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Welcome

Dear Participant:

It is my great pleasure to welcome you to Balatonfüred for Füred2013, the summer conference of Hungarian Medical Association of America. This year we gather again to learn from an extraordinary series of research topics presented by ambitious and talented young faculty, clinical residents, and medical students from around the country. The conference provides a great opportunity for meeting colleagues with similar interests, networking and building collaborations, and keeping abreast with current projects in basic, translational, and clinical research in Hungary.

We should remind ourselves that this scientific and social endeavor has emerged from the spirit of student exchange at the SUNY Buffalo Medical School, one of the most successful programs of HMAA. On behalf of the HMAA Board of Directors, I would like to express my sincere thanks to the leadership of our Hungary Chapter and the conference organizers for putting together another exemplary scientific and social agenda. They are indeed the best ambassadors for HMAA and for its mission of building and sustaining a bridge between medical professionals across the Atlantic.

Since the first meeting in 2009, the HMAA Füred conference has grown into a respectful occasion with close to 200 attendees, including an illustrious list of invited speakers, guests, and sponsors. This fact indicates the need for such events, but also speaks for the vision of the organizers who have chosen a spectacular location for the meeting. We are grateful to Professor Gábor Veress, long-time physician-in-chief of the Szívkorház, for offering, once again, this historic and elegant venue to hold the conference. Last but not least, we truly appreciate the support of Dr. István Bóka, mayor of Balatonfüred, for hosting our conference in one of Hungary's most beautiful cities!

With best wishes,
György Baffy, MD, PhD
HMAA President



A. PLENARY SESSION I.:

EDUVITAL-Complex Trends in Health Education/Prevention

A/1 INTRODUCTION; THE EDUVITAL CONCEPT

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The present state of health of our society and its long-term prospects assign indispensable tasks to every responsible person. Therefore, as *doctors, biologists, psychologists, teachers, sociologists, bioethicists and health policy experts*, we have launched the EDUVITAL NET Non-profit Society for Health Education.

We believe that health awareness largely depends on the widespread availability of modern biomedical and psychosocial knowledge, as well as on the personal motivation of each member of the society. Although proactive interaction between the expert and the individual is essential in every age-group, children and the young generation deserve special attention, with respect to shaping the future pattern of healthy lifestyle and the sustainability of the achievements.

How can we offer modern, useful and practical knowledge?

We intend to provide *complex, comprehensive and reliable* information on modern basic genetics, environmental awareness, nutrition, culture of movement, including the most important questions of school health, mental health, psychosomatic disorders, healthy aging, family and bioethics.

Science-based novel approach that is accessible and easily attainable

Based on our dissemination, we intend to initiate professional, interdisciplinary open discussions on issues related to the development of medicine and psychosocial science, as well as on professional initiatives wishing to renew traditional medicine.

A/2 CHILDREN'S INTELLECTUAL DEVELOPMENT IN GLOBALIZED WORLD

Prof. Dr. Anna Tompa

Department of Public Health, Semmelweis University

The development and technical achievements of mankind have made life in the 20th-21st century more tolerable, however, this has led to relatively good living conditions, higher life expectancy for more than seven billion people on Earth. At the same time the overuse of natural energy sources increased the pollution level in the environment causing green house effects and globalization of consumer society. High price has to be paid for development since with the advance of technology and motorization very great forces have been liberated from the depth of the Earth in the form of crude oil, natural gas and carbon. When these are combusted large amounts of carbon dioxide toxic metals and other pollutants have infiltrated the atmosphere accelerating global warming. By creating comfort and affluence, advanced transport means, making homes more comfortable, cooling techniques all the energy is exploited which the Earth has accumulated over billions of years in mineral resources. The ratio between poor and rich has risen from 1: 35 to 1 : 80. This uneven distribution causes international tension and imposes almost impossible tasks on international aid agencies in caring for the victims of war and ensuring medical supplies for the wounded. Besides the wars, the more desperate refugees form gangs of robbers turning cities into metropolises of fear. The aggression level of all mankind has risen. Organized crime does not spare children either, pornography is spreading. Increased acts of aggression have been carried out on children, but even children are involved in aggressive actions. There are 800 million people starving in the world and 2.5 million children starve to death per year. The neurosis of the civilized world is aggression and alienation and with the negligence of their souls the spread of drugs, alcohol and smoking especially among youth is spreading. The intensified stress and the unhealthy throbbing of the indiscriminate consumer society have the full support of international capital and the media. It is not only the desperately poor who feel the contrast but both sides of the world suffering from diseases. We are reminded of this contrast day after day, on television which shocks the youth and those

who wish to find a solution in their own way. There are more than 20 metals concern of residential exposure especially toxic to mental development in children . Interestingly, small amounts of these elements are common in our environment and diet and are actually necessary for good health, but large amounts of any of them may cause acute or chronic toxicity (poisoning; antimony, arsenic, bismuth, cadmium, cerium, chromium, cobalt, copper, gallium, gold, iron, lead, manganese, mercury, nickel, platinum, silver, tellurium, thallium, tin, uranium, vanadium, and zinc). Heavy metal toxicity can result in damaged or reduced IQ and mental productivity. Today these problems are globalized and unified by fast growing open societies and by the telecommunication, affecting life styles and socializations all over the world.

A/3 COLONISATION OF THE HUMAN BODY – DISADVANTAGES OF CIVILIZATION

Prof. Dr. Ferenc Túry

Institute of Behavioural Sciences, Semmelweis University

There are many cultural determinants of the human body. The presentation tries to interpret the influences of the civilization on the body from the viewpoint of medical anthropology and behavioural sciences. The human body became a „colonised” object of consumer society, the advertising industry and media. There are some modern forms of changing the body, e.g., tatoo, piercing, plastic/cosmetic surgery, body building, or the fitness and beauty industry. The sociocultural background of eating disorders reflect these influences. As a consequence, the body is the center of new obsessions: e.g., the Adonis complex of males means the overconcern relating to the masculine body, or the orthorexia is a dependence of healthy food.

Many of these phenomena include self-destructive behaviours. The modern civilization challenge the responsibility towards our body.

A/4 COHESIVE SOCIETY HEALTHIER INDIVIDUALS. STRENGHT AND WEAKNESS OF COMMUNITIES AND MINORITIES

Dr. Bea Dávid PhD habil.

Institute of Mental Health, Semmelweis University

For the past 20 years numerous researches have proved the strong relation between socioeconomic status and public health. Evidence suggests that income inequality is a key determinant of public health and mortality. (Wilkinson 1996; Kawachi and Kennedy 1997) Both on the individual, as well as on the societal level the feeling of belonging to others and being valued by others are strong protective factors against illness and ensures better mental health status. Better public health figures can be achieved if social cohesion, the level of societal integration is strengthened, ie. if people trust each other, care about each other and feel responsible for each other.

Based on the social cohesion approach my presentation gives an insight into the „Hungarian case”. Showing the relevant data and figures I attempt to explain the present from the past, and suggest some steps for the future.

A/5 EPIGENETICS....."YES, WE CAN!"

Prof. Dr. Andras Falus

Department of Genetics, Cell- and Immunobiology, Semmelweis University

From a biological point of view, the complex diseases are all multifactorial disorders, which means that the susceptibility to the disease is determined by interactions between multiple genes, gene networks, but also involves important covalent modifications of DNA and histones of non-genetic (epigenetic), environmental factors. In the last years immense amounts of genetic data were collected (e.g. GWAS/ENCODE results). Although we may now know the DNA sequences and variants in a genome, the uncovering the way how regulatory factors do a cell know which genes to turn on and which to turn off requires epigenetic studies, as well. Many epigenetic factors are closely related to our lifestyle. If it is true, one cannot avoid a further, provocative question whether the epigenetic modifications (a „cell memory”) could even be transmitted to the next generation of an organism? This last question is very important since it raises the point as to whether our lifestyle affects our children and grand-children. The conscious change of the lifestyle (e.g. diet, exercise, stress management, social elements,

etc), may basically alter the outcome of the complex diseases and life-span.

In this lecture, evidences will be summarized that „yes, we can” change our lifestyle, we can modify our inherited risk factors, we can significantly decrease the severity of the diseases and we can elevate the chances for healthy aging.

A/6 MEDICINAL PLANTS IN DENTAL PREVENTION

Dr. Bálint Bencze

PTE-ÁOK Institute of Laboratory Medicine

Introduction: Mouthwashes used in daily dental prevention consist mainly of synthetic active agents increasing the chemical exposure of the body. Aims: Our goal was to develop and analyze a new mouthwash based solely on natural medicinal herbs and volatile oils. Materials and methods: Our mouthwash was prepared by 40% ethanol extraction of 6 well known medicinal plants completed with 3 different antimicrobial essential oils. Antimicrobial effects of the mouthwash were examined on oral pathogens *Staphylococcus aureus*, *Streptococcus sanguis*, *Escherichia coli*, *Lactobacillus plantarum* and fungi like *Candida albicans*, *C. Krusei*, *C. glabrata* and *C. parapsylosis*. We used disk diffusion and tube dilution methods. Direct bactericide effect was studied by fluorescence microscopy with propidium-iodide stain. Bioautography was performed on Merck F254 silica layer, using *Staphylococcus aureus* and the above mentioned bacteria and fungi. 5 µl, 10 µl, 15 µl of mouthwash with gentamicine and/or fluconazole controls were tested. Flavonoid spectrum of our mouthwash was analyzed by densitometry after separation on silica layer. The effect of mouthwash on the saliva proteins was examined by SDS-PAGE (Laemmli). Results: The inhibition zone of the mouthwash was 8±1mm, by Corsodyl® 20±2mm, by ethanol 0mm, respectively (disk method). In tube assay the mouthwash showed a dose dependent effect with highest inhibition effect of 188.7 times slower multiplication rate compared to the control. In the propidium-iodide assay the 40% ethanol control contained 4%, while the mouthwash treated sample expressed 92% dead bacteria. In bioautography, the largest inhibition zone of our mouthwash was 9±1mm, the controls were 6±3

mm; in the tincture we could separate 12 different flavonoids and the salivary protein pattern was not changed after mouthwash exposure. Conclusion: Our completely natural mouthwash prepare possesses significant antimicrobial effect, is rich in flavonoids and does not modify salivary proteins.

Keywords: mouthwash, dentistry, prevention, plants, natural

A/7 EVALUATION OF A CREDIT COURSE ON LEARNING METHODOLOGY AIMING TO IMPROVE THE MENTAL HEALTH OF MEDICAL STUDENTS

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2009 szeptemberében követéses vizsgálat indult a Debreceni Egyetemen tanulmányaikat akkor kezdő, elsőéves magyar és angol nyelven tanuló orvostanhallgatók körében annak vizsgálatára, hogy a tanulmányokkal járó megterhelés hogyan és milyen mértékben változtatja a hallgatók lelkiállapotát, lelki egészségét. A korábbi adatfelvételek során megállapítható volt, hogy az orvostanhallgatók lelki egészsége jelentősen romlik a második évben az első évhez képest. Ugyanakkor a pszichés terheléssel való megküzdéshez az orvosképzésben résztvevő hallgatóknak egyénileg kell támogatás után nézniük, nem kapnak ehhez szervezett segítséget. Ennek a helyzetnek a javítására 2012 januárjában féléves, 30 órás kreditkurzus meghirdetésére került sor első és másodéves, magyar nyelven tanuló hallgatók számára, amelynek célja a kezdő hallgatók segítése volt a tanulmányokkal való megbirkózásban. A kurzus témái közt szerepelt a tanulmányok és vizsgák során alkalmazható relaxációs technikák áttekintése és gyakorlása, a tananyag strukturálásának lehetőségei, az elmetérképek alkalmazása, a prioritizálás és súlyozás fontossága, az időgazdálkodás módszerei, a vizsgadrukk kezelése, valamint viselkedés szimulált vizsgahelyzetekben. A kurzust két, jelentős oktatási tapasztalatokkal rendelkező, orvos végzettségű oktató tartotta. A kurzus megkezdésekor, illetve annak zárásakor is kérdőíves felmérés történt, amelynek eszköze a fentebb említett követéses vizsgálatban alkalmazott kérdőív rövidített változata volt, melyet a hallgatók jellegével láttak el, ennek révén

lehetőség volt a hallgatók kurzus előtti és utáni állapotának egyénenkénti megítélésére is személyazonosságuk feltárása nélkül. A résztvevők közül 15 hallgatónak volt értékelhető kérdőíve kurzus előtt és után is, közel fele-fele arányban nők és férfiak. Az eredmények alapján a kóros mértékű pszichés stressz ($p=0,008$) és a perfekcionizmus mint diszfunkcionális attitűd ($p=0,007$) átlaga a kurzus végére szignifikánsan csökkent, a dinamikus önbizalmat jellemző koherencia-érzés átlaga szignifikánsan nőtt ($p=0,029$). A depresszió és szorongás csökkent, de ennek mértéke nem volt szignifikáns. A speciálkurzus növelte a hallgatók megküzdési kapacitását.

Keywords: mental health, medical students, pilot, intervention, psychological stress

B-C MULTIDISCIPLINARY SESSIONS I-II-III.

B. Lung and cells session I. – Pulmonology

B/1 EFFECT OF HYPOXIA AND CIGARETTE SMOKE ON THE HYPOXIA-INDUCIBLE FACTOR 1A (HIF-1A) AND HEAT SHOCK PROTEIN 72 (HSP72) SYSTEM OF THE ALVEOLAR A549 EPITHELIAL CELLS

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Introduction: Smoking is the main risk factor of chronic obstructive pulmonary disease (COPD). In COPD alveolar hypoventilation caused by obstruction leads to alveolar hypoxia. We examined the effect of hypoxia and cigarette smoke on the expression of hypoxia-inducible factor 1 α (HIF-1 α) and inducible heat shock protein 72 (HSP72). Methods: We analyzed mRNA expression of HIF1 α and HSP72 in immortalized alveolar epithelial cells (A549)

using RT-PCR. The following groups were analyzed: FiO₂ 20,9% (control); 13 $\pm$ 1%; 6 $\pm$ 1%; 1 $\pm$ 1% and treatment with cigarette smoke extract (CSE). Changes in cell count and apoptosis were assessed. Results: Under hypoxic conditions cell count grew significantly (FiO₂ 13 $\pm$ 1%: 13,33x10⁵; FiO₂ 6 $\pm$ 1%:13,2x10⁵; FiO₂ 1 $\pm$ 1%: 2,86x10⁵ vs. normoxia FiO₂ 20,9%: 7,73x10⁵; $p<0.01$), whereas decreased when treated with CSE. Severe hypoxia and CSE treatment significantly lowered the HIF-1 α mRNA expression. HSP72 mRNA expression increased in normoxia, while decreased in both hypoxic and CSE treated cells. Conclusions: Hypoxia increases while CSE treatment decreases cell number. HSP72 mRNA decreases following hypoxic or CSE induced cellular stress, while severe hypoxia and CSE treatment decreases HIF-1 α mRNA expression of A549 cells.

