUMAN EMBRYONIC STEM CELL-DERIVED ENDOTHELIAL CELLS: KEY FOR VASCULAR REGENERATION?

Edit Gara, Zsuzsanna Lendvai, Judit Skopál, Zsolt Bagyura, Tamás Németh, Annamária Kosztin, Béla Merkely, Gábor Földes

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Keywords: stem cell, endothelial cell, vascular regeneration

Introduction: Cardiovascular derivatives of stem cells are promising candidates for future tissue replacement therapy, disease modelling and drug testing. In our study we focused on human embryonic stem cell (hESC) -derived endothelial cells (hESC-ECs).

Aim: The aim of this study was to develop hESC-ECs in vitro, to characterize their phenotype by gene expression profile and immunoreactive endothelial markers. We studied the viability, survival and function of hESC-ECs in vivo and characterized the re-implanted cells and their angiogenic profile.

Methods: In our experiments undifferentiated H7 human embryonic stem cells were differentiated into mesoderm, endothelial line. After two weeks CD31-positive cells were separated from the differentiating culture using magnetic activated cell sorting method. The hESC-ECs were transplanted subcutaneously into 3 months old athymic nude rats - using Matrigel extracellular matrix as a scaffold.

Results: hESC-ECs are positive for CD31, vWF, ve-cadherin immunocytochemistry staining, they form capillary-like tubules on Matrigel, and take up acetylated-low density

lipoprotein. As assessed by real-time quantitative PCR, hESC-ECs express endothelial genes. Both arterial (EphrinB2, Notch1-2) and venous (EphB4, FLT4) markers are abundantly expressed. Human umbilical vein endothelial-cells (HUVEC) were analysed as positive endothelial control. Two weeks after the implantation, immunohistochemistry proved that hESC-ECs form capillary-like structure in vivo. After re-isolated from rats, hESC-ECs remain viable in culture. The mRNA levels of angiogenic genes are increased during the engraftment (Angiopoietin2/GAPDH mRNA levels: preimplantation: 1 ± 0.11 , postimplantation 86.23 ± 26.34 ; Apelin/GAPDH mRNA levels: preimplantation: 1 ± 0.05 , postimplantation: 1197.42 ± 703.75 , $n=5$, $p<0.05$).

Conclusion: Our results proved that hESC-ECs show endothelial characteristics in vitro. They form capillary-like structures and may support angiogenesis in vivo. The separation of arterial and venous subpopulation of hESC-ECs warrants further investigations. Human embryonic stem cell-derived endothelial cells and other hESC-derived cardiac tissue cells can be a promising future therapeutic, drug testing and diseases modelling option in the cardiovascular field.

N/2 MICROEMBOLIC SIGNAL DETECTION DURING DIFFERENT LEFT ATRIAL ABLATION TECHNIQUES FOR ATRIAL ABLATION TECHNIQUES FOR ATRIAL FIBRILLATION. RELATIONSHIP WITH POSTOPERATIVE COGNITIVE FUNCTION

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Keywords: atrial fibrillation, catheter ablation, doppler ultrasound, microparticles, cognitive function

Background: Clinically silent cerebral ischemia (SCI) has been recently demonstrated on diffusion MRI after pulmonary vein isolation (PVI). Although the clinical relevance of these brain lesions

is unknown, they raise a new concern regarding the safety of the procedure. The occurrence of these lesions has been shown to correlate with the ablation technology used: phased radiofrequency (RF) ablation has been associated with the highest, while cryoablation with the lowest incidence of SCI. We compared the occurrence of bubble formation seen on intracardiac echocardiography (ICE) and microembolic signals (MES) detected by transcranial Doppler using these two ablation techniques and the longer-term effects of the procedures on cognitive function.

Methods: 26 procedures in 25 patients (age: 51 ± 13 years; female:male 5:20) undergoing PVI for paroxysmal or persistent AF were assigned to 3 different treatment groups: I: cryoballoon (CRYO) ablation and conventional intraprocedural anticoagulation regime with target ACT > 250 sec (7 procedures); II: ablation using multipolar duty-cycled radiofrequency (RF) catheters (PVAC) with target ACT > 250 sec (12 procedures); III: ablation with PVAC catheter using a more aggressive anticoagulation protocol with ACT > 350 sec (7 procedures). Bubble formation (few, moderate, shower) was assessed on ICE and the number of MES was detected in both middle cerebral arteries using TCD with the ability to discriminate between solid and gaseous emboli. A battery of neuropsychologic tests were also performed in these patients and in six controls with AF but no intervention at baseline and 6 weeks postablation.

Results: Strong correlation ($r = 0.89$) was found between the degree of bubble formation on ICE and the number of MES in all groups. PVAC ablation is associated with significantly more MES even when a more aggressive anticoagulation is applied. Most of MES are gaseous in nature with both techniques. Clinical stroke/TIA did not occur in any patient. No significant changes in neuropsychologic tests were found in the 3 ablation groups when compared to control patients. ($p = 0.8$).

Conclusions: Duty-cycled RF ablation is associated with significantly more MES even when a more aggressive anticoagulation is applied. Most of MES are gaseous in nature with both techniques. PVI has no short-term

effect on cognitive function regardless the ablation technology used.

N/3 PATIENTS WITH HEART FAILURE DISEASE ARE TREATED WITH RESYNCHRONISATION THERAPY FOLLOWED BY ECHOCARDIOGRAPHY

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Keywords: heart failure, echocardiography, resynchronisation therapy, reverse remodeling

The systolic heart failure (HF) is a chronic disease with various etiologies. The decrease of systolic heart function is in the background of symptoms. During the standard pharmacological treatment of HF there is another important part of it this is cardiac resynchronization therapy (CRT). The main part of CRT is synchronize the asynchronous movements of left ventricular (LV) with biventricular pace maker. The efficiency of this treatment is characterized by the increase of ejection fraction (EF).

The aim of our prospective study is follow patients with echocardiography who have received in CRT therapy and examine the reverse remodeling in these patients. 54 patients with HF had been selected till now. After 6 weeks we found expressive improvement in LV systolic (54.89 ± 1.239 vs 50.78 ± 1.57 mm, ns.), diastolic (65.76 ± 1.265 vs 64.11 ± 1.287 mm, ns.) diameters and the index of ventricular myocardial contraction dP/dT (586.6 ± 31.55 vs 803.3 ± 55.90 Hgmm/s, ns.). On the second time 3 month later we saw significant improvement considering starting-point. (systolic diameter: 54.89 ± 1.24 vs 46.95 ± 2.39 mm, $p = 0.0022$; diastolic diameter: 65.76 ± 1.27 vs 59.25 ± 2.81 mm, $p = 0.0180$; dP/dT: 586.6 ± 31.55 vs 1052 ± 143.5 Hgmm/s, $p = 0.0157$). In EF we saw significant improvement after 6 weeks (28.44 ± 0.65 vs 34.00 ± 1.30 %, $p = 0.0003$) and has been showed much more expressed increasing after 3 month (28.44 ± 0.65 vs 36.10 ± 1.74 %, $p = 0.0004$).

Our results provide supporting evidence that CRT made also morphologic and functional changes in the LV. The good

effects of the therapy are appeared in a few months later and caused tangible improvement in patients' quality of life.

N/4 INHIBITION OF $\text{Na}^+/\text{Ca}^{2+}$ EXCHANGER REDUCES THE ARRHYTHMOGENIC CONSEQUENCES OF THE INCREASED LATE Na^+ CURRENT

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Keywords: action potential, Ca^{2+} transient, Ca^{2+} overload, sodium current, NCX

Introduction: Excessive increase in late Na^+ -current (INaL) often leads to cardiac arrhythmias by prolonging the action potential duration (APD) or by causing $[\text{Ca}^{2+}]_i$ overload. The $\text{Na}^+/\text{Ca}^{2+}$ -exchanger (NCX) has been suggested to participate in this process: rise in Na^+ influx increases the reverse activity of NCX, thus concomitant Ca^{2+} influx occurs which can lead to arrhythmogenesis. Therefore, the primary aim of this study was to investigate the interrelationship between INaL, and INCX by elucidating the effect of partial NCX inhibition on Na^+ -induced Ca^{2+} -overload.

Methods: Action potentials were recorded using conventional microelectrode technique on canine ventricular papillary muscles. Ionic currents (INa, INCX) were determined using patch clamp technique and $[\text{Ca}^{2+}]_i$ shifts were monitored by a Ca^{2+} sensitive fluorescent dye on isolated canine ventricular cells. We use ATX or veratrine as INa activator and SEA0400 as a selective NCX blocker.

Results: 2 nM ATX markedly increased the INaL and the magnitude of the Ca^{2+} transient and considerably prolonged the APD. 1 μM SEA0400 significantly inhibited the NCX current without shortening the APD or decreasing the Ca^{2+} transient. When INaL was activated with ATX, the reverse NCX current was also increased. Application of SEA0400 prevented the coupled

enhancement of the NCX current. 1 μM SEA0400 considerably restricted the ATX-induced increase of the Ca^{2+} transient, but cannot reversed the APD prolongation.

Conclusions: The interaction between INaL and INCX can be attenuated by selective NCX inhibition, therefore it may be a promising therapeutic perspective against cardiac arrhythmias by restricting Na^+ -induced Ca^{2+} load.

N/5 GENETIC AND ENVIRONMENTAL INFLUENCES ON CARDIOMETABOLIC RISK FACTORS: A TWIN STUDY

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Keywords: prevention, twin study, cardiometabolic risk, metabolic syndrome, heritability

Introduction: Both genetic and environmental factors may play role in the pathogenesis of type 2 diabetes and cardiovascular diseases. The magnitude of genetic and environmental influences may vary in different populations.

Objectives: Fourteen different risk factors were simultaneously assessed in monozygotic (MZ) and dizygotic (DZ) adult twin pairs without diabetes and known cardiovascular diseases in order to determine the genetic and environmental influences on cardiometabolic risk factors.