Keywords: COPD, hypoxia, cigarette, smoke, HIF-1 α , Hsp72

B/2 IS THE EXHALED BREATHPRINT INHERITABLE?

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Introduction: The exhaled breath contains thousands of volatile substances whose production can be changed in various respiratory and systemic diseases. The electronic nose is analogue to the mammalian olfactory system, and consist of various carbon polymer sensors. The binding of the volatile gas molecules to the different sensors causes resistance changes, which are analyzed by a built-in computer and a "breathprint" is generated. Previously, e-nose has been able to separate the lung cancer under some conditions based on the "breathprint", but it is still unclear whether the "breathprints" are

determined by genetic or environmental backgrounds. Methods: 20 monozygotic (MZ) and 8 dizygotic (DZ) twin pairs participated in the study. We collected 2 air samples from each volunteer with a previously validated technique. The samples were analyzed with e-nose including 32 sensor signals. Principal component analysis was performed using the principal components (PC1, PC2 and PC3). Univariate genetic structural modeling was also done. Results: The breathprint was highly reproducible within subjects ($r=0.75$, $p<0.001$). Both the MZ ($r=0.66$) and DZ ($r=0.76$) twins significantly and highly correlated with each other ($p<0.05$). Adjusted for sex and age, shared environmental factors determined 93% and 94% of the variations of PC1 and PC2, respectively, while 54% of PC3. Unique environmental factors were responsible for the remaining variance. No genetic effects were found. Conclusions: Exhaled air "breathprint" is not inheritable, but strongly influenced by shared environmental factors.

Keywords: electronic nose breathprint biomarker twin exhaled volatile compound

B/3 ASSESSMENT OF OBJECTIVE AND SUBJECTIVE SYMPTOMS OF OBSTRUCTIVE SLEEP APNEA IN CHILDHOOD

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Introduction: Obstructive sleep apnea (OSA) in childhood is a common, but underdiagnosed disease. The gold standard of the diagnosis is polysomnography (PSG), but also the screening of the disease is needed. In our study, we analyzed the results of our sleep questionnaire for parents and compared it with the polysomnographic data of the patients. Methods: between May 2011 and September 2012, 102 children (age: 2-18 years, 52 % male) were examined with PSG at the 1st Department of Paediatrics, Semmelweis University. We assessed sleep quality with questions regarding to the sleep related problems occurring during a week. We analyzed the relationship between the frequency of OSA related symptoms (breathing difficulty, restless sleep, snoring and breathing pause; symptom

score) and the objective severity of OSA (apnea-hypopnea index (AHI), oxygen desaturation index (ODI)). Results: 31 children had mild, 12 moderate, 19 severe OSA. We have divided the children according to their symptom score into four equal groups. Children with the highest symptom score had significantly higher AHI and ODI than children in the lowest score group (lowest score vs. highest score, AHI: 4.2 ± 10.4 vs. 11.1 ± 15.7 ; $p=0.045$, ODI: 4.3 ± 10.6 vs. 11.8 ± 16.4 ; $p=0.037$). Among school-age children (age > 7 year) symptom score showed a moderate, positive correlation with AHI and ODI (AHI: $r=0.502$ $p=0.012$, ODI: $r=0.505$ $p=0.010$). Conclusion: the results of our questionnaire showed a good correlation with objective parameters of OSA. Therefore, it can be a potentially useful tool in the screening of OSA, but the validation is still needed.

Keywords: obstructiv sleep apnoe, polysomnography, screening of OSA, questionnaire, 4 symptoms

B. Lung and cells session II. – Immunology – Cell Biology

B/4 ROLE OF MACROPHAGES IN THE SURVIVAL OF MEGAKARYOCYTES IN THE SPLEEN

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Introduction: The spleen in both man and rodents is a complex lymphoid tissue performing multiple hematopoietic and immunological functions. The red pulp exerts auxiliary erythromyelopoietic activities, partly manifested by the presence of macrophages and megakaryocytes. It is not known what local tissue factors promote the survival of megakaryocytes. In our work we investigated the relationship between macrophage subsets and megakaryocytes. Methods: Amongst the macrophage lineage the marginal zone macrophages were identified by their sialoadhesin/CD169 (IBL-13) or MARCO (IBL-12) expression, red pulp macrophages by their F4/80 or IBL-15 epitopes, and megakaryocytes were detected by IBL-17 mAb and were evaluated by AnaliSYS software. The relationship between megakaryocyte survival

and presence of macrophages was investigated using various murine models; BALB/c mice following the administration of clodronate liposomes depleting macrophages, and in mice deficient for Nkx2-3 homeodomain transcription factor with progressive atrophy of splenic red pulp both in resting and TPO-agonist Nplate/romiplostin-treated mice. Results: We found that the splenic megakaryocytes show a cellular association in territories populated by F8/40-positive macrophages. Following clodronate treatment all macrophage subsets were eliminated, which was associated with the complete disappearance of megakaryocytes. In Nkx2-3 deficient mice with the near-complete lack of red pulp macrophages the megakaryocytes were undetectable, and TPO-agonist Nplate treatment also failed to induce megakaryocyte production in mutant spleens. However, the distribution of megakaryocytes in bone marrow was indistinguishable from normal controls. Conclusion: Our findings indicate that the red pulp macrophages in murine spleen play an important role in the homeostasis of extramedullary megakaryocyte pool, which is severely impaired in conditions with defective macrophage survival.

Keywords: megakaryocytes, Nkx2-3, macrophages, spleen, Nplate

B/5 DOES THE EXPRESSION OF THE FUSION PROTEIN NFH-GFP MODIFY THE COMPORTMENT OF A NON-NEURONAL CELL LINE (NIH-3T3)?

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Introduction. Neurofilaments are the most important components of the intermediate filament network in neurons. Previous researches showed that NFL molecules alone have the ability to form minimally assembled structures in transfected fibroblast cells, however they are not able to build complete filamentous network by themselves. NFH and NFM molecules seem to be necessary for neurofilament assembly. At the same time, fibroblast cells change their behaviour when a new part of intermediate filament system is introduced in them. These results let a new

question emerge whether there is a difference in comportment of fibroblast cells after NFH transfection or not. In this study, two groups of cells have been observed, a transfected type group with NFH-GFP in it and also a wild type group with NIH-3T3 mouse fibroblast. Methods. Four aspects have been measured during the research – cell proliferation, pseudopod number, pseudopod length and cell size. Results have been obtained for the most part with immunohistochemistry and microscopic techniques such as fluorophore staining probe. Results. Significant differences have been found in cell size and pseudopod number due to NFH-GFP transfection. Heavy type neurofilament molecules have an effect on cells' area and pseudopod length for certain reasons, namely both value increased as a matter of the transfection. Conclusion. Heavy type neurofilament units are likely to be the cause for this phenomenon but the mechanisms are not entirely clear therefore further experiments should be performed.

Keywords: NFH-GFP, NIH-3T3, cytoskeleton, Neurofilaments, Intermediate filament group

B/6 EXOSOMES MAY MEDIATE REMOTE ISCHEMIC PRECONDITIONING IN ISOLATED RAT HEART

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Mpharm, Peter Ferinandy

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Introduction: The extent of injury the heart can withstand during a prolonged ischemia can be limited by brief ischemia-reperfusion cycles applied either on a remote organ (remote ischemic preconditioning, RIPC) or on the heart (IPC) prior to the lethal ischemic insult. Its underlying mechanisms are still unclear. Exosomes (30-100 nm) are membrane-bound vesicles released by most cells as a means of intercellular communication. It is plausible that these particles are involved in propagating RIPC. Thus, the aim of our study was to test whether cardioprotection by RIPC is mediated by exosomes. Hypotheses: (1) IPC triggers release of exosomes from the heart (2) The preconditioned coronary perfusate contains

exosomes and elicits RIPC (3) Exosomes are necessary for eliciting the cardioprotection afforded by RIPC . Methods: Isolated Langendorff-perfused rat hearts were preconditioned by short ischemic insults. Coronary perfusates were collected and transferred to other isolated hearts, which underwent 30 minutes of global ischemia. After 2 hours of reperfusion infarct size was determined by TTC staining. Exosomes were isolated from the perfusate by ultracentrifugation and their presence was confirmed by particle analysis and electron microscopy. Results: Preconditioned coronary perfusate reduced infarct size in non-preconditioned hearts. Cardioprotection by preconditioned perfusate was comparable in extent to that afforded by IPC. Vesicle-depleted perfusate failed to induce cardioprotection. Exosomes and microvesicles (100-1000 nm) were detected in the preconditioned perfusate. Conclusions: Exosomes and microvesicles may play an essential role in the propagation of RIPC. The analysis of these particles can reveal cardioprotective mediators involved in RIPC and potentially lead to the development of novel anti-ischemic therapies.

Keywords: ischemia-reperfusion injury, cardioprotection, remote ischemic preconditioning, exosomes, microvesicles

C. Basic sciences: Anatomy, Biochemistry and Biophysics

C/1 INVESTIGATIONS ON THE THREE HIT THEORY OF DEPRESSION ON THE BED NUCLEUS OF STRIA TERMINALIS

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Introduction: Based on three hit theory genetic predisposition, epigenetic factors and chronic stress lead to manifest depression. The shortage on pituitary adenylate cyclase-activating polypeptide (PACAP) can cause depression-like behavior. The role of corticotropin releasing factor (CRF) in the hypothalamuspituitary-adrenal axis is well known in stress adaptation response; however the significance of extra-

hypothalamic CRF is largely elusive. We hypothesized that the three hit theory is applicable on mice and extra-hypothalamic CRF neurons in the BNST could be affected. Methods: 38 male PACAP heterozygote mice were exposed to 15 or 180 minutes maternal separation on postnatal days (PD) 1-14 vs. non-deprived controls. Half of the mice each group was exposed to chronic variable stress on 106-120 PD. The stress paradigm was validated by measuring the adrenal weight. Indirect CRF immunolabeling was performed on the sections of BNST. Results: Mice carrying all three risk factors showed significantly higher CRF specific signal density and showed 58% higher CRF immunoreactive cell counts in BNSTov. In subjects without maternal deprivation this alteration did not occur. Adrenal weights in mice exposed to both maternal deprivation and stress was significantly elevated. In conclusion the rise of adrenal weight demonstrates the adaptation to stress, and supports the validity of the model. CRF neurons in the BNST change their functions if all three risk factors of depression coincide. The use of three hit theory of depression in PACAP heterozygote mice seems to be a promising model for mood disorders, and requires further investigation.

Keywords: PACAP, Depression, CRF, stress, BNST

C/2 INTRAVENTRICULAR MICROINJECTION AND ELECTROPORATION FOR INVESTIGATING DEVELOPMENT OF SPINAL DORSAL HORN IN RAT EMBRYOS

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In utero electroporation (IUE) is a modern and useful tool for investigation of the embryonic development that can be used in those of species in that conventional transgenic technology is difficult to perform. This method includes injection of DNA vector into living embryos through the uterine wall followed by electroporation that results expression of the foreign gene by the neighbouring cells. The aim of our study was to apply the IUE method in rats to investigate spinal cord development focusing on the superficial laminae of the dorsal horn. We used time mated rats in the experiment; the operations were made in deep anaesthesia at

gestational days ranging from 14.5 to 16.5. After the sagittal incision of the abdominal wall, the pregnant uterus horns were prepared out of the abdomen. With continuous moistening, we localized the fourth ventricle through the uterine wall by using fibre optic illumination which was followed by the injection of the DNA vector (pmaxGFP) solution into it with a mouth pipette attached glass capillary. We let the injected solution diffuse from the ventricle to the central canal before the electroporation was performed. The uterus then was placed back to the abdominal cavity, and the surgical section was closed by double layer suture. Embryos collected, fixed and processed for histological examinations at the brainstem and cervical spinal cord levels after 1-6 days of their postoperative survival and the GFP expressing cells were investigated by epifluorescent microscope. The survival rate of embryos was approx. 40% after the in utero manipulation. Migrating GFP labelled cells were found in the brainstem and upper spinal segments as well proving the success of the electroporation. We were also able to detect labelled cells with neuron morphology in the superficial layers of the dorsal horn only one day after the electroporation.

Keywords: embryonic development, transgenic technology, intraventricular microinjection, in utero electroporation

C/3 TESTING THE RECOVERY FROM C-TYPE INACTIVATION OF SHAKER K⁺ CHANNELS WITH LOCKED-OPEN ACTIVATION GATE

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Introduction: The voltage-gated Shaker-IR potassium channels have two distinct gates, an activation and an inactivation gate. The functional crosstalk between these gates is well-established, the status of the inactivation gate influences the movement of the activation gate. However, none of the previous studies determined whether the coupling between these gates is bi-directional or not. We hypothesized that the locking the

activation gate in the open configuration prevents recovery from C-type inactivation. **Methods:** To test this hypothesis we engineered cysteines at positions 476 of the pore forming S6 segments in a Shaker-IR background. The T449A/V476C channels were expressed in tsA-201 cells. Channels were trapped in the open state by Cd²⁺ bridges between a cysteine in one subunit and a native histidine in a neighboring subunit. Experiments were performed with excised inside-out patches. **Results:** 2s long depolarizing pulses to +50 mV were applied first in the absence and then in the presence of 20 μ M Cd²⁺. The duration of Cd²⁺ application was 0.2s or 1.0 s long. In both cases Cd²⁺ was added intracellularly to the fully inactivated channels. Between the pulses the patches were held at -120mV for 60s. The analysis of the peak currents showed that under control conditions nearly 100% of the channels recovered from inactivation, whereas the extent of recovery from inactivation was irreversible decreased by Cd²⁺ exposure. **Conclusion:** The lack of recovery from inactivation of the locked-open channels suggests that closure of the activation gate is essential for the recovery from C-type inactivation.

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

C/4 INVESTIGATION OF INTERACTIONS BETWEEN RAR AND RXR USING FLUORESCENCE CORRELATION

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Nuclear receptors are transcription factors that are able to regulate gene expression in a ligand dependent manner. They play a central role in cell differentiation, growth, and death. We investigated interactions and dynamics of retinoic acid receptor (RAR) and retinoic X receptor (RXR) acting in a dimer in living cells. Their operation is described by the nuclear receptor molecular switch model. In the absence of ligand receptors are bound to DNA associated with a corepressor complex, and repress

transcription. In the presence of agonist (Vitamin A derivative) receptors change their conformation, and the corepressor complex is replaced by coactivator complexes resulting in gene transcription. Nowadays, this model is being changed for a more dynamic one due to intense investigations in the field. In our studies we wanted to determine the affinity of the receptors to chromatin and to each other in the absence and the presence of ligand. We transfected HeLa cells with nuclear receptors marked by fluorescent proteins (GFP, mCherry). We monitored changes in mobility by fluorescence correlation spectroscopy (FCS), a method capable of following the dynamics of fluorescent molecules with high sensitivity. Previously we revealed that agonist treatment decreased the mobility of GFP-RAR or GFP-RXR molecules transfected alone. Our new results show that co-transfection of the two receptors decreases their mobility even in the absence of ligand. This is probably due to the increased affinity of the RAR-RXR complex to the chromatin as compared to that of the monomers. Later, we want to determine the dissociation constant of RAR-RXR dimers, and its dependence on ligand treatment by using fluorescence resonance energy transfer.

Keywords: nuclear receptors, fluorescence correlation, spectroscopy, molecular switch

C/5 THE MECHANISM OF ACTION OF ELISIDEPSIN IN NORMOXIA AND HYPOXIA
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Introduction: Elisidepsin is an experimental chemotherapeutic drug, which acts by destroying the cell membrane. The stability of lipid rafts depends on the number of hydrogen bonds, which is increased by the enzyme fatty acid hydroxylase (FA2H), which can only work in the presence of an appropriate concentration of oxygen. Methods: Cells were cultured in an atmosphere containing 1% oxygen. FA2H expression was analyzed by immunofluorescent staining. The sensitivity of cells to elisidepsin (IC50) was determined by measuring the activity of mitochondrial dehydrogenases. Lipid rafts were visualized by transfecting cells with GPI-

anchored GFP (GPI=glycosyl-phosphatidylinositol) and their aggregation state was measured by number and brightness (N&B) analysis. Membrane permeability was assessed by propidium iodide uptake. Results: Hypoxia decreased elisidepsin sensitivity and its effect correlated with the IC50 measured in normoxia, which strongly correlated with the expression level of FA2H. Hypoxia did not have any effect on the most sensitive cells. According to N&B measurements hypoxia decreased the aggregation state of GPI-GFP. GPI-GFP and fluorescently labeled elisidepsin colocalized in confocal microscopic images. The binding and the membrane permeabilizing effect of elisidepsin is characterized by different half maximal concentration, and the latter is highly cooperative. Conclusions: Elisidepsin binds directly to lipid rafts. Hypoxia generally decreases elisidepsin sensitivity by modifying the structure of lipid rafts and decreasing the level of hydroxylated lipids. Our results could explain the variable efficacy of the drug in clinical trials.

Keywords: chemotherapeutic drug, hypoxia, lipid rafts, fatty acid-2-hydroxylase, cooperativity

D. PLENARY SESSION II.:

Medical Imaging session – Radiology

D/1 ORBITAL ULTRASOUND ON ORBIT

Dr. Zsolt Garami

Methodist Hospital, Houston/USA

D/2 PREDICTORS OF THE NAPKIN-RING SIGN IN CORONARY CT ANGIOGRAPHY

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Background: certain morphological pattern in coronary CT angiography (CCTA), a hyperdense ring-like structure surrounding a hypodense center, described as “napkin-ring” sign, (NRS) is

associated with advanced coronary plaque as defined by the AHA classification. Objective: The purpose of this study was to identify histologic characteristics of advanced coronary atherosclerotic plaques that are related with the detection of the napkin-ring sign in coronary CT angiography. Methods: CCTA was performed in 7 human donor hearts. Histological slicing and stainings were performed in 1 mm increments of each major coronary artery. Histology was co-registered with the CT-data and classified according to the modified AHA classification. Results: Advanced plaques were present in 139 (23%) of 611 cross sections. Of these 33 (24%) demonstrated an NRS in CCTA. NRS plaques were associated with greater non-core plaque area (median 10.2 vs. 6.4 mm², $p < 0.01$) and larger vessel area (median 17.1 vs. 13.0 mm², $p < 0.01$). The area of the necrotic/lipid core was larger in plaques with NRS (median 1.1 vs. 0.5 mm², $p=0.05$). Angiogenesis tended to be more frequent in plaques with NRS (48% vs. 33%) whereas micro-calcifications tended to be more frequent in plaques without NRS (27% vs. 46%) ($p=0.06$ and 0.07 respectively). In a multivariate analysis, necrotic/lipid core area (OR=1.9), non-core plaque area (OR= 1.6), and total vessel area (OR=0.9) independently predicted the appearance of the NRS in coronary CT angiography. Conclusion: Delineation of NRS in CCTA is independently linked to the size of the necrotic/lipid core, the size of the non-core plaque and to the vessel area as measured in histology of advanced coronary atherosclerotic plaques.

Keywords: Napkin-ring sign, Coronary CT Angiography, Coronary Artery Disease, Atherosclerotic plaque, Histopathology

D/3 COMPARATIVE EXAMINATION OF MAGNETIC RESONANCE CONTRAST AGENTS ON LOW AND HIGH MAGNETIC FIELD

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Purpose: Magnetic resonance imaging (MRI) is one of the most developing and promising fields of medical imaging. Our research aim is to

compare MRI contrast media and different solutions on Earth-field and on clinical MRI with 1.5T magnetic field. Methods and materials Experiments were performed on an Earth-field MRI device and on a 1.5T clinical MRI scanner. Different concentrations of Na, Mn and Gd containing solutions and three types of contrast media (Omniscan, Optimark, Dotarem) were investigated. T1 and T2 relaxation time measurements were performed five times in a row and five times separately as a control on the Earth-field device for each concentration. T1 and T2 mapping were performed on 1.5T. Evaluations were performed using dedicated softwares and special mapping program packages. Results were summarized into a database.

Results Relaxation times of paramagnetic solutions and contrast agents changed according to the concentrations. Relaxation times were correlated on 1.5T magnetic field and on the Earth's magnetic field, but shortening of relaxation times were noticed even in lower concentrations on Earth-field. The concentration differences of diamagnetic solutions has no effect on relaxation times. Discrete changes of temperature have no influence on relaxation times.

Conclusion Paramagnetic solutions (containing Mn and Gd) has effect on relaxation times, specific to the solution's type and concentration. EfnMR measurements were more accurate on low contrast-media concentrations comparing to experiments on 1.5T device. T1 relaxation times were significantly different ($p<0,05$) on low and on high magnetic field of paramagnetic compounds solutions we studied. The presented research can be a forerunner of developing new contrast media and biomarkers that can support new clinical applications on both low and high field MRI.

Keywords: magnetic resonance imaging, contrast media earth-field imaging, paramagnetic substance mapping

D/4 DEFINING THE OPTIMAL SYSTOLIC PHASE TARGETS FOR DUAL-SOURCE CORONARY CTA

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Purpose: Dual-source computed tomography angiography has been shown to maintain diagnostic image quality over a wide range of heart rates and rhythms by using an absolute reconstruction delay time after the R-R interval, because the length of systole is a relatively fixed physiologic phenomenon versus diastole. However, the ideal phases of the R-R interval using this method have not been defined. **Methods** We analyzed images reconstructed between 200 and 420 milliseconds (msec) after the R-wave at 20 msec intervals in 10 patients, using 6 coronary landmarks (ostial right coronary artery, first acute marginal branch, posterior descending artery, left main coronary artery, first obtuse marginal branch, and second diagonal branch). A workstation was used to precisely locate X, Y and Z coordinates for each landmark in all phases to calculate velocities. Differences in velocities were assessed by analysis of variance for repeated measures; Bonferroni post-hoc tests were used for multiple pairwise comparisons. **Results** 720 landmarks were measured (6 locations at 12 systolic time points in 10 patients). The mean lowest velocity timepoints for each coronary segment were significantly different, ranging from 240 msec (lowest mean velocity 38.6 mm/s) in the second diagonal segment, to 340 msec (lowest mean velocity 37.8 mm/s) in the ostial right coronary artery segment. **Conclusion** During an absolute delay of 200 to 420 msec after the R-wave, the ideal reconstruction interval varies significantly among coronary segments. Thus a narrow range of systolic intervals, rather than a single phase, should be acquired.

Keywords: coronary, computed tomographic angiography, coronary artery motion, systolic phase, image reconstruction, ideal systolic intervals

D/5 OBJECTIVE EVALUATION OF EMBOLIZATION OF THORACIC ENDOVASCULAR AORTIC REPAIR BY TCD AND BY AORTIC CALCIUM SCORE

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Introduction: Thoracic Endovascular Aortic Repair (TEVAR) placement has become a widely acceptable treatment alternative to open repair of the thoracic aorta. As surgeons are continually pushing the limits of these devices, the device companies make necessary device improvements. Cerebral embolization during TEVAR is well described and potentially the most catastrophic event during the procedure. There is a lack of objective data on how device modifications influence embolic rates, so our aim is to quantify the number of microembolic signals (MES) detected by Transcranial Doppler (TCD) during TEVAR using two different generations of endovascular devices and correlate with MES with calcium score (CS) of the aorta, landing zones, and clinical outcomes. **Methods:** Twenty-four patients with thoracic aortic aneurysms (TAA) were managed by TEVAR. Twenty (20) TAG and 4 cTAGs (W.L. Gore & Associates, Flagstaff, Arizona) were implanted and monitored using TCD during the entirety of the procedure. Calcium score was calculated on a TeraRecon workstation with automated selection and measurement tools. A Hounsfield Unit (HU) cut-off value set at 80. Imaging and procedural details were entered into a combined database. Data was collected retrospectively. **Results:** The average of MES calculated for the diagnostic segment (DS) before TEVAR placement and during device placement (DP) for all cases of the TAG and cTAG 8/46 and 5/11 respectively. The pigtail catheter and device placement generated the highest MES counts during the procedure. The decrease in MES using the cTAG was independent of aortic calcium score/volume (11cc vs 12cc total volume). Embolic counts to right / left (Rt/Lt) sides were overall equal. **Conclusions:** The ability of TCD to detect cerebral emboli helps in the identification of the procedural steps, most likely to cause stroke. The use of techniques that limit the wall contact, like endovascular robot may prove to be beneficial.

Keywords: TCD, Thoracic Endovascular Aortic Repair, calcium score, thoracic aortic aneurysm, microembolic signal

D/6 ST ELEVATION, POSITIVE CARDIAC BIOMARKERS, NEGATIVE CORONARY ARTERIOGRAPHY; THE ROLE OF CARDIAC MRI

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Approximately 5% of coronary angiographies performed due to acute coronary syndrome fails to reveal organic coronary disease. In some cases currently applied diagnostic procedures are not informative enough in the diagnosis of underlying disease. The aim of our study was to investigate the diagnostic role of magnetic resonance imaging (MRI) in patients with the suspicion of ST-elevation myocardial infarction (STEMI) but without significant coronary artery disease. Our prospective study was performed from 2007 to December 2011, during this period coronary angiography was performed in 2851 pts with the suspicion of STEMI. In 70 pts (2.4%) coronary angiography failed to reveal organic coronary disease. The 70 patients (58 males, mean age: 35±15 years) underwent acute cardiac MRI examination in the first 7 days. In long and short axis planes ECG synchronized „cine movie”, T2-weighted STIR, and delayed contrast enhancement images were taken. Using cine images both ventricular end-diastolic (EDV) and end-systolic volumes (ESV), ejection fractions, masses, wall motion disturbances, on delayed contrast enhancement images myocardial damage, on STIR images regions with oedema was evaluated. Cardiac MRI examination proved acute myocardial infarction in 9 cases (6 males), Tako-Tsubo cardiomyopathy in 5 cases and myocardial contusion in 1 case. In five patients MRI showed no cardiac disorder. In fifty patients (46 males) characteristics of myocarditis were found: subepicardial oedema and subepicardial delayed enhancement in 44 and 50 cases, respectively. In pts with myocarditis left ventricular ejection fraction was: 54.7±8.7%, ESV index 39±12 ml/m², EDV index 91.5±17 ml/m²,

with quantitative analysis 5% of LV mass was necrotic. In most cases (30 pts) basal inferolateral region was affected. There was no correlation between left ventricular subepicardial necrotic mass and ejection fraction. In cases of clinical features of ST-elevation infarction and normal coronary angiography cardiac MRI examination can prove the diagnosis, providing exact morphological and functional information of the diseases.

Keywords: the role of cardiac MRI, cardiac MRI, ST elevation, negative coronary arteriography, differential diagnosis, myocarditis

D/7 DIAGNOSTICS AND MONITORING OF ABDOMINAL SOLID TUMORS WITH DIFFUSION-WEIGHTED WHOLE-BODY IMAGING WITH BACKGROUND BODY SIGNAL SUPPRESSION (DWIBS) IN CHILDREN

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Introduction: Neuroblastoma and Wilms tumor are the 13-16% of pediatric malignant diseases. More than 70% of the patients are under the year of 5. Beside the children's good recovery tendency, in the cases with bad prognosis it's important to have an early diagnosis and keep a strict monitoring procedure after the treatment. CT should be avoided due to radiation exposure. Children are known to have a higher inherent sensitivity to the negative effects of ionizing radiation. Diffusion-weighted whole-body imaging with background body signal suppression provides functional information of the entire body in a non-invasive manner and can be used for the detection of pathologic processes. Method: Retrospective study of children suffering from Neuroblastoma or Wilms tumor and treated at the 2nd Department of Pediatrics at Semmelweis University since 2009. The aim of this thesis is to investigate the potential of Diffusion weighted whole-body imaging with background body-signal suppression (DWIBS), and suppose this technique for the substitution of examination with contrast agents. Results: DWIBS has a high sensitivity. Specificity is lower, because changing in diffusion can occur not only in malignancies, but in inflammation, necrotic or

apoptotic processes as well due to a higher cellular density or loss of cell membrane integrity. Conclusion: Since DWIBS can be similarly applied to obtain volume measurements and is able to detect early changes in function (decreasing viability) in areas involved with tumor before structural changes may become visible, it may be a promising tool in monitoring response to therapy.