Methods: A total of 101 (63 MZ and 38 DZ) adult twin pairs (n=202; mean age: 44.3±15.8 years) was investigated. Past medical history was recorded and physical examination was carried out. Fasting venous blood samples were taken for measuring laboratory parameters. For assessing heritability, the structural equation (A-C-E) model was used.

Results: The following risk factors proved to be highly or moderately heritable: weight (88.1%), waist circumference (71.0%), systolic blood pressure (57.1%), diastolic blood pressure (57.7%), serum creatinine (64.1%), fibrinogen (59.9%), and hsCRP

(51.9%). On the contrary, shared and unique environmental influences had the highest proportion of total phenotypic variance in serum total cholesterol (46.8 and 53.2%), serum HDL-cholesterol (58.1 and 14.9%), triglycerides (0.0 and 55.9%), fasting blood glucose (57.1 and 42.9%), fasting plasma insulin (45.4 and 54.5%), serum uric acid (46.0 and 31.3%), and serum homocysteine (71.8 and 28.2%).

Conclusion: Our study suggested that genetic and environmental factors have different magnitude of influence on cardiometabolic risk factors. The better understanding of genetic and environmental contribution to certain cardiometabolic risk factors could play an important role in designing prevention and treatment strategies.

Special Focus Session

O. Neuroimaging session

O/1 IS YOUR BRAIN SIMILAR TO THE FACEBOOK? VISUALIZATION AND MATHEMATICAL ANALYSIS OF STRUCTURAL AND FUNCTIONAL BRAIN NETWORKS.

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Keywords: functional MR imaging, diffusion tensor imaging, neuroimaging, MRI, brain

The quest to study the connectional anatomy of the brain was recently re-electrified by emerging in vivo neuroimaging technologies like diffusion tensor imaging or resting state functional MRI. Diffusion tensor MRI allows performing probabilistic tractography - an approach that visualizes virtual brain pathways and furthermore helps to elucidate the structural connectome of the human brain. Functional MRI is able to uncover widespread hemodynamic

fluctuations in the brain during rest, this technique is called resting state fMRI or r-fMRI. The time course of signal intensity fluctuations in specific frequency domains show characteristic synchrony across the brain; this is the backbone of functional connectivity hypotheses.

This new type of “brain-mapping” endeavor aims to provide novel mathematical models that describe the specific patterns of interconnections between gross brain areas in normal and pathological scenarios. One practical approach is to image the brain networks as mathematical graphs and then to perform classical analyses describing how the information can travel across the elements of the graphs. The truly quantitative output of these studies is often correlated with biomarkers describing the normal human cognition and behavior.

In our talk, we give a short review about the theoretical background and also provide a showcase of interesting achievements in connectome mapping. Moreover, we exemplify the graph theoretical representation of the human connectome with an in-house developed tool with special focus on the following topics: (1) networks in high-level functioning autistic adults, (2) general correlates of intelligence, (3) analysis of the structural and functional networks of the human thalamus.

O/2 NEUROSONOLOGY

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Keywords: brain, ultrasound, tcd, tcdd, duplex

Transcranial Doppler (TCD) is called the “doctor’s stethoscope for the brain,” and the use of TCD with portable carotid and vertebral duplex scanning provides structural and physiologic imaging extension of the neurologic examination. Ultrasound expands the ability of clinicians to detect, localize, and quantify disease and to evaluate hemodynamic responses, thus providing tools for a neurovascular examination at bedside.

TCD is noninvasive, safe, and cost-effective bedside test for evaluating cerebrovascular circulation in real time. TCD shows the

spectral flow waveforms, blood flow direction, velocities, and intensity in the intracerebral vessels, adding physiologic information to the anatomic images obtained with other imaging modalities. TCD also can detect collaterals through the ophthalmic, anterior communicating, and posterior communicating arteries caused by hemodynamically significant carotid stenosis or vertebrobasilar lesions. TCD remains the only method for detecting in real time embolization of the cerebral vessels and even more. TCD provides essential, real-time, hemodynamic information about intracranial circulation that is complementary to other static brain-imaging modalities.

O/3 GENETIC INFLUENCES ON CEREBROVASCULAR HEMODYNAMICS

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Keywords: heritability, environment, twin study

To assess the contribution of additive genetic, shared and non-shared environmental factors to variation in middle cerebral artery (MCA) mean flow velocities (MFV) and pulsatility indices (PI) and to investigate a possible association between MFV and PI with arterial stiffness. One-hundred and sixtythree (163) Italian and American twin pairs [86 monozygotic and 77 dizygotic, 53±13 years, mean±standard deviation] underwent transcranial Doppler sonography of the MCA. Brachial and aortic augmentation index (Aix_{bra} , Aix_{ao}), aortic pulse wave velocity (PWV_{ao}) were measured by TensioMed Arteriograph. Heritability of left and right MFV was 34.7% (95% confidence interval, CI, 0.1 to 75.2%) and 28.1% (95% CI, 2.5 to 59.7%). Shared environmental factors explained the largest variance of MFV (left: 50.5%, 95% CI, 20.5 to 73.3%; right: 39.1%, 95% CI, 0.0 to 67.8%). No genetic contribution was found, and a CE model best fitted the twin correlations for PI. Unique environmental factors explained 54.9% of right PI (95% CI, 42.4 to 70.2%) and 66.6% of left PI (95% CI, 46.3 to 87.6%), while shared environmental factors determined the remaining variance in PI. No significant negative correlations were found between bilateral MFV, PI and the following parameters: Aix_{bra} , Aix_{ao} , and PWV_{ao} (correlation between MFV and arterial stiffness indicated $-0.346 > r > -0.278$; $p < 0.001$ without age-adjustment). Shared and unshared

environmental factors influenced both MFV and PI, while genetic factors played a moderate role in determining MFV. No association was found between systemic arterial stiffness and cerebral hemodynamic variables.

O/4 WHAT KIND OF MESSAGES BEAR MUMMIES? - A MULTIDISCIPLINARY APPROACH TO UNDERCOVER A PIECE OF ANCIENT EGYPT

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Keywords: mummies, CT, histology, electronmicroscopy, molecular biology

The two mummies of Déri Museum, Debrecen had a barely known history. Till now we were aware about only the last 120 years, when Franz Ferdinand, prince of the Austro-Hungarian Monarchy received and after Frigyes Déri bought them. The earlier history of these humans has been uncovered thanks to the scientific methods of the 21st century.

Whole body CT scans and 3D reconstructions, conventional histology and electronmicroscopic examinations of the bone and molecular biology methods were performed in addition to the historical background. This multidisciplinary project clearly demonstrates the necessity of the tight cooperation of the diagnostic specialists - that is not only important to explore ancient cultures and habits, but important in an everyday healthcare practice manner, too.

The mummies guide us to an ancient world and to an up-to-date workflow of diagnostic professionals.

O/5 ADVANCE IMAGING OF BRAIN TUMORS

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The introduction of MRI into clinical practice has been among the most important of all advances in the care of

Patient's with brain tumors. The role of neuro-imaging is no longer a tool to simply evaluate structural abnormalities and identify tumor-related complications but has evolved into a science that incorporates functional, hemodynamic, metabolic, cellular, and cytoarchitectural alterations. Where previously, pathological and anatomical imaging has offered information about histologic diagnosis, past imaging has never incorporated information about the actual

Biological behavior of these neoplasms. Today, there is a multitude of new imaging techniques that have

Revolutionized neuro-oncologic imaging. Neuro-imaging of brain tumors can be divided in four broad categories:

1. Tumor diagnosis.
2. Preoperative treatment planning.
3. Intraoperative imaging.
4. Postoperative care and treatment response.

The current standard of neuro-imaging for brain tumor evaluation is anatomical magnetic resonance imaging (MRI) with gadolinium-based intravenous contrast agent, providing highly sensitive tumor detection and characterization, far superior than any other imaging modality. MRI has been found more sensitive than CT in the detection of asymptomatic progression. However, MRI suffers from non-specificity when in vastly different pathologic processes that appear to be similar on imaging. In the last decade, there has been an increase in the development and application of various functional imaging techniques such as MR spectroscopy (MRS), and diffusion/perfusion-weighted MR imaging (DWI/PWI). The advances of MRI is its multiplanar capability, superior contrast resolution, and flexible protocols that play an important role in assessing tumor location and extent, in directing biopsies, in planning proper therapy, and evaluating therapeutic results. Preoperative imaging of

a brain tumor plays several important roles including characterization of the brain tumor ,providing preliminary information of tumor type and grade, establishing a differential diagnosis, providing sufficient anatomical detail for surgical planning, and identifying tumor-related complications such as hemorrhage, hydrocephalus, herniation, or mass effect. Intraoperative imaging has improved neurosurgical morbidity and increased the amount of tumor resected, which is associated with improved quality of life and increased survival of patients. Postoperative imaging is important to monitor treatment response and detect tumor progression as early as possible. Imaging often will detect tumor progression before there is clinical deterioration.

Multidisciplinary session VI.:

P. Biochemistry session

P/1 INFLUENCE OF PROTEIN PHOSPHATASE-1 INHIBITORY PROTEINS ON THE DEPHOSPHORYLATION OF RETINOBLASTOMA PROTEIN

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Keywords: protein phosphatase-1, retinoblastoma protein (pRb), pRb-dephosphorylation, LIM-kinase-2 (LIMK-2), kinase enhanced phosphatase inhibitor (KEPI)

Introduction: The phosphorylation level of retinoblastoma protein (pRb) plays an important role in the regulation of cell cycle, and therefore has a major impact on the survival of malignant cells. Protein phosphatase-1 (PP1) has been considered as one of the pRb phosphatases, however its direct role in the dephosphorylation has not been fully established. The goal of our study was to investigate the role of PP1 and possible PP1 inhibitory proteins in pRb-dephosphorylation.