Keywords: Neuroblastoma, Wilms-tumor, DWIBS MR, Pediatrics, Innovation

D/8 TRANSCRANIAL DOPPLER (TCD): THE PREMIER MULTIDIMENSIONAL MONITORING MODALITY FOR CAROTID INTERVENTIONS

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Introduction: TCD during carotid endarterectomy (CEA) has traditionally been regarded as an embolization detection system. TCD additionally determines flow velocity, flow direction in the MCA and ACA. These are the attribute needed to make a real time technical decisions (shunt placement, BP management), to evaluate efficacy of the intervention and to direct immediate salvage when necessary. TCD assistance for shunt selection and for stroke detection during carotid endarterectomy was investigated. Method: MCA monitoring was performed during CEA. Previously established criteria of an MCA velocity (V) drop of more than 50% was used to determine the need for shunt placement. Results: 102 (24 females, 78 male, 68 average age) had monitoring of 54 right, 48 left sided CEAs. Shunts were placed in 41 (41%), shunting was determined by MCAV. A major embolization preclamping was the event that provoked our single postoperative stroke with normal cerebral angiogram, but watershed lesions on MRI. 3 additional postoperative cerebral angiograms were performed after MCAV velocity did not improve post clamp release. This prompted 2 reoperations and where we detected 1 terminal ICA occlusion with string sign and 1 hyperperfusion (doubled MCAV) treated with hypoventilation and MAP decrease. Conclusion:

Our study suggests the potential value of TCD beyond simple embolic detection. MCAV plays a major role in guiding our CEAs, potentially decreasing shunt injuries, procedure time and bleeding.

Keywords: TCD, Carotid endarterectomy (CEA), real-time decision, shunt, stroke

D/9 CHARTING THE DEVELOPING BRAIN IN UTERO: FUNCTIONAL MRI STUDIES OF THE FETUS

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Endeavors to explicate the architecture and functional capacities of the human brain confront its vast complexity most pronouncedly when describing the interactions and interconnections of its neuronal processing units. Efforts in this direction gave rise to the notion of connectomics, research investigating large-scale interactions mediated by axonal fibers (structural connections) or characterized by causality or co-activation of distributed domains (functional connections). The processes that shape the connectome into its mature form during in utero development are yet poorly understood in humans. In this study, we benefit from the advent of “resting state” functional MRI, a technique which enables to chart the co-activation of brain areas. This can be utilized to image developing fetuses noninvasively, in utero. These observations will be integrated into a temporal (week-by-week) atlas of fetal connectome development in which structural imaging is combined with depiction of the brain connectivity. In the preliminary phase of the research project, the group already succeeded in acquiring a large set of fetal fMRI data. Radiological image processing software was optimized to tackle the problems of image artifacts and fetal motion. As a result, the main

commissural, association and thalamo-cortical connectivities can be visualized in the second and third trimester of development. The noninvasive structural and functional mapping of fetal brains is a pioneering field in human brain research. Ultimately the project could result in insights into the relationship of functional and structural connectivity during development and re-organization, providing for surrogate markers for clinical evaluation, function loss, and neurodevelopmental diseases.

Keywords: radiology, neuroscience, functional MRI, fetal development, brain connectivity

D/10 THE 3D EXAMINATION OF THE LOWER LIMB'S AXIAL PARAMETERS IN CHILDREN

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INTRODUCTION: The examination and understanding of the lower limb's anatomical and biomechanical properties is essential to define reference values, to understand the mechanisms of impairment, and to develop adequate therapeutic methods and instruments. The EOS device is a new method in the field of radiology, which produces 3D reconstruct able, stereo images of the skeleton of a physiologically positioned (standing or sitting) patient with low dose radiation. The goal of our study is to define the lower limb's axial parameters in age-divided groups and to determine their sexual characteristics. **METHODS:** We have reconstructed 508 child's (age 4-16 year) lower limb EOS 2D/3D image, while measuring more geometrical parameters. All of the examinations were made with orthopaedic indication to diagnose a disease, but no deformation was found, which could change the biomechanics of the lower limb. We have analysed the items statistically by paired sample t-test, Welch test and regression analysis. **RESULTS:** We have found sexual differences in factors influencing the axial parameters in the following cases: The mechanical angle of the femur increases from 92,297° to 93,027° in boys and 92,989° to 93,399° in girls. The tibial mechanical angle is around 88° in boys, and 89° in girls. The mechanical tibiofemoral angle decrease from

1,220° to -1,775° in boys, and 1,030° to 0,289° in girls. The femorotibial rotation increase from -1,350° to 3,361° in boys, and 1,825° to 7,472° in girls. The HKS (the angle between the anatomical and mechanical axis of the femur) has shown no relation with gender. It's value increases from 3,946° to 4,444°. **CONCLUSION:** We could determine parameters, which have not been defined in this age-group before or just by studies with a limited population or accuracy. We can confirm the characteristics of the lower limb's age and gender related development.

Keywords: Lower limb, Axial parameters, EOS, Children, 3D reconstruction

E. LUNCHTIME SESSION

E/1 MASS PSYCHOGENIC ILLNESS- THE LEROY CASES AND THE EFFECTS OF SOCIAL MEDIA

Dr. Laszlo L. Mechtler

Dent Neurologic Institute, Buffalo/USA

F. MULTIDISCIPLINARY SESSION IV. -

Surgery session

F/1 LAPAROSCOPIC, SINGLE PORT LAPAROSCOPIC AND ROBOTIC SURGERY - NEW ADVANCEMENTS OF LAPAROSCOPIC AND ROBOTIC SURGERY

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University of California, Davis Dept. of Surgery

The introduction of laparoscopic surgery in the 1980s opened the door for general surgery to enter the computer age. Some surgical procedures, such as laparoscopic cholecystectomy became quickly and widely

accepted; some has taken a longer learning curve and acceptance (gastric bypass, colectomy). In recent years new forms of minimally invasive surgery have been introduced. In this paper we will review these advances. Natural orifice and single port surgery has been introduced about 7 years ago. Natural orifice surgery is still in experimental phase and only performed in a few selected centers. It involves entering the abdominal cavity through a natural orifice: via the mouth and stomach; via the rectum; or the vagina. Various surgical procedures (cholecystectomy, appendectomy, and nephrectomy) can be performed with a scarless procedure. Potential severe complications (leak at the entry site) and lack of proper instrumentation are hindering acceptance of this technique. Single site access surgery, on the other hand, is becoming more and more used for various procedures. It has the advantage of reduced scarring by entering the abdomen at the umbilicus. All the instrumentation and the camera are introduced through a special port. The development of these special ports and instruments are facilitating the acceptance of these procedures. Long term studies are not available yet to demonstrate significant benefits of these procedures to conventional laparoscopy. Robotic assisted surgery continues to evolve in general surgery, especially in complex procedures, where the main advantages (stable camera platform, articulating instruments, 3-D imaging and ergonomically correct position of the surgeon) are important. Robotic assisted single port surgery has been introduced about 2 years ago, with promising early results. Endoluminal surgery and intraoperative real time imaging are currently introduced, and will be available in the near future.

Keywords: laparoscopic surgery, robotic surgery, minimally invasive surgery, single port surgery, natural orifice surgery

**F/2 SURGICAL MYOCARDIUM
REVASCLARIZATION FOLLOWING
PERCUTANEOUS CORONARY INTERVENTION IN
THE DEPARTEMENT OF CARDIAC SURGERY
UNIVERSITY OF DEBRECEN BETWEEN 2007-2012
Péter Csizmadia, Tamas Debreceeni, Tamas Szerafin**

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Cardiology, University of Debrecen**

Background: Percutaneous coronary intervention (PCI) is the most common treatment for revascularization of ischaemic myocardium. Following successful PCI 15-30% of patients require repeated coronary intervention. **Objective:** This study examines the outcome, morbidity and mortality of cardiac surgery following percutaneous coronary intervention. **Patients and methods:** Between 1. January 2007. and 31. December 2012. 592 patients underwent isolated CABG after PCI in our department. 146 women and 446 men with the mean age of $60,6 \pm 9$ at the time of surgery. **Results:** More often restenosis developed after initially successful PCI or progression of the coronary artery disease, less cases PCI failure and unsuccessful intervention were the indication for CABG. At the first procedure the patients who had 1 or 2 vessel disease, by the time of the surgery mostly 3 vessel disease was developed. Therefore the mean number of the distal anastomoses was higher. **Conclusion:** Based on our results an increasing number of patients PCI procedures have been performed before they are referred to CABG. The interval between PCI and surgical myocardium revascularization, moreover the high rate of patients with multivessel disease emphasise the importance of proper patient selection before PCI.

Keywords: coronary intervention, revascularization, myocardium, surgical

**F/3 MORPHOLOGICAL AND FUNCTIONAL
CHANGES DURING TRIGGERED LIVER
REGENERATION**

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Introduction: Selective portal vein ligation (PVL) results of ipsilateral atrophy and hypertrophy of contralateral liver segments. The aim of the present study was to examine the morphological

and functional changes during this process. Methods: Male Wistar rats (n=70) underwent PVL. The portal venous supply of the 80% of whole parenchyma was ligated (lobes III-VII). The animals were sacrificed 0, 12 hours, 1, 2, 3, 5, 7 days after PVL. Histological examination (necrosis, apoptosis, mitosis, glycogen content) was performed. Wet-to-dry and liver regeneration ratio were calculated. Bile secretion was performed by selective bile cannulation before and 7 days after PVL. Results: Liver regeneration rate was 7 days after PVL 266,2% in lobes I-II and 18,8% in lobes III-VII. The division of cells in regenerated lobes were found significantly higher 1 day after PVL (54.6 vs. 0.2) and reached maximum by 48 hours (56.3 vs 0.2). Apoptosis scores were the highest in the portal vein ligated lobes 2 days after PVL (43.6 vs. 0). Necrosis scores were the highest in the portal vein ligated lobes 1 day after PVL. Oedema content of both the regenerated and portal vein ligated lobes increased moderately. During selective-bile-duct cannulation, bile-flow in contrast to the control increased in regenerated lobes (30,3% vs. 71,6%) and decreased in portal vein ligated lobes (69,6% vs. 28,8%). Conclusions: According to our data it can be suggested that PVL induced liver regeneration causes not only weight increase, but functional recovery as well.

Keywords: portal vein, ligation, liver regeneration, bile secretion, morphology

F/4 INTERACTION OF POSTCONDITIONING AND TOLL-LIKE RECEPTORS IN MESENTERIC ISCHEMIA-REPERFUSION

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Background. Ischemic-reperfusion (I-R) injury of the small intestine occurs most frequently following superior mesenteric artery (SMA) occlusion. Applied at the onset of reperfusion, postconditioning - brief, repetitive, alternating cycles of reperfusion- and reocclusion, prior to

the vessel's free reperfusion -, seems as a suitable method for attenuating tissue damage. As part of the innate immune system, toll-like receptors (TLRs) play an important role in the pathogenesis of I-R injury. The aim of the study was to examine the effects of postconditioning on local TLR expression-, and on local redox- and systemic inflammatory states. Methods. Male Wistar rats underwent 60 minutes of SMA clamping, and 360 minutes of reperfusion. The animals were randomized into 3 groups: SHAM-operated, I-R control (IR), and Postconditioned (PC). Postconditioning was performed in 6 cycles of 10-10 seconds of reperfusion and reocclusion each. Following the end of reperfusion, blood and tissue samples were taken for further histological analysis, and measurement of local TLR mRNA expression. Furthermore, an intestinal mucosal section was homogenized for the assessment of local redox state. Serum TNF- α and IL-6 levels were also measured. Results. Compared to the I-R control group, the postconditioned group presented milder tissue injury, increased TLR mRNA expression ($p<0,05$), and lower TNF- α ($p=0,002$)- and IL-6 ($p=0,004$) serum concentrations. Paralelly, postconditioning amended the mucosal redox state by increasing the number of -SH agents (I-RDuodenum: $1,41\pm0,24$ mmol/l; I-RJejunum: $1,44\pm0,2$ mmol/l; I-RIleum: $1,31\pm0,31$ mmol/l; PCD: $1,88\pm0,13$ mmol/l; PCJ: $2,04\pm0,47$ mmol/l; PCI: $1,65\pm0,18$ mmol/l), and H+-donor activity (I-RD: $76\pm13\%$; I-RJ: $71\pm9\%$; I-RI: $56\pm22\%$; PCD: $93\pm6\%$; PCJ: $83\pm15\%$; PCI: $69\pm10\%$). The total mucosal reducing power was also enhanced (I-RD: 256 ± 52 AS/g; I-RJ: 233 ± 33 AS/g; I-RI: 231 ± 46 AS/g; PCD: 304 ± 66 AS/g; PCJ: 324 ± 65 AS/g; PCI: 294 ± 41 AS/g). Conclusions. Postconditioning proved capable of modulating intestinal mucosal TLR mRNA expression, and attenuating intestinal I-R injury following SMA occlusion.

Keywords: small intestine, ischemia-reperfusion, postconditioning, toll-like receptors, arteria mesenterica superior

F/5 MEDICAL CHALLENGES OF HEALING TUMORS OF HORSESHOE KIDNEY

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Introduction The horseshoe kidney is the most common type of renal fusion anomaly. Every urologic disease, including malignancy has been described in the horseshoe kidney. Prognosis is dependent on the same factors as in nonfused kidney. Highly variable vascular supply and the bridge of renal tissue that connects the left and right renal moieties can be challenging when planning surgical intervention. **Methods** A case of a renal cell carcinoma within a horseshoe kidney is presented. A 47-year-old Caucasian man presented with acute epigastric pain of several hours. He was afebrile and physical examination revealed no abnormalities beyond epigastric tenderness. CT angiography demonstrated 4cm large tumor of the right side. Kidney was receiving supply from two arteries on both side. A transperitoneal hand-assisted laparoscopic heminephrectomy was performed on the right side. There were no intraoperative complications. **Results** The histopathology examination showed pT1a, grade 2-3 carcinoma clarocellulare. The patient remains asymptomatic 12 months after his partial nephrectomy, with stable renal function. **Conclusion** With this case we would like to highlight, that radiographic imaging studies can play a vital role for guiding minimally invasive intervention and that less blood loss, less adhesions due to the laparoscopic techniques can lead to much faster recovery.