Methods: The catalytic subunit of PP1

(PP1c) was silenced by transfection of siRNA in HeLa cells. Vectors coding Flag-tagged KEPI (kinase enhanced phosphatase inhibitor) and LIMK-2 (LIM-kinase-2) were transfected into MCF-7 and HeLa cells, respectively. The efficacy of the transfections was checked via Western blot analysis and immunofluorescence. The viability of cells was assessed by MTT assay. **Results:** The silencing of PP1c resulted in increased phosphorylation level of pRb. Both KEPI and LIMK-2 include a phosphorylatable peptide sequence that is necessary for the potent inhibition of PP1. Expression of KEPI in MCF-7 cells led to its phosphorylation by endogenous kinases and inhibition of PP1 reflected in enhanced pRb-phosphorylation. Similarly, expression of LIMK-2 in HeLa cells decreased protein phosphatase activity leading to increased pRb-phosphorylation.

Conclusion: Our results indicate the essential role of PP1c in determining the phosphorylation level of pRb, which is also regulated by PP1 inhibitory proteins. Thereby PP1, LIMK-2 and KEPI could be considered as potential drug targets with therapeutic means in different kinds of malignancies.

P/2 NEW POTENTIAL BIOMARKER IN SEPSIS: SERUM ACTIN/GELSOLIN RATIO

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Keywords: actin, gelsolin, predictive value, western blot, enhanced chemiluminescence.

Introduction: Except procalcitonin, the specificity and predictive value of biochemical markers in early diagnosis and monitoring of sepsis is poor. In severe sepsis and septic shock the necrotizing cells release actin in excess into the circulation which are eliminated by plasma gelsolin and other actin binding proteins. When the amount of released actin exceeds its elimination capacity, gelsolin concentration decreases and free G-actin levels increase in the blood. Free actin promotes development of MOF and ARDS.

Methods: In our study we monitored serum actin and gelsolin levels in septic patients (n=8) for 3 – 5 days and tried to find correlation between classic laboratory parameters and outcome of the disease (predictive value). Sera were electrophoretized by SDS-PAG (Laemmli). After separated proteins were transferred to nitrocellulose membranes relative amounts of actin and gelsolin were determined by quantitative chemiluminescent (ECL) western blot. The signal of the samples were referred to that of an internal standard (serum of a healthy individual) and data were given as ECL ratios.

Results: Septic patients showed decreased gelsolin levels (20 – 50%) compared to the control. Furthermore, when actin ECL ratios were referred to gelsolin ECL ratios, data for surviving patients were only 2 – 3 times higher than 1,0 (arbitrary unit of control) while non surviving patients showed 8 – 16 times higher values than that of the control. CRP and procalcitonin data did not correlate closely with survival rates.

Conclusion: Our method gives data on the overall catabolic state of septic patients predicting the outcome of the disease.

P/3 REGULATION OF CASKIN1 SCAFFOLD PROTEIN BY EPHB1 TYROSINE KINASE

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Keywords: scaffold protein, Caskin, Ephrin receptor, SH3 domain, tyrosin phosphorylation

Introduction: Caskin scaffold proteins are typically present in neuronal cells, particularly, in the post synaptic density (PSD). Caskin1 is able to form a complex with the Cask proteins; therefore it is referred to as Cask-interacting protein. By the means of yeast two hybrid screening we have identified earlier a number of

interacting protein partners of Caskin1, including Abi2 and Nck adaptor proteins.

Methods and results: Here we demonstrated that EphB1 receptor tyrosine kinase can recruit Caskin1 through the adaptor protein Nck. Upon activation of the receptor kinase, Nck SH2 domain binds to one of its tyrosine residues, while Nck SH3 domain interacts with the proline-rich domain of Caskin1. Complex formation of the receptor kinase, adaptor and scaffolds proteins results in the tyrosine phosphorylation of Caskin1 on its SH3 domain. The phosphorylation sites were identified by mass-spectrometry as tyrosines 296 and 336. To reveal the physiological consequence of this phosphorylation, CD spectroscopy was performed. This measurement suggests that upon tyrosine phosphorylation the structure of the Caskin1 SH3 domain changes dramatically.

Conclusion: Taken together, we show here that the scaffold protein Caskin1 can form a complex with the EphB1 tyrosine kinase via the Nck protein as a linker. Translocation of Caskin1 to the plasma membrane leads to its tyrosine phosphorylation on its SH3 domain. Although we were not able to identify any physiological partner of the SH3 domain so far, we could demonstrate that phosphorylation on conserved tyrosine residues results in marked changes in the structure of the SH3 domain.

P/4 ACTIVATION GATE OPENING PRECEDES C-TYPE INACTIVATION IN SHAKER POTASSIUM CHANNELS

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Keywords: C-type inactivation, structural rearrangement, cysteine modification, recovery from inactivation, Shaker potassium channel

Introduction: The voltage-gated Shaker-IR potassium channels have two distinct gates, an activation and an inactivation gate. The functional crosstalk between these two gates is well-established, but none of the previous studies correlated the opening of

the activation gate, formed by the bundle crossing of the S6 segments, with the development of inactivation, which is associated with the structural rearrangement in the selectivity filter. We hypothesized that opening of the activation gate must precede C-type inactivation.

Methods: To test this hypothesis we engineered cysteines at positions 474 of the S6 segments in a Shaker-IR background. The T449A/V474C channels were expressed in tsA-201 cells. The opening of the activation gate was monitored by the accessibility to Cd²⁺ from the intracellular side. The irreversible binding of Cd²⁺ renders the channels non-conductive, thus the cysteine modification can be monitored by ion current measurements. The experiments were performed with excised inside-out patches.

Results: The applied protocol consists of three consecutive short (5ms) depolarizations to +50mV. Between the first two pulses the patch was held for 20s in the absence and presence of Cd²⁺ on a test potential, at which no macroscopic current can be detected, but channel inactivation occurs. Then the patch was held at -120mV for 60s which was followed by the third depolarizing pulse. The analysis of the peak amplitudes showed that the extent of recovery from C-type inactivation is decreased by Cd²⁺.

Conclusion: Based on these results we suggest that activation gate opening always precedes structural changes associated with C-type inactivation.

Q. Surgery-Anesthesiology-Pathology-Oncology-Otorhinolaryngology session

Q/1 EFFECTS OF THE METHANE TREATMENT ON THE EARLY MORPHOLOGICAL AND FUNCTIONAL CONSEQUENCES OF THE EXPERIMENTAL MESENTERIC ISCHAEMIA AND REPERFUSION

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Keywords: intestinal, ischaemia, reperfusion, methane, morphology

Introduction: We have demonstrated that exogenous methane (CH₄) reduces the biochemical consequences of the inflammatory response during experimental mesenteric ischaemia-reperfusion (I/R). The effects of CH₄ administration on I/R-caused mucosal damage are unknown, thus our goal was to investigate the structural and functional changes of the mucosa during I/R with or without CH₄ treatments during reperfusion.

Methods: We have monitored the effects of a 45-min ischaemia followed by 1 hr of reperfusion in anesthetized rats. Control, I/R, I/R with methane treatment (I/R+Met) groups were used (n=9 each); in I/R+Met animals artificial air containing 2.5% CH₄ was administered in the last 5th min of ischaemia and for 10 min during reperfusion. We have analysed the dynamics of morphological changes of the mucosa with in vivo fluorescent confocal laser scanning endomicroscopy (OptiScan, Australia) with iv fluorescein, FITC-dextran and topical acriflavine staining. Functional changes were evaluated by intraluminal fluorescent dextran, to quantify epithelial permeability (EP) and with iv administered Evans blue to measure the vascular permeability (VP) index).

Results: Increased epithelial shedding was observed in the I/R group with a 50-fold increase of the EP index (I/R: M=53.9 vs control: M=0.9) and VP index (I/R: M=0.34 vs control: M=0.09) compared to the control group. The CH₄ treatment prevented the loss of the epithelium and significantly decreased the EP (I/R+Met: M=13.1) and VP indices, respectively (I/R+Met: M=0.13).

Conclusion: Normoxic CH₄ inhalation prevents reperfusion damage of the small intestinal epithelium, as confirmed by the decreased EP and VP indices.

Q/2 EFFECT OF POSTCONDITIONING ON LOCAL AND SYSTEMIC INJURY FOLLOWING SUPERIOR MESENTERIC ARTERY OCCLUSION IN RAT

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Keywords: ischemia, reperfusion, postconditioning, SIRS, MOF

Introduction: The ischemia-reperfusion injury of the small intestine is a condition of high mortality, which occurs following superior mesenteric artery (SMA) embolization or circulatory redistribution. The aim of the study was to evaluate the local and systemic effects of postconditioning in a rat model of small intestinal ischemia-reperfusion.

Methods: Male Wistar rats underwent 60 min ischemia by the clamping of the SMA, followed by 6 hrs of reperfusion. The animals (n=30) were randomized into three groups: sham-operated, control-, and postconditioned. Postconditioning was performed at the very onset of reperfusion by 6 alternating cycles of 10-10 seconds reperfusion/reocclusion, for a total of 2 min. Intestinal mucosal microcirculation was monitored with a laser Doppler flow meter representatively throughout both ischemia and reperfusion. At the end of the reperfusion blood and tissue (small intestine, lungs, kidney, liver) samples were taken.

Results: Histologic results presented increased damage in control-group lungs, kidney, liver and small intestine in comparison with the postconditioned-group. The injury was supported by significantly higher dry/wet weight ratio (p=0.026), and serum levels of creatinine (p=0.013), ASAT (p=0.038), LDH (p=0.028) and CK (p=0,038) in the control-group. The postconditioned-group showed improved intestinal mucosal microcirculatory

parameters (pRT=0.001; pPM=0.0002), and lower serum IL-6 levels (350 pg/ml vs. 168 pg/ml), as well as significantly higher mucosal antioxidant concentration.

Conclusions: Postconditioning was able to decrease not only local, but the systemic damage intensity also, after a small intestinal ischemic-reperfusion episode.

Q/3 EFFICACY OF DIFFERENT TYPES OF FLUID THERAPY IN PATIENTS WITH SUBARACHNOID HEMORRHAGE: A PROSPECTIVE, RANDOMIZED STUDY

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Keywords: subarachnoid hemorrhage, triple-H therapy, vasospasm, crystalloids, colloids

Introduction: Triple-H therapy (3HT; hypervolemia, hemodilution and hypertension) is often utilized to prevent and treat cerebral vasospasm after aneurysmal subarachnoid hemorrhage (aSAH), although the preferred agent is still a question under debate. We designed a prospective, randomized study to evaluate whether crystalloid-based (Lactated Ringer) or colloid-based (Voluven) 3HT is more effective in the treatment of cerebral vasospasm.

Methods: Hunt-Hess I-II-III patients with documented aSAH were randomized into two groups: 1) LR-group: 15-40 ml/kg Lactated Ringer daily or 2) Vv-group: standard 15 ml/kg Lactated Ringer and 15-50 ml/kg Voluven daily. Patients received additional vasoactive drug treatment when it was needed. Transcranial Doppler and NIH Stroke Scale were assessed daily. 30-day outcomes were measured with Glasgow Outcome Scale (GOS) and Barthel Index (BI). We defined the primary endpoint as the occurrence of vasospasm and the secondary endpoints as the 30-day outcomes (mortality, GOS, BI).

Results: 38 patients were randomized to the

LR-group, and 34 patients were randomized to the Vv-group. No differences were detected between the two groups with respect to vasospasm. 30-day clinical follow-up assessments did not demonstrate any significant group differences neither with BI ($p=0,11$) nor with the 30-day mortality rate ($p=0,65$). However, results of GOS were significantly better in the LR-group ($p=0,018$).

Conclusion: Based on the data in this study there is no difference between the efficacy of the crystalloid-based and the colloid-based preventive 3HT.

Q/4 POSSIBLE ANTI-TUMORIGENIC USAGE OF ANGIOSTATIN IN ONCOTHERAPY

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Keywords: angiostatin, chimera, neovascularisation, anti-tumorigenesis, oncotherapy

Introduction: Angiostatin, a cleavage product of plasminogen kringle domains, is an endogenous angiogenesis inhibitor which can decrease tumorous growth. However, angiostatin is instable so therapeutic usage is complicated.

Our goal was to design an angiostatin-protease chimera which produces angiostatin in situ and in vivo after activation.

Methods: PCR amplified protease, angiostatin cDNA and elements needed for expression in bacterial and eukaryotic cells were ligated into an adequate vector in the same reading frame. The plasmid was used for transfecting different cell lines to achieve in vitro and in vivo production. Aorta ring assay served for monitoring endothelial proliferation in presence of transfected cells. BALB/c mice were injected with transfected and wild type 4T1 breast cancer cells to quantify tumor growth in time.

Results: The chimera was purified from E. Coli and its autocatalysis was observed using SDS-PAGE: the full chimera (80 kDa) appeared if isolation happened in presence of protease inhibitor. Endothelial

proliferation in hanging drop culture stopped when chimera expressing cells grew at the bottom. The aorta ring assay became negative on transfected cell lines. In vivo tumor progression was tested using 20 independent clone lines. Mice injected with transfected 4T1 cells only started growing cancerous tissue 10 days after infection and their tumor progression proceeded with slower rate compared to control animals. Metastases occurring in these mice showed smaller diameters as well.

Conclusion: Our chimera cleaves active angiostatin and develop its anti-tumorigenic effect as demonstrated both in vitro and in vivo experiments. Patent application is in process.

Q/5 BIOMARKER EXPRESSIONS OF HEAD AND NECK CARCINOMAS ARISING AT DIFFERENT ANATOMICAL LOCALIZATIONS

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Keywords: head, neck, cancer, biomarker, expression

AIMS: The objective of our study was to evaluate and to compare the biomarker expressions of head and neck squamous cell carcinomas (HNSCC) arising at different anatomical sites.

PATIENTS and METHODS: We enrolled 124 patients with HNSCC into our study. Among them, 7 had oral, 25 oropharyngeal, 13 hypopharyngeal and 79 had laryngeal cancer. We prepared Tissue Microarrays (TMA) made from the patients' tissue samples and used immunohistochemical staining for the detection of four conventional (Ki67, p53, EGFR, p16ink4) biomarkers and a relatively new (Collagen XVII/BP180) marker. The TMAs were digitalized, and the histological evaluation was performed on computers using a special software. We considered the expressions positive if more than 25% of the tumor cells were stained with the used biomarker. For statistical analysis, we performed Pearson's Chi-square tests.

RESULTS: The p16ink4 and Ki67 expression rates of the tumors in the supraglottic

region were significantly higher than those of the tumors in other laryngeal and hypopharyngeal regions. Though, the Ki67 expression rates of the tonsillar tumors (palatine and lingual tonsil) were significantly higher than those of the oral, hypopharyngeal, and other oropharyngeal tumors. The other biomarkers were also detectable in the majority of the tumors, but significant differences were not revealed.

CONCLUSIONS: According to our results, the tumors of the oropharynx cannot be regarded as one entity. Additionally, we can state that tonsillar and supraglottic tumors have similar biomarker-expression profiles. A possible explanation for this phenomenon is that these structures undergo similar embryologic development.

Q/6 RECONSTRUCTION OF TRACHEA AND SOFT TISSUE DEFICIT IN PATIENT WITH TRACHEOSTOMY USING SUPRACLAVICULAR ARTERY ISLAND FLAP

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Keywords: trachea reconstruction, tracheostomy closure, supraclavicular composite island flap, tracheotomy, reconstruction

Authors present a case of a 52-year-old female patient, who underwent an urgent tracheostomy because of life threatening heavy breathing. Later total thyroidectomy was carried out. The atypical tracheostomy required to be closed, also in case of a tracheal instability the missing anterior wall had to be reconstructed with rigid tissue. The authors decided to prepare a supraclavicular artery osteocutaneous flap, which was harvested from the shoulder as an island flap, a thin bone chip was taken from the coracoid process of the scapula, and it was placed into the defect. The bone chip was sutured to the trachea wall. The donor site was closed primarily. After reviewing the literature this flap is useful

for head and neck reconstruction in a wide range of cases. Not only the satisfactory functional and cosmetic result, but also the fact that the donor site does not need skin grafting may take this flap more popular.

Q/7 EXAMINATION OF CLINICOPATHOLOGICAL PROGNOSTIC FACTORS IN NEUROENDOCRINE TUMOURS OF PANCREAS

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Keywords: pancreas, neuroendocrine, tumor, classification, prognosis

Introduction: Pancreatic neuroendocrine tumors are considered potentially malignant tumors, their classification has gone through several changes during the last few years. Both the European Neuroendocrine Tumor Society (ENETS) and the Union for International Cancer Control (UICC) classify these tumors according to stage, whereas the WHO classification is based on the proliferative activity.

Objectives: In our study we compared the efficiency of the different classifications from the viewpoint of prognosis.

Materials and methods: We analyzed the clinicopathological parameters of 34 neuroendocrine tumors of the pancreas. We then evaluated the roles played by these parameters and the various classifications in the prognosis using statistical methods (chi-square test and Fisher's exact test).

Results: The grade values obtained on the basis of the Ki-67 index and mitotic figures showed correlation. The Ki-67 proliferation index had a significantly higher value in case of tumors with lymph node metastasis. Based on grade and stage, insulinomas showed significantly better prognosis. We found differences in stage regarding tumors infiltrating surrounding structures. In case of tumors classified into the carcinoma group and giving lymph node metastases according to the WHO classification, the development of metastases at distant sites is expected.

Conclusions: The three classification

systems customary in the diagnosis of neuroendocrine tumors of the pancreas, the hormone production as well as proliferation tendency of the tumors are all suitable for assessing the prognosis. We suggest the parallel application of both grading systems when assessing the proliferative activity. In the pathological findings it is essential to indicate the classification used.

R. Lunch Symposium

R/1 ANTIFERTILITY EFFECTS OF FLUPENTIXOL IN ADULT MALE RAT

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Keywords: Flupentixol, testosterone, gonadotropin, sperm, rat

Introduction: Flupentixol is an anticonvulsant drug. Its side effects on reproductive functions have not been sufficiently studied. This study was designed to evaluate the effect of Flupentixol on pituitary-gonad axis and spermatogenesis in adult male rats.

Methods: 40 adult male rats Wistar strain were randomly divided into five groups. Animals in group1(Control group) were injected with any treatment. Animals in group2 (Sham group) received the three-component solvent (propylenglycol, ethanol and distilled water in a ratio of 5:2:3) in a corresponding volume,i.e.,1ml/kg.bw. Animals in groups 3, 4, 5 received Flupentixol dissolved in solvent), respectively, in doses of 50,100,150 mg/kg.bw/day i.p. for 21 days. At the end of the study, blood gonadotropins (LH and FSH) levels as well as testosterone of rats in five groups were determined. The animals were sacrificed, then, spermatogram and histological changes of their testes were studied under light microscope.

Results: The results show that in Flupentixol treated groups, particular experimental group 3, blood testosterone levels were

significantly decreased as compared to the control group. Plasma concentrations of LH, FSH assayed and there were no significant differences among the Flupentixol treated groups as compared with control group. Body weight in Flupentixol treated relatively increased. However, sperm density and testes weight were not different from those of the control group.

Conclusions: These findings indicate that Flupentixol has a relative suppressive influence on reproductive function in rats. We suggest that Flupentixol directly affects production of testosterone in leydig cells or centrally increased estradiol biosynthesis subsequently lowered testosterone levels by negative feedback.

R/2 NEUROSONOLOGY – STETOSCOPE FOR THE BRAIN!

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Transcranial Doppler (TCD) is the "doctor's stethoscope for the brain". It is non-invasive, safe and cost-effective bedside test in evaluating the cerebrovascular circulation. TCD shows the blood flow direction and velocity in the intracerebral vessels, adding physiologic information to the anatomical images obtained with other imaging modalities. TCD can also detect potential collateral flow signals in the ophthalmic, anterior communicating, and posterior communicating arteries caused by hemodynamically significant carotid stenosis. TCD remains the only method to detect asymptomatic embolization but does even more. TCD provides essential "real" time, hemodynamic information about the intracranial circulation compared to "static" brain imaging modalities.