Keywords: horseshoe kidney, carcinoma clarocellulare, laparoscopic heminephrectomy, minimally invasive intervention, CT angiography

F/6 IN-HOSPITAL MORTALITY AND MORBIDITY OF OPEN SURGICAL AND ENDOVASCULAR TREATMENT OF ELECTIVE INFRARENAL AORTIC ANEURYSM

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Open surgery and stentgraft implantation may both mean surgical solutions for infrarenal aortic aneurysms (AAA). The number of aortic endovascular procedures increased significantly in the last decades, but the indication of the preferred method in patients who are fit for surgery is still not clear. Inconsistent data are available about in-hospital mortality and morbidity in centres with different level of expertise in open and endovascular technique. We studied the in-hospital mortality and morbidity of open surgery and stentgraft implantation in the cases of elective AAA. Our aim was to determine whether our results support stentgraft implantation to become the first treatment of choice in this cohort. We analyzed the hospital chart data of elective early mortality, cardiovascular, pulmonary, gastrointestinal and renal complications in the last five years, retrospectively. We compared the results of patients treated with open and endovascular technique. We performed open surgery in 433 patients. The average age was 69(±8) years. 77% suffered from hypertension, 39% had ischemic heart disease. The in-hospital mortality was 2.0%, all other type of complication added up to 13.8%. Pneumonia occurred in 2.7%, gastrointestinal complication was noticed in 2.3%, pulmonary embolism and renal injury in 2-2%, wound infection, urinary tract infection, acute myocardial infarction, stroke and acute tubular necrosis requiring hemodialysis in less than 2%. Stentgrafts were implanted in 83 patients. The average age was 73(±9) years. The early mortality was 2.0%. Pneumonia occurred in significantly more patients (p=0.042). There was no significant difference in the ratio of any other complications. Our results show that the in-hospital mortality of the AAA-patients with small or moderate risk for open surgery is not inferior to those treated with stentgraft implantation. Our data do not support to use stentgraft implantation as the first choice of treatment in patients fit for open surgery with long life expectancy.

Keywords: Infrarenal Aortic Aneurysm, Mortality, Morbidity

F/7 EARLY PHASE INVESTIGATION OF CRITICAL ILLNESS NEUROMYOPATHY IN SURGICAL PATIENTS

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Introduction In the last few years it has been shown that critical illness associated neuromuscular disorders appear early in the course of critical illness. They predispose the patients to protracted weaning from the ventilator, prolonged intensive care unit and hospital stay and higher mortality. **Methods** 21 critically ill surgical (APACHE II score ≥ 12) patients were enrolled in this observational study aged $63,52 \pm 16,9$ years. Routine non-invasive nerve conduction study of bilateral median and ulnar nerves was performed on five consecutive days starting within at most two days after admission, then weekly follow-ups were carried out. **Results** On the first examination 18/20 patients had $>20\%$ motor and sensory amplitude reduction with preserved conduction velocity. During the five day follow-up 4 patients showed improvement, 7 patients showed no change and 10 patients' results worsened in the overall. Weekly follow-up was possible in 8 patients. 3 of these patients showed further electrophysiological improvement, 2 patient showed further decrease and 3 patients' results stagnated. SAPS II and APACHE II severity score systems showed significant negative correlation with the daily change in electrophysiological parameters (Spearman's $r = -0,541$, $p < 0,001$). Mortality was higher in the patients with worse admission ENG and stagnant or declining tendency in the first week. **Conclusions** In the present cohort electrophysiological alterations appeared soon after the development of critical illness. Early phase alterations showed a strong negative correlation with patients' general condition and more severe electrophysiological alterations predisposed to higher mortality. But in several cases early alterations proved to be reversible.

Keywords: critical illness polyneuropathy, critical illness neuromyopathy, sepsis severity score, nerve conduction study

G. Head and neck regional medicine (Oto-rhinolaryngology and dentistry session)

G/1 EXAMINATION OF Ca^{2+} BINDING PROTEIN EXPRESSION AFTER KANAMYCIN TREATMENT IN THE INNER EAR OF WILD TYPE, HETEROZYGOUS AND PACAP-DEFICIENT MICE

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Pituitary adenylate cyclase activating polypeptide (PACAP) is a multifunctional neuropeptide with well known neuroprotective and neurotrophic effects. Recently, we have shown that PACAP protects cochlear cells against oxidative stress-induced apoptosis in vitro, but there are no data about its effects in ototoxic insults in vivo. In this study we examined the effect of a single dose of ototoxic kanamycin treatment (1mg/g) on Ca^{2+} binding protein expression in hair cells of wild type, heterozygous and PACAP-deficient mice. We treated 5-day-old mice with kanamycin and 2 days later we examined the Ca^{2+} binding protein (parvalbumin, calretinin) expression of the hair cells with immunohistochemistry. Control animals received physiological saline. We found that the hair cells of control PACAP-deficient mice showed more pronounced parvalbumin and calretinin immunopositivity compared to control wild-type mice. Kanamycin induced a significant elevation in Ca^{2+} binding protein expression in hair cells of wild-type and heterozygote mice, but the baseline higher expression in PACAP-deficient mice did not change after the treatment. Elevated endolymphatic Ca^{2+} is deleterious for the cochlear function, against which the high concentration of Ca^{2+} buffers in hair cells may protect. The increased immunoreactivity of Ca^{2+} binding proteins in PACAP-deficient and heterozygous mice provide evidence for the important role of endogenous PACAP in hair cell

development. Kanamycin induced a significant elevation in Ca²⁺ binding protein expression in hair cells of wild type and PACAP-heterozygous mice, which permits these groups to be used as an experimental model for studying the effects of exogenous PACAP by simultaneous kanamycin and PACAP administration. The baseline higher expression in PACAP-deficient mice did not change significantly after the treatment, therefore further investigations are necessary to examine the exact role of endogenous PACAP in ototoxic insults.

Keywords: PACAP, Ototoxicity, Aminoglycoside antibiotics, Hair cell damage, Ca²⁺ binding proteins

G/2 CLINICOPATHOLOGICAL FEATURES OF HEAD AND NECK CANCERS AND THEIR RELATION TO BIOMARKER-EXPRESSION

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INTRODUCTION: Prognosis of head and neck squamous cell carcinomas (HNSCCs) is considerably poor (5-year overall survival: 50%). Though these tumors belong to the same histopathological entity, they possess different clinicopathological characteristics. In our study, we compared the biomarker-expressions of HNSCCs arising from different anatomical localizations and evaluated their correlations with the clinical parameters. **METHODS:** 226 patients having HNSCCs were enrolled into our study. We prepared Tissue Microarrays (TMA) made from the patients' tissue samples and used immunohistochemical staining for detecting the biomarkers (Ki67, p53, EGFR, p16ink4, Collagen XVII). The histological evaluation was performed on computers using the Panoramic Viewer software. Expressions were considered positive when more than 25% of tumor cells were stained. We performed Chi-square tests and Kaplan-Meier survival analysis. We compared the biomarker-expressions according to conventional anatomical classification of the tumors then performed comparisons by and between subsites. **RESULTS:** The survival rate of patients with p16-negative cancer was significantly lower than that

of patients with p16-positive disease. The Ki67-positivity was associated with worse prognosis and a higher rate of lymph node metastasis. Factors such as T and N stage, diameter of the tumor and the histological grade significantly affected the prognosis. Ki67-expression rates of the tonsillar tumors were significantly higher than those of the oral and other oropharyngeal tumors. Additionally, regarding the laryngeal cancers, the Ki67 and p16-positive tumors were significantly more frequent in the supraglottic area. **CONCLUSIONS:** We considered proven that the HNSCCs cannot be regarded as a homogeneous entity based on their biomarker-expressions. Regarding the close correlation between p16-expression and HPV infection, we assume that HPV plays a role not only in tonsillar carcinogenesis, but in the development of supraglottic cancers, too. Additionally, we can declare that the supplementation of the conventional TNM-system with biomarker-profile could lead to a more precise prognostic score.

Keywords: head, neck, cancer, biomarker, survival, prognosis

G/3 HEARING DEVELOPMENT OF HEARING IMPAIRED CHILDREN WITH DIFFERENT ETIOLOGICAL BACKGROUND AFTER COCHLEAR IMPLANTATION

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Introduction: GJB2 gene mutation resulting in prelingual sensorineural deafness is the most common cause of congenital hearing impairments. Cochlear implantation (CI) replacing the deficient auditory function may enable the affected children to understand the environmental sounds better. In addition, it supports integration into the society. **Patients and methods:** Subjects aged 2-4 suffering from prelingual hearing loss were selected with confirmed GJB2 mutation, other genetic factors or unknown etiology. On the basis of intraoperatively evoked stapedius reflex threshold levels, impedance telemetry, postoperative threshold- and comfort levels as well as the results of auditory and speech tests, a

comperative study was performed. Results: Hearing and speech development of patients with GJB2 mutation shows better outcome results compared to children with other origin of deafness. Conclusion: The findings indicate that the etiology of hearing impairments has a great influence on psychophysical and objective electrophysiological parameters of the speech processor as well as the postoperatively acquired communication skills of the children.

Keywords: cochlear implantation, genetics, deafness, children, hearing development

G/4 GJB2 GENE MUTATIONS IN HUNGARIÁN PATIENTS WITH SENSORINEURAL HEARING LOSS

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Introduction: The c.35delG mutation of the GJB2 gene is the most common cause of hereditary non-syndromic sensorineural hearing loss in Europe. This mutation in homozygous form causes profound hearing loss, while in heterozygous form a wide spectrum of hearing impairment. In our study the frequency of c.35delG mutation were examined in patients with severe profound hearing loss and the patients with heterozygous c.35delG mutation the sequence analysis of GJB2 and GJB6 genes were tested as well. Methods: 108 Hungarian patients were selected with severe- to profound sensorineural hearing loss. The DNA isolated from blood. The GJB2 c.35delG mutation was investigated with PCR-RFLP methodology. The total coding regions of GJB2 and GJB6 genes were sequenced bidirectionally. Results: Among the investigated patients the c.35delG mutation were found in 13 cases (12%) (homozygous form: 7 patients (6,5%); heterozygous form: 6 patients (5,5%)). Beside the c.35delG mutation the sequence analysis of the GJB2 gene were found further two mutations in compound heterozygous form (35delG/W24X, 35delG/313del14). In the GJB6 genes was not detected any alteration. The genotype-phenotype

correlations have found for the homozygote types 6 prelingual, profound and 1 postlingual, progressive hearing loss. Four heterozygous patients with mutation in 1 allele had postlingual, severe and progressive hearing loss, and by the two compound heterozygote types prelingual, profound hearing impairment. Conclusion: The allele frequency of the GJB2 c.35delG was 9.25% in our investigated patients. The GJB2 c.35delG mutation frequency in Hungary lowers than other European countries using similar patient selection criteria. The mutation frequency varied in different countries, it may be due to the variety of population, further the choice of selection criteria. The study design has a huge impact on the result of the genetic epidemiological investigations concerning c.35delG allele frequency. In compound heterozygote patients the hearing impairment is like by homozygote patients.

Keywords: sensorineural hearing loss, GJB2 c.35delG, frequency, severe profound hearing loss

G/5 STRENGTHS AND WEAKNESSES OF RESTORATIONS USING PARAPULPAR PINS

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Introduction. With the advent of dental composite materials with adhesive systems, the need for a retention points, improve fixation seals significantly decreased. However, the treatment of cavities II and IV classes for black, especially when defects that occupy a large area. To avoid complications and to increase the mechanical retention, which will avoid complications it's advised to use different types of pins. To achieve better retention anchor pins in non vital teeth and in vital teeth in order to keep the vitality of the teeth, and to ensure better retention advisable to use parapulpal pins. Aim. Using parapulpal pins allows you to restore the major defects of dental hard tissues in one visit, in our time it is a fairly common requirement of patients who are guided by their time or financial resources, so we decided to identify strengths and weaknesses of restorations using parapulpal pins. Methods. Using the Thread mate system of parapulpal pins we made restorations of cavities II and IV classes (Black's classification) Results.

Our study showed the use of parapulpal pins in the restoration of frontal and posterior teeth with extensive cavities or fractures of crowns or of the cutting edge. Summary. Though the use of pins gives an opportunity to get better retention and durability of restorations, but there are some disadvantages and contraindications for using of parapulpal pins. Application of parapulpal pins is limited to cases when the thickness of dentin and form and cutting edges' dental anatomy meets the application pins. Parapulpal pins are not used, if the X-ray determined large cavities and tooth dentin narrow layer between it and the enamel-dentine connection. Use pins is not recommended for cutting edge thinned and increased transparency area (to avoid translucence). Pins are not used as the only means of retention of extensive defects of vital teeth in their application we should be guided not only by common indications for use, but consider each case individually taking into account both the advantages and disadvantages of the given method.

Keywords: parapulpal pins, pulp restorations, vital fractures

G/6 ASPECTS OF BURNOUT SYNDROME AMONG DENTISTS OF TRANSKARPATIA

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Introduction. Burnout syndrome is a psychological state resulting from prolonged exposure to job stressors. In the light of social change and a transformation in the work situation, interest in the problem of burnout has grown over the past decade. There is no generally accepted definition of burnout, or binding diagnostic criteria. According to the most common description at present, burnout syndrome is characterized by exhaustion, depersonalization and reduced satisfaction in performance. Because of its aetiopathogenesis, burnout is today mainly regarded as the result of chronic stress which has not been successfully dealt with. Because healthcare workers, especially dentists are characterized by a high level of work-related stress, a factor known to increase the risk of burnout syndrome, we sought

to work out a method to avoid the burnout syndrome among dentists. **Methods.** It was a review, testing and questioning of 43 dentists using the Maslach Burnout Inventory. **Aim.** Because healthcare workers, especially dentists are characterized by a high level of work-related stress, a factor known to increase the risk of burnout syndrome, we sought to work out a method to avoid the burnout syndrome among dentists. **Results.** Our study showed the clinical manifestations and characteristics of occupational stress and burnout among practicing dentists based on their specialization. The individual predisposition to the negative effects of occupational stress in relation to the typological features of the personality of each dentist was found. Evaluated and found that the subjective picture of stressors in professional dentists differs as the stress factors are variable and different in each specialization. We found a severe level of burnout syndrome of dental surgeons (13%) whereas the overall level of burnout syndrome was 48,4 %. **Summary.** So as the level of burnout syndrome among the dentist is high we suggest examination of doctors, including an analysis of social, clinical, psychological parameters, allows to identify occupational stress and burnout syndrome in the early stages of their formation, to reduce their negative impact on the health of the doctor.

Keywords: stressors, Burnout syndrome, exhaustion, dentists, stress

G/7 CAN VISUAL EVOKED POTENCIAL PREDICT AMBLYOPIA?