Previous studies have attempted to identify specific TCD criteria for the middle cerebral (MCA) and Internal Carotid Artery stenosis/occlusions using the gold standard of cerebral angiography. Several studies have compared TCD with digital subtraction (DSA), CT angiography (CTA), magnetic resonance (MRA) angiography in the acute

stroke setting with variable accuracy (60-91%) to detect intracranial pathology. Based on a battery of detailed diagnostic TCD criteria using specific flow findings accuracy can be improved. TCD accuracy for detecting the MCA or ICA lesion is superior to other intracranial locations such as vertebral and basilar artery occlusion. Numerous studies have been performed in the literature to derive carotid duplex parameters for angiographically confirmed carotid stenosis including detailed logistic regression modeling of duplex criteria based on angiographic data. However no large study has been performed which attempts to derive TCD/CD criteria based solely on CT/CTA data.

Transcranial power motion mode Doppler (PMD/TCD) is now available with digital TCD that simultaneously sample 33 gates over 60 mm of intracranial space. Specific flow signatures are seen with PMD/TCD which provides simpler identification of the insonated artery and specific signatures of stenosis and occlusion. Transcranial duplex Imaging has advantages over TCD by showing the images of the intracranial anatomy and arteries by duplex B-mode, while you are still measuring velocities with Doppler.

TCD detection of embolic particulate matter as well as gas bubbles has been well-validated in laboratory and animal models. The intensity of the Doppler signal of an embolus traveling in blood depends on the size and acoustic impedance. Air, for example, has much lower acoustic impedance than blood and, therefore, reflects sound waves to a greater extent. This fact was exploited early in the use of Doppler in order to detect decompression sickness in deep-sea divers in the 1960s. Differentiating gas from particulate matter with a high level of sensitivity has been reported and would help determine the embolic source but it is still under investigation.

The minimum detectable diameter of gaseous emboli has been reported at 10 microns while particulate emboli can be detected from 40 microns. Based on Consensus Committee guidelines, certain technical criteria must be met to qualify as

microembolic signals (MES) by TCD. If microembolic signals (MES) are seen on both the side of the carotid stenosis and the contralateral side, the origin of embolus may be from a central source, e.g., the heart or aorta. Unilateral MES more likely result from carotid lesion, plaque.

PFO Detection by agitated saline injection and Vasomotor reactivity testing are the other billable test we can perform with the same machine.

Limitations:

Two major limitations exist with TCD impeding its widespread use. It is a true operator-dependent, hand-held technique requiring detailed 3 dimensional knowledge of the intracranial arterial anatomy. More critically TCD is hampered by the 10-15% rate of inadequate temporal windows most commonly seen in elderly female patients.

A newer technology called Power Motion-mode TCD (PMD/TCD) appears to improve window detection and simplifies operator dependence of TCD by providing multi-gate flow information simultaneously in the Power M-mode display.

S. Special Teaching Session:

Cardiovascular prevention

S/1 PREVALENCE AND MORTALITY OF CARDIOVASCULAR DISEASES

Mark Canning

United States of America Embassy in Budapest, Hungary

In the US, more than 2 million heart attacks and strokes occur each year, resulting in 800,000 cardiovascular deaths. Cardiovascular disease is still the leading cause of death in the United States, and is responsible for more deaths annually than cancer, chronic lower respiratory disease, and accidents combined. This is not just the result of recent changes to the ways we eat, work, and spend our free time. In fact, since 1900, cardiovascular disease has been the leading cause of death in the U.S. every year except 1918. Both the prevalence and mortality have been so high for so long. However, mortality rates have dropped

significantly over the last decade. It is worth asking why this happened, and what can be done to lower both mortality and prevalence even more. About 83 million American adults, roughly one third of the adult population, have 1 or more types of cardiovascular disease. The major risk factors for CVD include tobacco use, high blood pressure, high blood cholesterol, diabetes, physical inactivity, and poor nutrition. Smoking prevalence has decreased from baseline levels by 16%. This is the result of medical interventions, but to an even larger extent, social pressures.³ Medical therapies have also dramatically reduced blood pressure and cholesterol, with uncontrolled high blood pressure prevalence dropping by 30% and high cholesterol dropping by 25% from baseline. During the first decade of this century, death rates resulting from coronary heart disease and stroke fell by $\approx 30\%$. This shows that the efforts of public health advocates, researchers, and clinicians can dramatically reduce cardiovascular mortality. But much more needs to be done on the other risk factors: physical activity, body mass and diet, which not only didn't show improvement, but are indicating increased risks. If these factors can't be addressed through other means, social pressures, ban on large sodas, chips tax, etc; there will be pressures to increase the use of medical therapies, such as the polypill, including for asymptomatic or even healthy people.

S/2 NONPHARMACOLOGICAL TREATMENT OF HEART FAILURE

Prof. Dr. Béla Merkely

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No abstract available.

T. Hands-on-Session

Emergency medicine session

T/1 URGENCY CARE ON EACH LEVEL

Dr. István Éger

Hungarian Medical Chamber

No abstract available.

T/2 "PROFESSION FOR THE LIFE!" THE SYSTEM OF THE HUNGARIAN NATIONAL AMBULANCE SERVICE

Pál Győrfi

Hungarian National Ambulance Emergency Service

The Hungarian National Ambulance Service (HNAS) is an integrated statewide health-care organization. Saving human lives and providing extra-hospital emergency medical attendance are the main tasks of the organization. Beside the different medical services (104 telephone number), the HNAS also plays an important role in the transportation, as the organization is responsible for the carriage of those particular patients whose condition demands special interventions during the transportation. The HNAS is an integrated system during 1948, when it was founded. The organization employs 7055 person on 231 stations throughout the country. Our team attended almost 1 million patients and covered 33 million kilometers. Our goal is to build up a new European system of services on the basis of our traditional values. Our EU supported development projects are aiming the modernization of the corporate management system, the arbiter systems as well and the improvement of the infrastructural network. Beside the changes, we preserve our basic principles, our watchword is still "Profession for the Life!".

T/3 EMERGENCY MEDICINE: INTEGRATED DISCIPLINE IN THE UNITED STATES

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**Keywords: emergency, board
certification**

Summary: In the United States we see 120 million emergency visits a year. There are two basic emergency service models these years. The Anglo-American model and the German-French model of care-- wide spread in Europe. The Anglo- American model is based on a centralized emergency medicine system of care, with a well organized emergency departments where all citizens with any real or conceived emergency can enter or brought in with an ambulance and taken care of. The emergency departments are well centralized units of care where all sub specialists take care of patients in consultation with emergency physician who is in charge of the department and ultimately responsible for the patients. Emergency Medicine is the 23th sub specialty in the United States consisting of 3-4 year residency training followed by Board Certification examination. This examination has to be repeated every 10 years. There are 36.000 emergency physicians in the United States about the total Hungarian physician population. Emergency care in the United States is pyramidal with Level IV departments, very basic to Level I very advanced Departments, most of them university based. Due to the large size of the United States these systems are well integrated as needed be it a helicopter or bicycle paramedic interceptors. as transport means. The future of emergency medicine is under way with computer integration and tele-medicine. It is well defined subspecialty with its own body of literature and research.

Multidisciplinary session VII.:

U. Dentistry session

U/1 PREVENTION AND CORRECTION OF NEGATIVE ATTITUDE TO DENTAL TREATMENT IN SCHOOL CHILDREN

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Keywords: children, pain, fear of treatment, behavior

Introduction. Epidemiological studies in dentistry show that the percentage of people who fear the dentist is in the range from 3 to 43%. Relations in the system of a doctor and patient are one of the important problems in dentistry. Not enough attention in our country given the improvement of psychological and pharmacological methods of correcting the behavior of children during dental treatment, although the difficulty in relationships with patients has been around even that children's dentist is forced to communicate simultaneously with two subjects child and accompanying person, and each of them on their level.

Methods. It was a review, testing and questioning of 63 patients 6-9 years old children and their parents. Aim. Investigate the causes of negative attitude to dental treatment. Results. According to our testing because of fear of dental treatment 6% of primary school children and 25% of teenagers refuse to visit a dentist, also because of anxiety and lack of motivation dentistry correction behavior during treatment requires 70% of children in school. Common causes of fear in dental patients include a high level of general anxiety, there are other fears, lying position in the dental chair, the state of helplessness and dependency, inability to monitor and influence the course of treatment, the possibility of weakness and loss of control over their behavior. According to the literature almost 90% of children requiring correction of the reaction behavior. The negative behavior of children during dental treatment, often manifested increased physical activity significantly affects the quality of medical procedures and is one of the reasons for the reluctance of young dentists working in pediatric dentistry. While waiting dental patients receiving dental clinics are often seen as signs of emotional distress and fear that can lead to autonomic disorders such as syncope, hypertensive crisis, arrhythmias, and neurological disorders. Thanks sedative preparation patients remain in full consciousness, review the treatment, use stop- signals are susceptible to psychological help.

Conclusions. During our research we found out that application of psychological and

pharmacological correction of the behavior of children during dental treatment allows make the dental treatment less time consuming for the doctor and more gentle for children who fear dental procedures, also to eliminate the need for general anesthesia.

U/2 SURFACE COATING EFFECTS ON MORPHOLOGY AND ON MARKER EXPRESSION OF RAT DENTAL PULP STEM CELLS' NEURODIFFERENTIATION

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Keywords: stem cell, neurodifferentiation, coating

Objectives: Our group developed a protocol for neural differentiation of human dental pulp stem cells, the method is not completely applicable for rat dental pulp stem cells (rDPSC). Our aim was to find optimal parameters for differentiation of rDPSC cultures.

Methods: Cells were isolated from rat's lower incisors, and cultivated under standard conditions. As neural differentiation first we activated the PKA-PKC system and induced the cells with growth factors. Cells were maintained for two more weeks with bFGF and retinoic-acid containing media. Differentiation was performed on fetal calf serum (FCS), laminin (LA), poly-L-lysine (PLL), poly-L-lysine/laminin (LYLA), ornithin/laminin (ORLA) and on untreated surface (NTC). Marker expression was studied with Q-PCR.

Results: Within 24 hours, cells attached to the surface displaying similar morphologies. We observed three different cell types: fibroblast-like cells, epitheloid cells, and large, flat cells. In the first step of differentiation cells formed ridges on FCS coating, but spread out on other surfaces. During the induction, the proportion of cells with neural morphology increased, but during the first maturation stage it decreased. To the second maturation stage neuronal-like cells were visible on LYLA, ORLA and PLL surfaces. At the end of the

differentiation, the expression of neural markers such as neurofilament medium and neuron specific enolase increased six times and twice on LYLA and ORLA surfaces in compare to NTC.

Conclusion: Neural morphology was more evident and neural markers elevated while rat pulp cells were cultured on combination of lysine-laminin and ornithin-laminin.

V. Rainbow session – colorful actual questions

V/1 DEVELOPMENT AND DISTRIBUTION OF HEALTH RELATED CONTENT ON STATE-OF-THE-ART DIGITAL PLATFORMS

Imre Hild

YBL Club, Budapest

Keywords: distribution, digital, state-of-the-art, health related

There is a wide variety of digital multimedia platforms available to content owners to distribute their content to a global audience. The presentation will give an insight into the development of these platforms, what are the available opportunities to health care professionals to use, utilize and monetize the current platforms and what the forecasts say about the future

V/2 MEDICINE SPEAKING SEVEN LANGUAGES - TEACHING AND TESTING TECHNICAL LANGUAGE IN SEMMELWEIS LANGUAGE COMMUNICATION CENTRE

Dr. Éva Kovács, Dr. Katalin Vincze Sárközyné

Language Communication Centre, Semmelweis University

Keywords: our history, our activities, courses, plans, American exchange students

In my lecture I am going to present the language teaching system used in Semmelweis L.C.C. which is unique among the medical schools of Hungary for being the only place where six living languages are taught besides Latin. Following a brief

historical survey, I will talk about our basic activities, teaching and exams including university final and state examinations.

Besides describing our courses, I will also speak about our other activities, for example doing translations for university institutes or compiling technical dictionaries and teaching materials. Finally I am going to talk about our plans among which teaching Hungarian to American exchange students and make them acquainted with Hungarian culture is meant to have an outstanding role.

V/3 ACTUAL QUESTIONS OF DOPPING AFTER THE OLYPIC GAMES

Dr. Ágnes Tiszeker

Hungarian Antidopping Kft.

No abstract available.

V/4 SPENDING CUTS AND CENTRALIZATION IN HUNGARIAN HEALTHCARE AS A RESPONSE TO THE INTERNATIONAL FINANCIAL CRISIS

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Keywords: I11 – Analysis of Health Care Markets, I13 – Health Insurance, Public and Private, I15 – Health and Economic Development

The Bismarckian model of mandatory social health insurance scheme was replaced by a tax-financed system, closely resembling to the British NHS model. The network of hospitals previously owned by local governments was nationalized and the Ministry responsible for healthcare became the owner of the entire hospital sector. The right of patients to choose hospitals was strictly limited.

On the financial side, the government has made cuts of public health expenditures in the order of 1% of GDP.

W. Teaching Session

Iron Metabolism Session

W/1 REGULATION OF IRON METABOLISM - THE ROLE OF THE HORMONE HEPcidIN

Dr. Katalin Sipos

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Keywords: iron, anemia, hepcidin, regulation

Iron is one of the essential nutrients of every living organism. The level of iron in the body is regulated efficiently as well as its recirculation. Hpcidin, the hormone which regulates iron metabolism in vertebrates was discovered in 2000. First it was described as an antimicrobial peptide. The major effect of hepcidin is the initiation of the break down of ferroportin, an iron exporter molecule. This way iron is not entering the blood stream. This effect explains the development of anemia of some chronic diseases.

The expression of hepcidin is regulated by many factors, including iron level, hypoxia, inflammation, activity of erythropoiesis. The regulation of hepcidin expression in the cellular level is not known in every detail yet. Also it is important to know that there are significant differences among tissues in intracellular iron metabolism regulations.

Iron metabolism regulation disturbances may play a basic or additional role in some diseases like anemia, hemochromatosis, thalassemia, chronic inflammations and neurodegenerative diseases.

W/2 DIFFERENTIAL DIAGNOSIS AND TREATMENT OF ANAEMIAS

Dr. Miklós Egyed

Department of Haematology, Kaposvar Hospital, Kaposvar, Hungary

Anemia is a medical condition in which the red blood cell count or hemoglobin is less than normal, so the oxygen carrying capacity of blood is decreased. The normal level of hemoglobin is generally different in males and females. Because anemia is a symptom, the

underlying conditions must be determined. A new diagnostic algorithm, based on MCV, MCH, and the corrected reticulocyte count (entered to one liter blood in the last 48 hours) is presented. Practically, anaemia can be classified to 6 groups

- 1, hypochromic, hypo.-normocytic hyporegenerative.
- 2, hypochromic, hypo.-normocytic hyperregenerative
- 3, normochromic, normocytic, hyporegenerative
- 4, normochromic, normocytic, hyperregenerative
- 5, macrocytic, normo, -hyperchromic hyporegenerativ
- 6, macrocytic, normo, -hyperchromic hyperregenerativ.

About 45% of the whole anemia cases are belonging to group 1. and 2. As anemia is the result of disturbance in the hemoglobin synthesis, there are several abnormalities: iron deficiency, disturbances of porphyrin-hem, globin chain synthesis (thalassemia, hemoglobinopathy)

Anemia of chronic disease (ACD), pure red cell aplasia (PRCA), renal anemia belong to group 3, about 35% of anemia's. The group 4 has no clinical relevance, contains only regenerating conditions (recovery after bleeding...)

Group 5 ...express the defect of nucleic acid metabolism which is the result of lowering of pyrimidin base synthesis because of Folate and/or Vitamin B 12 deficiency, MDS can also cause macrocytic anemia. Group 6 contains hemolytic conditions (inherited and/or acquired hemolytic anemias). MCV is not extremely elevated, because it is the result of elevated reticulocyte count

We find our algorithm very simple, because it is based on only very few data.

W/3 POSSIBLE RELATIONSHIP BETWEEN IRON STORES OF THE BODY AND CARDIOVASCULAR DISEASES IN WOMEN

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Keywords: cardiovascular diseases, menopause, iron

It has been known for a while that women have lower risk for cardiovascular diseases at their younger age than men at the same age. Because this time interval is before menopause, this fact was connected to the hormones produced by the ovaries in women. These days the role of estrogens in protection against cardiovascular diseases is not clear. Scientific evidences prove that other possible factors cause the difference between sexes in the cardiovascular morbidity rates. One of these possible players is the amount of stored iron of the body. I plan to discuss this hypothesis and address the following questions: how to estimate the amount of stored iron? What are the consequences of increasing stored iron? What types of tissues are affected? Why is heart so vulnerable? How can we fight against high iron level?

X. Poster session III.: Clinical sciences

X/1 CROSSTALK BETWEEN THE SEPTIC ORGANISM AND NEUTROPHIL GRANULOCYTES

Ferenc Kolonics, András Béres

Department of Physiology, Semmelweis University

Keywords: PMN, neutrophil granulocyte, sepsis, immune system

Introduction: Sepsis and other diseases with systemic inflammatory response are intensively investigated in recent studies, although the pathomechanism and a definitive treatment are still unknown despite the many details found in this topic. Clinical findings confirm the central role of neutrophil granulocytes in the pathomechanism of systemic inflammatory response syndrome (SIRS). Sepsis is a SIRS caused by infective agents, which are in 80% of the cases bacteria, so neutrophils, the principal bactericidal cells are not only affected by the systemic inflammation, but they also participate in eliminating the causing factor of the SIRS.

Methods: We investigated human neutrophil granulocytes isolated from healthy volunteers and septic patients by

using a superoxide-detecting chemoluminescent assay and a semiautomatic bacterial surviving test.

Results: We observed some of the clinical evidences regarding septic neutrophil function: we found signs of decreased superoxide production capacity, preactivation and impaired bactericidal activity. We showed first that some of these tightly correlate with the general condition of the patients. We proved that altered neutrophil functions in SIRS affect the elimination of various bacteria differently, yet the localization and causing agent of the sepsis did not influence the effects of SIRS on neutrophils. We ruled out the role of septic physicochemical conditions behind these changes, and we observed that pretreatment with septic sera strongly influences neutrophil functions.

Conclusion: In our theory, bacteria and other noxa cause systemic inflammation in different ways, but this evolves into the same SIRS, which can be quantitatively different. We presume that these changes are serum mediated.

X/2 IMAGE RECONSTRUCTION AND POST-PROCESSING IN MEDICAL CT AND MR IMAGING - AN EXAMPLE USING EFMRI

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Keywords: efMRI, post-processing, imaging, Filtered back Projection (FBP), Fourier Transformation (FT)

The information-technological development has facilitated the evolution of digital imaging paving the way for mathematical algorithms to be exploited in all areas of science. The role of conventional image processing is being overtaken by digital imaging and post processing within the confine of medical diagnostic imaging.

Our aim is to demonstrate the various aspects of digital imaging focusing on post processing techniques, exploring "what happens in the background?". This will be demonstrated using an example of image

reconstruction on Earth's magnetic field using Terranova-efNMR device at Debrecen. Steps of image reconstruction: Filtered back Projection (FBP) is the most common technique used for the reconstruction of raw CT data. This procedure is based on supposition that the collected scanning image projection are Radon transform of linear attenuation coefficients. The basic steps of the FBP are: image pixel normalization and filtering, back projection and corrections. Another method is iterative reconstruction. Its algorithm calculates the projection CT images, and then compares the resulting image of the real measured projection image. Fourier Transformation (FT) is the algorithm used in MR imaging reconstruction. The raw MRI data is collected in so-called K-space and inverted into 2D and 3D images using FT. Image contrast and resolution can be improved using various filters. We studied the improvement methods for efNMR scans' post-processing.