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Introduction: Although the prevalence of amblyopia (lazy eye) is 4-6%, its early screening has not been solved yet. The dynamic random dot correlogram evoked visual evoked potential (DRDC-VEP) is an electrophysiological method to examine binocular vision, which can be applied in infants. We have been testing this method in our Human Electrophysiological Laboratory among 1-8-month-old infants for 5 years. In the present serial study we started the follow-up of those infants who had been examined by DRDC-VEP previously and are in preschool age now. Our goal

is to determine whether DRDC-VEP could be a suitable tool for the clinical investigation of binocularity, thereby an early predictor of amblyopia. Methods: We have examined 24 children aged 3-6 years, including 22 who showed normal binocularity in the VEP test performed during infancy, and 2 cases where the DRDC-VEP response was absent until their age of 8 months what could indicate the disorder of development of the binocularity. The preschool screening set included monocular visual acuity examination, orthoptical tests and two stereo tests: the Lang-test and the DRDS-E. A child who failed any of the tests was referred to an eye specialist. Results: In the case of those two children who did not show any response to DRDC-VEP, visual pathology was confirmed: in one case hypermetropia, strabismus and amblyopia developed, while in the other child hypermetropia was diagnosed, which did not require treatment at the moment. In the other group nobody developed amblyopia, 19 children (86.36%) have normal vision and 3 children (12.25%) treatable refractive visual disorder, which normally do not lead to amblyopia. Conclusion: Based on our early results, the DRDC-VEP is a specific and a sensitive examination for amblyopia. It is important to notice that regular vision screening is crucial because some predisposing factor of amblyopia typically occurs after infancy.

Keywords: preschool screening, DRDC-VEP, amblyopia, Lang test, regular follow-up

G/8 Éva Kovács MD PhD, András Bíró
COMMUNICATION IN MEDICAL LANGUAGE IN
THE HEALTH SERVICE

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Communication in Medical Language in the Health Service The presentation is trying to find answers to the issues to what extent we can speak about communication in general or technical language as to the situations at the doctor's, in hospital or under therapeutic procedures. The presentation – using the method of observation - compares the expected usage and vocabulary touched by the subject „Medical

communication” and those used „in reality”. The findings are summarized focusing on the similarities, coincidences or differences. The author is trying to find the answer if the communication is of two ways i.e. whether the communication takes place between two persons (or more), or it is one way, because only one person „communicates something” - in our case a physician or a professional talks to an other person, i.e. to the patient, respectively. What should the word/terminology usage be like in course of the communication? – an analysis of opinions and ideas from interviews with medical students and physicians. Among who is the communication taking place? Between professional and patient, professional and professional? In the first case, the communication is more likely of informative character, built on instructions, while in the latter instance it is the change of knowledge and information that plays a primary role. Joining the topic of taboo and euphemism in negative medical prognosis, the results of a Ph.D. thesis are introduced. Finally, a few words are said about the preparation of students for the the Profex examination of technical language regarding the oral situation exercises, where the author tries to show how much the artificial situations reflect reality.

Keywords: communication between professional – patient, professional – professional, taboo, euphemism, PROFEX medical language examination

POSTER SESSION

H. Basic sciences

H/1 NOVEL KINASE INHIBITORS DESIGNED FOR TARGETED DELIVERY

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Introduction: In this study, our goal was to develop novel Sunitinib like kinase inhibitors, designed for peptide based drug delivery systems. This approach can lead to organ specificity, and increased efficiency compared to Sunitinib. **Methods:** We docked our primary test set, containing 150 virtual kinase inhibitor, into an available co-crystal structure of VEGFR-2 with Sunitinib (PDB code: 4agd). The docking studies were performed by YASARA Structure, an AutoDock 4.0 based software. We validated our docking results in vitro, measuring the IC₅₀ values of Sunitinib and Orantinib on VEGFR-2. Based on the in silico screening results, we selected and synthesized the most promising 18 molecules, bearing a carboxylic function, which allows us to bind them to different carrier systems, with covalent bond. We synthesized the ester derivatives of the selected compounds as well, with the aim of determining the total phosphorylation in vitro, in further cell culture studies. The purity of the compounds were determined using HPLC-MS and ¹H NMR techniques. After a single point in vitro screening, we selected 25 out of the 36 synthesized molecules to determine the IC₅₀ values against VEGFR-2, using TranScreener ADP2 assay. **Results:** The in silico calculations showed good correlation with the in vitro biochemical results (IC₅₀s against VEGFR-2: 5-10,000nM). Based on the IC₅₀ values we were able to select the best candidates for targeted delivery. **Conclusion:** We have designed and synthesized Sunitinib analogue kinase inhibitors bearing a carboxylic function. Some of the compounds showed submicromolar IC₅₀s against VEGFR-2 in a biochemical assay. Our future perspective is to test the ester derivatives in vitro. Furthermore, based on the in vitro results, we have selected the best free drugs and we are planning to bind them to peptide based delivery systems such as RGD peptides.

Keywords: Sunitinib, targeted delivery, kinase inhibitor, VEGFR RGD peptide

H/2 EFFECTS OF ENVIRONMENTAL ENRICHMENT ON EARLY DEVELOPMENT IN PERINATAL ASPHYXIA IN RATS

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Introduction: Investigation of beneficial or negative effects of various perinatal treatments in newborn rats has been in the center of interest of our research group for more than ten years. We have previously detected that perinatal asphyxia significantly retards the early neurobehavioral development of newborn rats, and environmental enrichment is protective in toxic lesion. In the present experiment we examined the possible protective role of complex environmental enrichment in perinatal asphyxial model. **Methods:** We examined full term pregnant rats, and induced 15 minute in utero asphyxia on the day of delivery. Pups were delivered by cesarian section following the asphyctic period. Litters were randomly cross-fostered and given to surrogate mothers. Every litter contained control, non-asphyctic pups and asphyctic pups. Number of surviving pups was 12 in each litter. We kept one half of the litters in normal cage, the other half in complex environmental enrichment until 5 weeks of age. Four groups were studied: non-asphyctic animals in normal cage (control), asphyctic in normal cage, non-asphyctic in environmental enrichment and asphyctic in environmental enrichment. We examined the early development of the nervous system from 3-21 day of age. Appearance of certain somatic parameters and neurological reflexes was detected. At the age of 4 weeks we performed motor coordination (foot-fault) test, and at the age of 6 weeks we examined the novelty-seeking behaviour. **Results, conclusions:** We obtained the already known results in asphyctic animals: weight gain, appearance of physical parameters and the onset of some reflexes were delayed compared to control animals. The developmental pattern of rats was not significantly changed by the environmental enrichment in control rats. In asphyctic injury, enriched environment significantly improved the neurological reflexes and somatic parameters, similar to our previous findings in toxic lesions. Performance of enriched asphyctic animals was improved in motoric coordination tests. Novelty seeking was also

significantly changed by asphyxia, and environmental enrichment had no protective effect in this test.

Keywords: rats, environmental enrichment, asphyxia, development, reflex

H/3 THE ROLE OF VENTRAL PALLIDAL D1 DOPAMINE RECEPTORS IN SPATIAL LEARNING VENTRAL PALLIDUM

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The ventral pallidum (VP) is located in the basal forebrain, and it is extensively connected with the mesolimbic dopaminergic system (MLDR). Its function is known to be important in learning and reward processes. In the ventral pallidum mainly D1 and D2 dopamine receptors can be found. We used neurochemical manipulations to investigate the role of D1 dopamine receptors of the VP in spatial learning. Bilateral stainless steel cannulae were implanted into the VP of male Wistar rats using stereotaxic surgical method. The D1 agonist SKF38393 was microinjected in 0,1 ug, 1 ug, or 5 ug doses into the VP, while the specific D1 antagonist SCH23390 was administered after to confirm receptor selectivity of the agonist's effect. The drugs were dissolved in 0,4 µl saline, and control animals received only this vehicle. Drug effects were investigated in Morris Water Maze (MWM) test. On day 1 and day 2 of the MWM test, the animals were conditioned. During the trials hidden platform finding latency was measured to assess the drugs' influence on spatial learning. In the MWM test, the D1 agonist in 1,0 µg dose significantly reduced the target finding latency, the other doses had no influence on the behavior. The SCH23390 specifically antagonized the agonist's effect. According to our findings, the D1 receptors of the VP have an important modulating role in spatial learning mechanisms. This function appears to be specific to D1 receptors because behavioral response to the agonist was abolished by microinjection of the antagonist. These results can lead to better understanding of learning mechanisms in general, and diseases that involve impaired function of the MLDR.

Keywords: D1 dopamine receptor, motivation, spatial learning, mesolimbic dopaminergic system

H/4 AGE-RELATED SHIFTS IN ACUTE CENTRAL CORTICOTROPIN EFFECTS ON ENERGY HOMEOSTASIS

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Introduction: In the background of age-related obesity and of aging anorexia complex age-related alterations in the catabolic [food intake (FI) reducing, metabolic rate (MR) enhancing] and anabolic (FI enhancing, MR- reducing) peptide systems may be assumed. Corticotropin-releasing factor (CRF) is an important hypothalamic catabolic mediator downstream of leptin and melanocortins. Our previous studies revealed age-related shifts in the catabolic responsiveness to intracerebroventricular (ICV) CRF infusion in rats: the weakest responsiveness was detected in the middle-aged, the strongest in the oldest group. **Methods:** We hypothesized that anorexigenic and hypermetabolic responsiveness to acute ICV CRF administration change with different dynamics during aging. Responsiveness of young adult, younger and older middle-aged, aging and old (3-, 6- and 12-, 18- and 24-month, respectively) male and female Wistar rats to acute ICV CRF injection (0.3 ug) was analyzed regarding parameters of energy balance. Anorexigenic effects were tested in an automated FeedScale system during 120-min re-feeding following 24-h fasting. Oxygen consumption (MR) was measured by indirect calorimetry (Oxymax). Colon (Tc) and tail skin temperature (Ts) were recorded by thermocouples in non-deprived animals. **Results:** Acute CRF injection suppressed FI and increased MR and Tc. In males both anorexigenic and hypermetabolic effects declined with aging. Females showed significant anorexigenic responsiveness in all age-groups. **Conclusion:** Age-related alterations in the responsiveness of male rats to central ICV CRF were similar to those of ICV CCK injections. In the background of gender differences variations in body weight/body composition and endocrine

factors (e.g. anorexigenic estrogen effects) may be assumed.

Keywords: aging, rat, catabolic, gender

H/5 TRANSIENT RECEPTOR POTENTIAL MELASTATIN-4 (TRPM4) MEDIATES VASOCONSTRICTION IN RAT MODEL

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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 (isometric measurements, preconstriction by about 5mN) and mesenteric (isobaric conditions, at 80mmHg) arteries. **Methods:** Arteries were isolated from Wistar-Kyoto (WKY) rats and experiments were performed in oxygenated Krebs buffer. **Results:** Initial diameter of the mesenteric arteries was $325 \pm 18 \mu\text{m}$ (n=9). Extracellular K⁺ (120mM) 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 (10μM, 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 (1μM-300mM), 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⁺ (60mM) 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).

The suspected TRPM4 activator, A23187 caused vasoconstriction accompanied by the rise of intracellular Ca²⁺-concentration in the arteriolar wall. The evoked vasoconstriction was antagonized by the inhibitor, 9-phenanthrol. **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.

Keywords: TRP, TRPM4, vascular biology, 9-Phenanthrol, A23187

H/6 BASIC AMINO ACIDS INDUCE MITOCHONDRIAL INJURY IN RAT PANCREATIC ACINAR CELLS

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Hegyi, Zoltan Rakonczay Jr**

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Introduction: Acute pancreatitis (AP) is the sudden inflammation of the pancreas. Large i.p. doses of basic amino acids induce AP in rodents, but the mechanisms mediating pancreatic toxicity remain unknown. Mitochondrial injury is thought to play a role in the pathomechanism. **AIMS AND Methods:** Our aim was to get insight into the mechanisms through which basic amino acids damage the exocrine pancreas. Pancreatic acinar cells were isolated from rat pancreas with enzymatic digestion. Isolated cells were treated with different concentrations (20-60 mM) of L-arginine, L-lysine or L-ornithine. The morphology of acinar mitochondria was monitored with electron microscopy. We measured intracellular Ca²⁺ concentration ([Ca²⁺]_i) by microspectrofluorometry using the Ca²⁺-sensitive fluorescent dye FURA-2-AM. The effect of basic amino acids on basal and cerulein-stimulated amylase secretion was tested. **Results:** We observed the swelling of mitochondria after incubating the cells for 2 hours with 20-60 mM basic amino acids. However, we did not detect any change in the [Ca²⁺]_i of cells in response to administration of basic amino acids, whereas marked Ca²⁺ signaling was found in response to 100 μM carbachol. Basal and cerulein stimulated amylase secretion was not influenced by basic amino acids vs the control group. **Conclusion:**

Our data suggest that basic amino acids are unlikely to cause pancreatitis via calcium signaling, they do not alter amylase secretion, but they injure mitochondria. Further experiments are needed to investigate the exact pathomechanism.

Keywords: pancreatitis, basic amino acids, mitochondrial injury

H/7 DIFFERENCES BETWEEN LIFESTYLE AND CLINICAL SYMPTOMS IN MYOSITIS PATIENTS: PHYSIOTHERAPY AND ITS BENEFITS

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Polymyositis (PM) and dermatomyositis (DM) are idiopathic inflammatory myopathies (IIM) belonging to systemic autoimmune diseases. Common symptoms are the symmetrical proximal limb muscle weakness and typical DM skin symptoms. In our experiments we have examined the data of 50 PM/ DM patients recruited by the Institute of Internal Medicine, University of Debrecen, Department of Clinical Immunology Clinic. Two subgroups were created: patients with and without physiotherapy DM/PM. In this study, we aimed to compare 5 parameters of the subgroups such as: clinical symptoms (muscle and skin symptoms, extramuscular involvement), laboratory parameters (LDH, GOT, GPT, CK), functional activity, quality of life and medications. These values were examined during a 3 years period of the remission of the diseases. Health Assessment Questionnaire (HAQ) and Stanford Questionnaire 36 (SF-36) were used to measure the quality of Life. In our findings, the patients with systematic physiotherapy had significantly lower LDH, GOT, GPT values in the third year and also the levels of the isoenzymes (CK, GOT, GPT, LDH) showed a more significant decrease comparing to the patients without physiotherapy. In the working subgroup, the values of quality of life showed greater improvement although these changes were not significant, probably due to the few patients. While at the beginning of the disease remission the distal muscle weakness was a common symptom in the subgroup without physiotherapy,

in the working group the Raynaud syndrome was more frequent. In addition, in the working group the muscle weakness was more severe symptom and consequently they more often received second-line therapy. Probably the more severe symptoms increased the motivation for the regular movement therapy. In conclusion, the physiotherapy can be an integral part of muscle regeneration which can form the therapy of myositis besides the gold standard steroid, or in severe cases with DMARD therapy.