There are many further possibilities in image processing which can be better understood by applying various algorithms. We are studying the methods of acquiring optimal contrast and resolution to be used for human diagnostic purposes.

X/3 A RARE COUSE OF GASTROINTESTINAL BLEEDING: SMALL BOWEL VARICES

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1: Semmelweis Hospital Miskolc

2: National Institute of Traumatology

Keywords: gastrointestinal bleeding, MDCT enteroclysis, small bowel varices, liver cirrhosis, portal thrombosis

To show the utility of MDCT enteroclysis in the diagnosis of small bowel varices.

Detection of small bowel varices is a challenging task and several invasive diagnostic techniques have been used for this purpose. Small-bowel varices are rare, compared with esophageal or gastric varices, most commonly associated with liver cirrhosis or portal thrombosis. They are clinically important because of the repeated episodes of bleeding. In our cases

patients were admitted because of a marked, repeated melena associated with mild anemia. Gastroscopy and colonoscopy revealed no abnormality. MDCT enteroclysis showed exactly small bowel varices supplied by the mesenteric vein with draining to systemic veins and liver cirrhosis or portal thrombosis. CT enteroclysis were performed using the following parameters: slice 1mm, with overlap scans, reconstruction interval 1mm, after administration of methylcellulose by nasojejunal tube, before and after infusion of 120 ml iv. contrast agent, at a rate of 4 ml/s with a scan delay of 35 and 70 seconds. Multiplanar and curved planer reformatted images were performed. Collimation was 16x0.75 mm. We founded pathological dilated vessels in the wall of the small bowel and in the mesentery. We have also found dilated draining veins. MDCT enteroclysis with neutral enteral and IV contrast is a good tool in detecting small bowel varices.

X/4 QUANTITATIVE MR IMAGING OF CHOLESTEATOMA WITH T1 AND T2 MAPPING

Andrea Horváth

Diagnostic Center of Pecs, University of Pecs

Keywords: cholesteatoma, HASTE-DW MRI, second-look surgery, T1 mapping, T2 mapping

Introduction: Middle-ear cholesteatoma is treated by tympanomastoid surgery. Since the risk of residual and recurrent disease is high, a second-look surgery is usually required. However, Magnetic Resonance Imaging (MRI), particularly the non-EPI half-Fourier acquisition single-shot turbo spin-echo diffusion weighted sequence (HASTE-DW) has been proved to identify residual and recurrent cholesteatoma non-invasively with high specificity and sensitivity. Nevertheless, this sequence provides only morphological information which might not be objective. Thus, our goal was to develop a quantitative MRI technique that provides a more accurate diagnosis.

Methods: 11 patients with the histopathologic and HASTE-DW MRI evidence of cholesteatoma were examined.

Besides the conventional T1 and T2 weighted images, axial and coronal, HASTE-DW, T1 map and T2 map images were performed on a 3 Tesla Siemens Trio MR scanner. After image registration, a mask was created on the T1 and T2 maps according to the HASTE-DW positivity. Afterwards, T1 and T2 relaxation times were calculated using MATLAB program.

Results: Our results showed long T2 relaxation times in all subjects, which provides objective information about the cystic structure of cholesteatoma

Conclusions: The combination of HASTE-DW MRI with quantitative MRI techniques such as T1 and T2 mapping provides accurate information about the cystic structure of cholesteatoma. Thus, with the further development of the method, patients could be prevented from unnecessary second-look surgeries.

X/5 COMPARISON OF PRIMARY BREAST CANCERS AND THEIR DISTANT METASTASES

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Keywords: breast cancer, metastasis, phenotypic change

INTRODUCTION: Our aim is to examine primary breast cancers compared to their distant metastases and also to monitor the patients' survival rate related to oncological treatment.

METHODS: We reviewed the autopsies done at the 2nd Department of Pathology of patients who died of metastatic breast cancer between 2001 and 2011. We examined 18 out of the 82 cases we found whose complete clinical documentation was available. Besides the primary tumors we examined altogether 61 distant metastases. For statistical analysis we used Statistica for Windows and SPSS Stat 17.

RESULTS: 66.7% of the primary tumors were IDC, 27.8% were ILC. Medullary carcinoma occurred only in one case. We

could only determine the immunohistochemical subtypes of the tumors in 15 cases. 2 were HER2 positive, 5 were triple negative, 4 were luminal A and 4 were luminal B. Poorly differentiated tumors prevailed among the cases (53.34%). Distant metastases were mostly found in liver (61.1%), bones (50%) and lung (38.9%). The proliferation rate in the primary tumors were significantly higher than in distant metastases (15.23 % vs. 3.31% $p = 0.001$). The hormone receptor status in the primary tumors and the distant metastases were concordant in 56.25% regarding ER and 60% regarding PR. In the other cases the receptors were identified in the primary tumors but the distant metastases were proved negative.

CONCLUSIONS: According to our research metastatic breast cancers are principally invasive ductal carcinomas. Nearly half of the tumors don't express ER and a phenotypic change can be occurred in the distant metastases.

X/6 INVESTIGATION OF ENDOGENOUS PACAP UNDER NORMAL AND PATHOLOGICAL CONDITIONS

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Keywords: PACAP, cytoprotective, knock out, retina, kidney

Introduction: Pituitary adenylate cyclase activating polypeptide (PACAP) is a widespread neuropeptide with a diverse

array of biological functions. Not surprisingly, the lack of endogenous PACAP therefore results in a variety of abnormalities. One of the important effects of PACAP is its neuroprotective and general cytoprotective role. PACAP protects neurons and other tissues against ischemic, toxic and traumatic lesions. Interestingly, development and tissue morphology under physiological conditions are not markedly different between wild type and PACAP deficient mice. However, mice lacking PACAP are more vulnerable to different insults, suggesting that endogenous PACAP also has protective functions.

Aims: The aim of the presentation is to summarize data on normal development and tissue structure under physiological conditions and to investigate the altered response of PACAP knockout mice under challenged conditions.

Methods and Results: The neurobehavioral development of PACAP KO mice during the first 5 weeks postnatal was not significantly different from their wild type mates. Light-microscopical structure of the intact retina and peripheral organs was not altered either. However, our research group provided evidence that mice lacking PACAP respond with a higher degree of injury in retinal ischemia. In peripheral organs, PACAP deficient mice have a negative histological outcome and altered cytokine response in kidney and small intestine ischemia/reperfusion injury. Increased inflammatory response has been described in subacute endotoxin-induced airway inflammation and in oxazolone-induced contact dermatitis.

Discussion: In summary, lack of endogenous PACAP leads to higher vulnerability in a number of injuries in the nervous system and peripheral organs, supporting that PACAP is part of the endogenous cytoprotective machinery.

Y. Poster session IV: Clinical sciences

Y/1 ANALYSIS OF SUICIDE ATTEMPTS WITH A FOCUS ON PRECEDING DISEASES, CAUSES AND METHODS

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Keywords: suicide, prevention, medication, alcohol, schizophrenia

The OSPI project (Optimised Suicide Prevention programs and their Implementation in Europe) has a new area of intervention in Hungary, the city of Miskolc. Unfortunately, the prevalence of suicide is particularly high in this community.

Our database that were thoroughly analysed consists of more than 2500 well-detailed cases recorded at the departments of toxicology, neurology and psychiatry in the last 3 years. The main goal was to reveal those physical diseases that are most commonly related to suicide attempts. We found that disc disorders, schizophrenia, epilepsy are significantly more frequent between suicidal people regardless of their gender. Alcohol dependency is significantly more often recorded among suicidal women.

Furthermore, we examined the reason of the suicide attempts. We can categorise the patients based on their motivation. The most common category is the “parasuicide pause”, when the person only tries to escape from a certain situation (39%). The “serious intent to die” is the second most common category (38%). The patients in the third group do not have any real suicidal motivation, it is just a parasuicide gesture (5%). Since the direct self-injury is hardly to be separated from other suicidal acts our research include those as well (10%).

The most common method of suicidal attempts is medication. We found that the quantity of the swallowed pills is highly correlated with the seriousness of the intention. The most common drugs are anxiolytics, psycholeptics and antiepileptics (Rivotril, Frontin, Xanax). Women often use some sort of cardiovascular medication as well.

Y/2 SPECTRAL CHARACTERISTICS OF SLEEP EEG IN RELATION TO INSOMNIAC AND DEPRESSIVE SYMPTOMS OF KIDNEY TRANSPLANT RECIPIENTS

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Keywords: insomnia, depression, kidney transplantation, spectral analysis, hyperarousal

Introduction: The prevalence of insomnia (I) and depression (D) is high among kidney transplant recipients. The hyperarousal of the central nervous system (CNS) might play a role in both conditions, which is characterized by high frequency activity (HFA) of the EEG. We investigated the relationship of insomnia and depressive symptoms versus HFA in sleep among kidney transplant recipients.

Methods: Forty-five kidney transplant recipients participated in the study (27 males and 18 females, mean age 48.2 ± 13.07 years, BMI $25.81 \pm 4.01 \text{ kg/m}^2$, GFR $49.97 \pm 18.05 \text{ ml/min}$). Symptoms of insomnia and depression were measured by the Athens Insomnia Scale (AISL) and the Center for Epidemiologic Studies-Depression Scale (CES-D). After one-night polysomnography sleep structure and spectral profile were characterized. HFA was measured within beta1 (15.25-25 Hz), beta2 (25.25-35 Hz), and gamma (35.25-45 Hz) frequency bands.

Results: Subgroup of patients with insomnia exhibited higher beta1 and gamma activity during REM sleep compared to patients without insomnia ($p < 0.005$; for both comparisons). In high depression score patients only beta1 activity was ($p < 0.005$) increased compared to low depression subgroup. The AISL score correlated with beta1 power in REM ($r = 0.363$; $p < 0.005$) and in non-REM ($r = 0.317$; $p < 0.005$), with gamma power in REM ($r = 0.317$; $p < 0.005$)

and in non-REM ($r=0.371$; $p<0.005$). The CES-D score had no significant correlation with the power spectra.

Conclusion: The correlation between the symptoms of insomnia and the increased neurocognitive activity of the CNS during sleep was shown for the first time in this population; thus the CNS hyperarousal might play a role in the emergence of insomnia among kidney transplant recipients.

Y/3 EFFECT OF ORAL CONTRACEPTIVE TREATMENT ON OXIDATIVE-NITRATIVE STRESS AND THEIR RELATION TO GLUCOSE METABOLISM PARAMETERS

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Keywords: OC, PARP

Background and aims: The metabolic side effects of oral contraceptive (OC) therapy are already described, however their pathomechanism are not well established. Oxidative-nitrative stress and concomitant poly(ADP-ribose)polymerase (PARP) activation play crucial role in the development of metabolic syndrome and type2 diabetes. Our aim was (1) to determine the effect of OC treatment on the oxidative-nitrative stress and PARP activation in blood components; (2) and to correlate them to glucose metabolism parameters.

Materials and methods: Plasma total peroxid level was measured by colorimetric method in (1) women taking OC (present

users); (2) women, who stopped OC treatment less than 5 years ago (recent users); (3) women, who stopped OC treatment more than 5 years ago (non-recent users); (4) and age matched never users before and two hours after oral glucose tolerance test (OGTT: 75g glucose). Tyrosine nitration and PARP activation was also determined by immunohistochemistry using anti-nitrotyrosine (NT) and anti-poly(ADP-ribose) (PAR) antibodies. HbA1c level was also measured. Results: Women using OC had elevated total peroxide levels both before (1357.4 ± 478.5 $\mu\text{mol/l}$ vs. 635.8 ± 173.6 $\mu\text{mol/l}$, 540.9 ± 194.8 $\mu\text{mol/l}$ and 627 ± 325.6 $\mu\text{mol/l}$, $p<0.05$) and 120 (1423.2 ± 372.9 $\mu\text{mol/l}$ vs. 640.8 ± 145.9 $\mu\text{mol/l}$, 558.1 ± 194 $\mu\text{mol/l}$, and 636.3 ± 323.4 $\mu\text{mol/l}$, $p<0.05$) and 120 minutes after glucose load. We found no difference between never, recent or non-recent users in PO levels. PARP activation was similar in all groups. Nitrosative stress was increased among recent users compared to never users and users 120 minutes after glucose load ($45.5\pm28.5\%$ vs. $13.9\pm16.2\%$ and $21.8\pm12.4\%$, $p<0.05$). There was no difference in glucose and insulin levels during OGTT or any insulin resistance parameters between any groups. On the other hand women who never used OC had higher BMI (28.9 ± 7 vs. 22.9 ± 2 , $p<0.05$) than present users. They had significantly more deliveries (2.6 ± 1.2 vs. 1.8 ± 0.8 and 1.7 ± 0.7 , $p<0.05$) compared to past users. According to a stepwise multivariate regression model, in present users, post load total peroxide level significantly correlates with the time of maximal insulin level ($B=7.926$ $\mu\text{mol/l}$, $p<0.05$) and the 180 minute insulin value ($B=7.162$ $\mu\text{mol/l}$, $p<0.05$) ($r^2=0.91$). In present users fasting NT staining correlates with isulinogenic index ($B=9.3\%$, $r^2=0.91$, $p<0.001$), fasting PAR labeling correlates with age ($B=3.9\%$, $r^2=0.623$, $p<0.05$), post load PAR staining correlates with the 90 minute glucose value ($B=79.2\%$, $r^2=0.572$, $p<0.05$). On the contrary, analyzing non-users revealed no correlations. Conclusion: According to our results, oxidative stress is elevated during OC treatment. Besides, in women taking OC oxidative-nitrative stress and PARP activation is much more effected by the glucose metabolism parameters,

which may contribute to their increased metabolic risk.

Y/4 THE IMPORTANCE OF THE ACE I/D AS WELL AS ACTN3 R577X POLYMORPHISMS IN THE PERFORMANCE OF THE HUNGARIAN ELITE ATHLETES

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Keywords: ACE, ACTN3, gene, sport, genomics

Introduction: The most extensively investigated genes in the area of sport genomics are the ACE I/D allele and the ACTN3 R577X polymorphism. Our primary aim was to find, whether the influence on the complex phenotype of the ACE I/D alleles and the ACTN3 R577X polymorphisms are enough strong to cause significant difference in the sport achievements?

Methods: 100 (62men, 38 women) successful and 52 (37 men, 15 women) unsuccessful athletes were investigated. In the successful group were been the athletes whose have first to third rank in Europe or World Championship. The athletes in the control (unsuccessful group) haven't any significant international sport achievement, but all of them are member of the Hungarian National Team. Genomic DNA was isolated from white blood cells following a standard protocol. For the statistical analysis the SSPT software was used, the data were analyzed with cross table analysis and the chi-square test. The border of significance was 0.05.

Results: The investigation of the allele frequencies shows significantly higher I allele frequency in the unsuccessful group, and lower D allele frequency in the successful group. The frequencies of R alleles were significantly higher in the successful than in the unsuccessful groups.

Conclusions: The results of our study suggest that the D alleles and the R alleles can give an advantage not only theoretically or between isolated circumstances, than between real competitive conditions.

Y/5 SUBJECTIVE AND OBJECTIVE MEASUREMENT OF ACCOMMODATIVE AMPLITUDE OF THE HUMAN EYE

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Keywords: accommodation, spherical aberration, keratometry, pupillometry

INTRODUCTION: Accommodation is the ability to increase dioptric power of the eye to focus for near distances. This study compared an objective accommodation measurement method (Grand Seiko WAM-5500 autorefractor) with subjective push-up test and also investigated, which ophthalmological parameters show significant correlation with the accommodative amplitude.

METHODS: 44 subjects, aged 36.4 ± 16.5 participated (range 19.1-78.5 years). Four methods were used to stimulate and measure accommodation: 1) subjective push-up test in free space 2) measurement of the anatomical parameters of the eye (keratometry, higher order aberrations of the cornea, depth of anterior chamber, axial length) with an optical method 3) measurement of changes in the anatomical parameters during the process of accommodation with Pentacam HR device 4) finally we made autorefractometric examinations and pupillometry with a new binocular accomodometer (Grand Seiko WAM-5500).

RESULTS: The amplitude of subjective accommodation was significantly higher than the accommodation measured with objective method ($p=0.6$). Significant correlation can be seen between age and the following parameters: the size of the smallest read text ($r=0.72$; $p<0.001$), spherical aberration measured with Pentacam HR ($r=0.46$; $p<0.001$), changing of the chamber depth during accommodation ($r=0.31$; $p<0.001$) and the resting pupil diameter ($r=-0.568$; $p<0.001$). With age the pupil diameter narrows increasingly ($r=0.25$; $p=0.02$). We haven't found significant correlation between the accommodative amplitude and the

keratometric parameters, the axial length, and other higher order corneal aberrations. CONCLUSIONS: The accommodative amplitude lowers with age, but the age-dependent changes in the shape of the cornea and the increased narrowing of the pupil partly compensates this negative effect.

Z. State-of-the-Art Session

Z/1 WINE AND HEALTH

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laureate**

Hippocrates of Kos recommended wine as a tranquilizer, analgesic, diuretic, anti-diarrheic and for the treatment of wounds. According to the Bible, Good Samaritans poured oil and wine into wounds. J. Caesar the great strategist forced his troops to drink one liter of wine per day in order to prevent gastrointestinal infections which could determine the result of the battle. Claudius Galenus, Pergamon recommended red wine for the treatment of gastrointestinal diseases and also for internal bleeding. Paracelsus described alcohol as the constituent of wine and coined the word: "Weingeist". He also recognized that the effect of wine depends on the dosage ("dosis facit venenum"). Recently it has been proposed that the low cardiovascular mortality rate in spite of high fat intake in France, is due to alcohol consumption correcting the adverse effects of animal fat. Several multicenter studies prove that moderate consumption of wine

has beneficial effects on cardiovascular risk factors. There is a U-shaped relationship between alcohol intake and survival rate: non-drinkers die more frequently than modest drinkers, but heavy drinkers also have a higher death rate due to liver disease, cancer of the gut, traffic accidents and heart disease. Modest consumption of alcohol has other benefits such as preventing diabetes and osteoporosis. Moderate alcohol consumption significantly improves the cognitive function in elderly people. Drinking wine may decrease the risk of chronic renal failure. Beer consumption reduced the risk of death from heart disease by 20%, but wine consumption by 32%. Women have a lower risk of heart disease and benefit less from wine or alcohol. Diabetics have a high risk of heart disease and benefit from modest doses of wine. Smokers benefit more from modest consumption of alcohol than do non-smokers. Improved survival in victims of myocardial infarction is seen with moderate alcohol intake. Alcohol increases the fraction of high density cholesterol, the „good” cholesterol and inhibits coagulation of blood. Phenols and flavones in wine reduce oxidative damage to components of the vessel wall and improve the function of endothelial cells, the inner coating of the vessels.

Hungary has more than twenty historical wine yards, whose products maybe not only recommended in moderate consumption to improve health and prevent diseases, but have been famous culinary delicacies all over the world for centuries!

EDITOR'S NOTE

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The help of the Program Committee Chairmen, Florina Zakany and Dr. Gabor Horvath; Drs. David and Adam Tarnoki is appreciated in forwarding the abstracts they received. No alterations in content were carried out.

With questions or suggestions, please contact the Editor at ssomkuti@abington-repromed.com.

Thank you,

Istvan Somkuti MD PhD

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