Keywords: Myositis, Physiotherapy, Functional activity, Quality of Life, Laboratory parameters

I. Clinical sciences I:

Chest (Radiology, Pulmonology, Cardiology)

I/1 FUNCTIONAL MRI REVEALS ABNORMAL NEUROVASCULAR RESPONSE IN MILD TRAUMATIC BRAIN INJURY

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Introduction: Functional magnetic resonance imaging (fMRI) is a potential tool in assessing functional disorders occurring in mild traumatic brain injury (mTBI). Previous studies aimed to reveal the neural background of impaired performance, however the findings were inconsistent. Here we test the hypothesis that abnormal cortical patterns may also be present during basic functions irrespective of symptoms or actual performance. Methods Twelve mTBI patients underwent structural and functional imaging within 3 days after injury, 8 of them also one month later. Functional imaging involved two tasks: finger tapping task to explore sensory-motor activation; and covert word generation task to activate language function. A control group of 12 matched volunteers were examined twice by the same imaging protocol and time interval. Results T1-, T2- and susceptibility weighted imaging revealed no pathology. Longitudinal analysis showed decreased activation at the sensory and motor areas during finger tapping task and reduced deactivation in the medial prefrontal cortex during covert word generation task at the acute phase compared to 1 month in the mTBI group. Conclusion Comparison of mTBI acute phase- and control

group data supported the finding of reduced activation during finger tapping task in the mTBI group.

Keywords: neuroimaging, fMRI, mTBI, motoric function, language function

I/2 'METABOLITE STUDIES AS A PRECLINICAL TOOL'

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As a prerequisite, radiopharmaceuticals have to be as stable as possible. Additionally, no mayor metabolites should interfere with the target tissue. To assure and quantify these metabolites, defined studies have to be performed prior to a first in man application of a new radiopharmaceutical. This thesis will deal with new methods for the quantification and qualification of metabolites: enzyme reactions, Michaelis-Menten kinetics, HPLC methods. These assays will be performed on the basis of FE@SUPPY, a PET-tracer for the adenosine A3 receptor. In one of the previous studies, conducted with the CES of porcine origin, stability of previously mentioned tracers FE@SUPPY, DFE@SUPPY and FE@SUPPY:11 were evaluated. In vitro CES experiments were conducted using incubation mixtures containing different concentrations of the substrates, porcine CES and phosphate-buffered saline. In addition, experiments were conducted with rats and knowing that metabolism in rats is several times faster than in humans conclusion was that [18F]FE@SUPPY should be stable for the typical time span of a clinical investigation. Having not yet evaluated the influence of human CES subtypes, similar testing will have to be conducted and compared with porcine and rat results. There is a demand for a suitable PET ligand for the Adenosine3 Receptor (A3R) both for in vitro and in vivo use. The molecules, based on a structure of [18F]FE@SUPPY and [18F]FE@SUPPY:11 did not yet find their way into human application. In preclinical experiments, it was showed that we have to focus on these molecules. The aim of the research is to

compare "in-vitro" data from porcine CES with "in-vitro" data from human origin. Focus of this research is to verify if human CES subtypes are able to metabolize FE@SUPPY, FE@SUPPY:11 and DFE@SUPPY in a comparable manner as porcine CES. Main questions are, (1) if there is a difference in degradation rates of these substrates and (2) which of these CES subtypes are mainly responsible for degradation of our tested substrates.

Keywords: Carboxylesterase, PET, Enzymes, Metabolites, Adenosine

I/3 FATAL ARRHYTHMIA WITH NO CASE HISTORY – WHAT DOES THE CMR SHOW?

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Introduction: A 33-year-old football coach with no history of serious illness collapsed during training. He was pulseless, and resuscitation was started within 4 minutes. The patient's ventricular fibrillation was terminated with a single DC shock. Methods: Cranial and chest CT scan showed normal anatomy. Coronary angiography revealed normal coronary arteries and LAD bridge formation. Echocardiography displayed normal heart chamber sizes and normal heart function. Using cardiac magnetic resonance imaging (CMR) normal right and left ventricular ejection fractions, moderately increased left and normal right ventricular volumes were measured, and left ventricular thinning and subepicardial late contrast enhancement was observed in the basal and middle part of the inferolateral wall. Subepicardial scar represented 14 % of the left ventricular mass. Results: The CMR scan uncovered signs of former myocarditis, and was not typical for arrhythmogenic right ventricular cardiomyopathy or ischaemia. As secondary prevention implantable cardioverter defibrillator (ICD) was implanted. Two months later, patient had a syncopic episode during training. The device recorded ventricular tachycardia (320/min) was terminated with a single shock. No arrhythmia was detected during

the three-year follow-up period. Conclusion: Myocarditis accounts for up to 10 % of sudden cardiac deaths in young adults. CMR is a diagnostic tool with high sensitivity and specificity in the identification of myocarditis. In most studies left ventricular ejection fraction is considered to be the best prognostic factor in myocarditis. However, recent evidence suggests that late enhancement appears to be an other good predictor of sudden cardiac death following myocarditis.

Keywords: myocarditis, CMR, late enhancement, sudden cardiac death, ICD

1/4 HIGH DIAGNOSTIC ACCURACY OF CARDIAC MAGNETIC RESONANCE IMAGING: DIAGNOSTIC DIFFICULTIES OF 27 YEARS

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Introduction: A 48yearold male patient's chest complaints started at the age of 21, duringextreme stress, syncope occured three times within a month. During a series of hospitalisation he had several cardiac examination while his atypical manifested structural heart disease found out. Methods: In his family's medical history his brother died in sudden cardiac death at the age of 25, autopsy discovered parenchymal degeneration of the myocardium. He was admitted in 1997 to a cardiology department with chest and left arm pain. Because of acute chest pain in 2006 and 2009 after detailed medical check ups, his ECG showed ischaemic signs, without typical signs of left ventricular hypertrophy, enzymes did not raise, treadmill test was normal. Echocardiography described moderately enlarged, hypertrophyc left ventricle, with no other alteration. During dipyridamol stress myocardial scintigraphy left ventricular anterior region showed inhomogenous activity distribution, perfusion reduction was not detected. In 2010 examinations performed because of frequent chest pain demonstrated no

further alterations. In 2012 invasive coronary angiography showed left dominant healthy coronary arteries. Ventricular angiography showed expressed left ventricular trabecularisation, cardiac magnetic resonance imaging (CMR) was recommended because of the suspicion of left ventricular noncompaction. Results: The CMR examination demonstrated, left ventricular hypertrophy (200 grams) predominantly in the apex (17 mm), and delayed contrast enhancement in the affected myocardium. The CMR justified apical hypertrophic cardiomyopathy with signs of tissue fibrosis. Holter monitoring did not prove ventricular arrhythmia, during stress test at 225 Watt chest pain, arrhythmia and ST alteration did not occur. Conclusion: After 27 years the CMR examination justified apical hypertrophic cardiomyopathy in the background of complaints. With choosing the appropriate imaging modality and with timely treatment, the progression of structural heart failure is preventable.

Keywords: HCM, apical HCM, structural heart disease, CMR, cardiac imaging

1/5 UNFAVORABLE EFFECTS OF PASSIVE SMOKING ON CHILDREN'S RESPIRATORY SYSTEM

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Introduction: The most common human addiction is smoking. The passive form of this is substantially dangerous to children as well, despite this fact many of them is at risk. Dr Panagiotis Behrakis says: "Passive smoking is the most common form of child abuse. It should be considered as a violation of the human rights." The aim: In my paper I'm looking for answers to questions, such as: despite the strong anti-smoking propaganda children how much are at risk in the case of passive smoking and this fact in what extent influences their health? I have studied the oftener symptoms, prevalence of the respiratory system, and the clinical appearance linked to passive smoking. Methods: I've made questionnaire assessment at the II. Pediatrics Clinic of Marosvásárhely, and at urban and country areas' child community among children

aged 1-8, during three winter months. I have studied whether they are affected by passive smoking, the frequency of respiratory diseases and the clinical appearance. Result: We studied 94 community children, 21 lives in city and 73 at country. 31% of these children are exposed directly to passive smoking, 15% has somebody who's smoking in the surrounding area (third hand smoke), and 53% is not in contact with smoke. 43% of children who are affected by passive smoking suffered respiratory disease during the three months, while just 12% of those who were not in touch with smoke. We examined 33 children assigned because of respiratory disease, 58% of them are a passive smoker, and 30% didn't get in touch with smoke. Conclusion: 1/3 of kindergartener children are exposed to the poisonous addiction of family members. These children get sick of respiratory diseases more often and more grievously. 2/3 of children assigned because of respiratory pathology are affected by passive smoking.

Keywords: passive smoking, children, respiratory system

MULTIDISCIPLINARY SESSION V.

J. Updates in Cardiology –Cardiology session

J/1What is the limit of capability to use the bioresorbable vascular scaffold?

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Number of deaths caused by coronary artery disease (CAD) in the USA is 145/100.000, while in Hungary it is 332/100.000. CAD is progressive, characterized by narrowing or even blockage of the arteries causing restricted bloodflow to the heart. Several risk factors can be modified by lifestyle changes, but due to other risk factors, the progressivity of the disease cannot be stopped despite all the aggressive pharmacological therapies. There is expectation for brand new devices and techniques in the therapy of CAD.

The first bioresorbable vascular scaffold (BVS) implantation around the world was performed by P. Serruys and his team in the Netherlands. In Hungary the first BVS was implanted in 2012. This was a second generation BVS. The stent fully resorbs in two years, leaving no irritative materials of degradation behind in the coronary artery and potentially regaining the physiological ability of vasomotion of the vessel.

One of the first institutes in Hungary was the Heart Institute of the University of Pécs, which had the opportunity to apply several BVS. In our lab the procedures were controlled by optical coherence tomography (OCT), which ensured the perfect apposition and sizing of the stents. Our first implantation was performed on a single lesion on the circumflex artery as a typical indication. Not only the usage of OCT was special in our cases, but also, that our second case was a multi-vessel intervention. In that this case, the patient had a very calcified and tortuous anatomy, we tried to find the limit of capability of BVS, so we applied it as an off label indication. Our presentation would like to present a follow-up on these two cases.

Keywords: coronary artery disease, myocardial infarction, interventional cardiology, bioresorbable, vascular scaffold, optical coherence tomography

J/2 Hemodynamic characterization of athlete's heart using left ventricular pressure-volume analysis in rat model

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Introduction: The development of professional sport and sudden cardiac death cases among athletes aroused emerging interest in sports cardiology. Several authors published data on exercise induced left ventricular (LV) hypertrophy but haemodynamic measurements are relatively scarce. We aimed to establish and validate the rat model of athlete's heart and provide a detailed functional characterization using the modern sophisticated method of pressure-volume (PV) analysis. Methods: The LV

hypertrophy was induced by forcing rats to swim 200 min/day for 12 weeks. The control group swam only 5 min/day. At the end of the study we performed histology, echocardiography and LV pressure-volume (PV) analysis with mikrotip pressure-conductance catheter. Results: Echocardiographic examinations showed LV hypertrophy according to the wall-thickness values. This was confirmed by post-mortem measured heart weights and hypertrophy on histology. On the catheter measurements we found no difference on heart rate, arterial pressure and LV end-diastolic volume between the two groups. The exercised rats had higher stroke volume and increased ejection fraction. Their PV loop derived load independent contractility indexes were significantly higher. We measured not only a larger stroke work but the maximal stroke power was also higher. Despite significant hypertrophy the LV stiffness was not increased but we found improvement in active relaxation. Conclusions: According to our results, we established a rat model of physiologic LV hypertrophy. It is the first study, which provides a detailed characterization of functional changes and hemodynamic relations in athlete's heart.

Keywords: cardiology, athlete's heart, cardiac hypertrophy, physiology, rat model

J/3 Cardiac effects of exhaustive exercise in a rat model

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Exercise has a preventive role in cardiovascular diseases. However, after exhaustive exercise (e.g., ultramarathon) the plasma level of cardiac necroenzymes is highly increased. We aimed at understanding the functional, biochemical and morphological changes in the heart after exhaustive exercise by using a rat model. Exhaustive load in the rats was exerted by swim training. The swimmer group had a 3-hour-long exercise with an added tail weight that was 5% of their body mass. The control group swam for 5 minutes. After a 2-hour recovery period we

performed left ventricular (LV) pressure-volume (P-V) analysis with a pressure-conductance microcatheter to investigate in vivo cardiac function. We performed histological examinations on the cardiac tissue and measured myocardial gene expression changes with qRT-PCR. The plasma concentration of cardiac troponin T ($0,131 \pm 0,022$ vs. $0,025 \pm 0,006$ ng/ml), creatine kinase and lactate dehydrogenase was significantly increased in the exhausted rats compared with the control. By monitoring the cardiac tissue histological sections we found myocyte fragmentation and leukocyte infiltration in the swimmers. The myocardial expression of anti-apoptotic bcl-2 decreased, while that of the oxidative stress markers thioredoxin and matrix metalloproteinase-2 increased after swimming. Invasive hemodynamic measurements showed increased LV end-systolic volume, thus decreased stroke volume and ejection fraction. LV contractility (Ees: $0,60 \pm 0,07$ vs. $0,90 \pm 0,05$ Hgmm/ μ l) and efficiency (Eff: 47 ± 1 vs. $58 \pm 2\%$) decreased in the swimmers. Our findings demonstrate that even a single but extremely exhaustive exercise damages the rat's heart. As such exercise gives structural and functional abnormalities, we stress that even one such exercise may be dangerous.

Keywords: necroenzymes, myocyte fragmentation, pressure-volume analysis, systolic function, contractility

J/4 Protective effect of vardenafil in a vascular ischemia-reperfusion model

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Introduction: Ischemia, the absence of blood supply is a very common cause of various pathologies, where the main goal was always the restoration of blood flow. However, reperfusion of ischemic tissues sometimes augments the damage caused by ischemia. Since the ischemia-reperfusion (I/R) injury also affects vascular grafts, efforts have been made to create novel storage solutions, which can minimize the damage to the graft before implantation. A

decreased level of I/R injury would contribute to the abolishment of acute and chronic graft failure. Vardenafil, a selective inhibitor of phosphodiesterase type 5 has been shown to be protective in myocardial I/R injury by enhancing the cGMP/PKG pathway. We investigated the effects of vardenafil in a vascular I/R model. Methods: Isolated thoracic aorta rings of rats were kept for 24 hours in cold physiologic saline or vardenafil supplemented saline. Reperfusion was simulated by addition of hypochlorite for 30 minutes. Contractile function and vasorelaxation was assessed, followed by histopathological and molecular biological assays. Results: Due to cold ischemic storage and reperfusion, endothelium-dependent vasorelaxation decreased, which was significantly improved by vardenafil. Vardenafil also significantly decreased DNA-strand brakes and increased cGMP levels in the injured aortic wall. Conclusion: In our experiments, pharmacological inhibition of the degrading enzyme of cGMP reversed the functional and structural damages caused by cold storage and warm reperfusion. These results support the view that cGMP-signalling plays a crucial role in the pathogenesis of I/R injury.

Keywords: ischemia-reperfusion, vardenafil, cold ischemia, storage solution, vascular graft

J/5 The effects of red wine on hemorheological parameters in healthy volunteers

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Introduction: Epidemiological evidences have indicated that moderate red wine consumption reduces the risk of cardiovascular diseases (French-paradox). **Methods:** Thirty-nine healthy, non-smoking male volunteers (age: 18-40 years) were assigned into two groups: subjects in the control group drank water, while in the red wine group consumed 200 ml of red wine each day at dinner for 3 weeks. None of the volunteers consumed alcohol for at least 3 weeks prior of the study. Blood was obtained in the morning of the first and last day of the study. Hematocrit (Hct), plasma (PV) and whole blood viscosity (WBV)

(Hevimet 40 capillary viscometer), red blood cell (RBC) aggregation (Myrenne and LORCA aggregometer) and deformability (LORCA ektacytometer) were measured and Hct/WBV ratio was calculated to determine oxygen carrying capacity. Hct was adjusted to 40%. Results: Hct and PV were not affected. WBV remained unchanged in the control group, but considerably decreased in red wine group compared to 3-week control samples. Hct/WB was significantly higher in those who drank wine ($p<0.05$). RBC aggregation significantly decreased in red wine group and became significantly lower compared to 3-week controls ($p<0.05$). Red wine significantly increased RBC deformability ($p<0.05$) at high shear stress. Summary: Our results show that moderate red wine consumption has beneficial effects on hemorheological parameters which may contribute to the French paradox. (TAMOP 4.2.1B)

Keywords: viscosity, deformability, aggregation, controlled, prospective

J/6 A Case Report of a Complicated STEMI - How Many Complications Can a Patient Survive?

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Introduction: The free wall rupture of the left ventricle is a severe mechanical complication of myocardial infarction. Despite the advances in surgical treatment the condition is associated with high mortality rate. Left ventricle aneurysm formation also has high long-term mortality rate without surgical intervention. **Case report:** A 56-year-old female patient without significant medical history was admitted with extensive anterior STEMI. Her coronary angiography showed occlusion of the proximal LAD. She underwent a successful PCI with 2 BMS implantation. 24 hours later cardiogenic shock developed requiring intubation and IABP insertion. Echocardiography revealed pericardial

tamponade, due to free wall rupture. The patient had an urgent surgical pericardial fenestration and haematoma evacuation with plication of the free wall rupture. 3 days later echocardiography showed severely depressed left ventricle function with large apical aneurysm. A week later her condition deteriorated, respiratory insufficiency caused by large left side haemothorax developed, with circulatory arrest, requiring resuscitation during the thoracocentesis. Her course was complicated by GI bleeding and sepsis also. Echocardiography done during the early rehabilitation confirmed giant apical aneurysm with spontaneous echo contrast. Despite HF medication the patient was in NYHA class IV. functional stage. MRI was done after her condition was stabilized. Beside aneurysm, large thrombus on the subendocardial surface of the left ventricle's anterior segment was diagnosed with EF as low as 17% and EDVI of 261 ml/m². 5 month after the primary event successful surgical reconstruction of the left ventricle was done. Follow-up echocardiography and MRI showed marked improvement in left ventricle function (EF: 34%, EDVI: 113.9 ml/m²). The patient was in NYHA class II. stage, without limiting symptoms during the last outpatient visit. Conclusion: Our case report demonstrated a successful multidisciplinary management of a STEMI patient with numerous, life threatening acute and subacute complications, which can result in a better chance of survival with good quality of life.

Keywords: STEMI, free wall rupture, aneurysm, heart failure, surgical intervention

J/7 Prognostic value of hematocrit to blood viscosity ratio in patients with stable and acute coronary artery disease

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Introduction: Hematocrit to blood viscosity ratio (Hct/BV) represents the oxygen delivery intensity, and thus it may refer to the development of ischemia. We investigated the

relationship between this parameter and mortality and morbidity due to ischemic heart disease. Methods: In our first study, we retrospectively analysed data of 78 patients with stable coronary heart disease who underwent elective diagnostic coronary angiography and were followed-up for a mean of 8.9 years. Patients having died of cardiac cause had significantly lower Hct/BV values (87±5 vs. 93±9 Pa-1s-1, p=0.022). Kaplan-Meier survival analysis showed the impact of Hct/BV on cardiac mortality (p=0.009). Receiver operating characteristic curve proved Hct/BV to be able to identify cardiac mortality (AUC=0.716, p=0.028). Hct/BV showed significant negative correlation with the number of hospital admissions due to cardiac events in patients who were alive at the end of the follow-up period (r=-0.377, p=0.03). Results: In another study, data of 124 patients admitted to our hospital due to acute coronary syndrome was analyzed. Blood samples were collected at admission, on the 2nd and 6th hospital day. Patients with lower Hct/BV values at admission reached the combined end-point of death, myocardial infarction and stroke more frequently during a 7-year-follow-up according to Kaplan-Meier survival analysis (49 % vs. 28 %, OR=2.47, p<0.05). After excluding patients undergoing revascularization (that probably affects survival) this was even more pronounced (59 % vs. 20 %, OR=5.7, p<0.05). Hct/BV determined from samples taken on the 2nd and 6th day showed no prognostic value, suggesting that therapy may influence Hct/BV and its impact. ROC analysis showed significant prognostic power for Hct/BV to predict the mentioned endpoint (0.676, p<0.05). Patients who needed more frequent hospitalization in the upcoming years had significantly lower Hct/BV at admission (r=-0.491, p < 0.05). Conclusions: Our results denote the prognostic value of Hct/BV in patients with stable and acute coronary artery disease as well.

Keywords: coronary heart disease, hemorrheology, hematocrit, viscosity, mortality

K. Pediatrics – Obstetrics and Gynecology session

K/1 Examination of PACAP38-like immunoreactivity in different milk and infant formula samples

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Introduction: Pituitary adenylate cyclase-activating polypeptide (PACAP) is a neuropeptide with important role in reproductive and developmental processes. PACAP has two bioactive forms: PACAP27 and PACAP38. Recently, we have described that PACAP38 is present in high levels in the milk of humans and ruminant animals. The aim of the first part of the study was to investigate PACAP38-like immunoreactivity (PACAP38-LI) in human colostrum, transitional and mature milk and we planned to detect the changes of PACAP38-LI during different periods of lactation. In the second part of the experiment we aimed to measure PACAP38-LI in fresh cow milk, pasteurized cow milk and commercial infant formula samples and to prove the presence of PACAP38 in infant formulas. **Methods:** PACAP38-LI was measured by radioimmunoassay (RIA). The presence of PACAP38 was determined by mass spectrometry (MALDI TOF/TOF) analysis. **Results:** We found that PACAP38-LI was significantly higher in human colostrum samples than in mature milk. PACAP38-LI did not show significant changes within the first 10-month period of lactation, but a significant increase was observed thereafter, up to the examined 17 months. We found that PACAP38-LI did not show any alteration in the foremilk and hindmilk samples. There was no difference in the PACAP38 content of fresh and pasteurized cow milk and in infant formula samples either. However, the hypoantigenic infant formulas contained significantly higher levels of PACAP38. The result of mass spectrometry indicates that the measured PACAP38-LI represents PACAP38 molecule in the infant formula. **Conclusion:** Our present data show that PACAP38 is relatively stable in the milk and it can withstand the manufacturing processes. The importance of PACAP in human milk is not known exactly, probably it plays a role in the development of the newborn nervous system, immunsystem and in the regulation of the

mammary gland. Further investigations are needed to evaluate the exact function of this neuropeptide in the milk. This work was supported by PTE-MTA "Lendület" Program, Arimura Foundation, OTKA K104984, TAMOP 4.2.1.B-10/2/KONV-2010-002, 4.2.2.B-10/1-2010-0029, 4.2.2.A-11/1/KONV-2012-0024.

Keywords: milk infant formula, PACAP38, MALDI, TOF/TOF radioimmunoassay

K/2 Assessment of sleep parameters in enuresis nocturna

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Introduction: The relation between sleep and nocturnal enuresis (NE) has been an area of discussion for many years. Children with enuresis are generally believed to have sleep that is too deep with decreased arousability. We investigated sleep characteristics in children with refractory NE. **Methods:** Between 2009-2012 seventeen children (mean age: 7.6 ± 2.5 yr, male 65 %) diagnosed with NE underwent single night polysomnography (PSG). Age and sex matched control group (CG) was collected from non-enuretic patients examined at the Sleep Laboratory of the 1st Dept. of Pediatrics (N=19, age: 6.6 ± 2.5 yr, male 63 %). Sleep parameters (total sleep time (TST), sleep architecture) were assessed and compared with age related normal values. Autonomic function of the two groups was estimated by circulatory parameters (blood pressure, heart frequency). **Results:** There was no significant difference in TST, percentage of deep sleep (NE vs. CG, 24% vs. 23%) and light sleep (NE vs. CG, 43% vs. 45%) between NE and CG. NE children had significantly less REM sleep than CG (NE vs. CG, 13% vs. 16%, $p=0.025$). Significant difference was found in the percentage of light and deep sleep between the normal values and both of the study groups (light sleep: NE vs. normal, 43% vs. 50%; $p<0.05$; deep sleep: NE vs. normal, 25% vs. 21%; $p<0.05$). Autonomic function did not differ between NE and CG as far as the measured parameters concerned. **Conclusions:** Our preliminary data suggests no alteration in sleep architecture in NE. Therefore,

to further evaluate cortical arousability in enuretic children a different methodology is necessary in the future.

Keywords: enuresis nocturna, sleep, polysomnography, REM, arousability

K/3 A special case of a 4-week old infant: osteomyelitis and destruction of the atlas and axis

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Introduction Cervical vertebral osteomyelitis involving the atlas and axis in childhood is distinctly unusual that could lead rapidly to devastation of vertebral body. The formation of a retropharyngeal abscess (RPA) may be the primary cause of the destruction of cervical vertebra. The purpose of the presentation to report an unique case of a 4-week old child with multiple abscess that penetrated cervical structures and destruated vertebrae C1-C2. **Methods** A 1-month old boy with multiple craniospinal and thoracal abscess was surgically treated. Therapy was initiated with antibiotics and immobilization. The follow-up examination was prepared with MRI, CT scans and functional X-ray diagnostics. Results Retropharyngeal and thoracal abscess were surgically removed. The child was positioned in a specific fixation device for 8 weeks and functional examination revealed no significant instability of cervical spine after 2 months. Under 3-year follow-up period, the boy presented no sign of neurological deficit and painless neck movements that are hypothetically possible through the remnants of the bony elements of C1-2 and the connective massive scar tissue formation after the inflammation. **Conclusion** C1-2 osteomyelitis is a very rare entity even in children. There is limited experience with treatment, but immobilization of the neck, surgical debridement, drainage and antibiotic treatment are advised. Under the follow-up will be decided the measurement of instability, the reconstitution of the affected

bones and ligaments, and necessity of surgical stabilization.

Keywords: osteomyelitis, atlas, axis, retropharyngeal abscess, pediatrics

K/4 Distinct features of uterine and circulating gamma/delta T cells during first trimester healthy human pregnancy

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Introduction: During the 1st trimester of healthy human pregnancy there is an alteration of immune parameters in the pregnant uterus. While our knowledge on NK cell function during gestation improves continuously, the mystery of the role of gamma/delta T cells in pregnant uterus or in peripheral blood of pregnant women is not completely solved. Here we are going to compare some phenotypic characters of decidual and peripheral gamma/delta T cells during the first trimester of healthy human pregnancy. **Methods:** Peripheral and decidual lymphocytes from healthy pregnant women undergoing elective pregnancy termination at 6-12 weeks gestation were used in this study. We detected the presence of peripheral and decidual Vdelta1+ and Vdelta2+ gamma/delta T cell populations and their CTLA4 expression by Flow Cytometry. CTLA4 is a cell surface molecule and recent results indicate that it is a powerful negative regulator of T cell activation. We also investigated the co-expression of different CD markers (CD56, CD4, CD8) on the different gamma/delta T cell populations. **Results:** Our results revealed an increased proportion of gamma/delta T cells among lymphocytes in the decidua, which are dominantly Vdelta1+. In our hands, decidual gamma/delta T cells preferentially express CTLA4. Among decidual Vdelta2+ T cells we detected a significant increase in CTLA4 expression compared to periphery, while no differences were found in the case of Vdelta1+ T population. In the decidua the number of gamma/delta TCR positive NKT like cells and the rate of CD4+ gamma/delta T cells were also changed. **Conclusion:** Increased CTLA4 expression by decidual Vdelta2+ T cells could

play a part in the control of these potentially cytotoxic lymphocytes. Our results show that decidual gamma/delta T cells form a unique cell population which differs from their peripheral counterpart, indicating that decidual gamma/delta T cells are able to play a role in the maintenance of pregnancy.

Keywords: healthy pregnancy, gamma/delta, T cells, subpopulations, CTLA4, control of cytotoxicity

K/5 The importance of the first trimester combined screening test for the detection of chromosomal aneuploidies

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By literature data, the most effective method detecting high risk cases for chromosomal aneuploidies is the first trimester combined test. The risk calculation is based on the maternal age and history, the ultrasound measurement of the nuchal translucency thickness and the level of placental hormones. In accordance with the requirements of the Fetal Medicine Foundation the test can provide a high sensitivity and low false-positive rate. Our goal was to examine the effect on reducing invasive interventions with the combined test. From 20th September 2011. to 31st March 2013. a total of 345 women were tested at the Department of Obstetrics and Gynecology of the University of Debrecen according to the FMF criteria. The risk assessment for Down syndrome, Edwards syndrome and Patau syndrome was carried out with the First Trimester Screening program Astraia and the results were subsequently analyzed by us. Out of the 345 patients 148 (42,8%) were 35 years old and over, but only 15 (4,3%) of the patients turned to have a high risk ($>1:150$) for trisomy 21 and 2 for trisomy 18. We offered invasive prenatal testing for them, and 1 case with trisomy 18 was detected from chorionic villi or amniotic fluid. 30 patients with a risk below the cut-off finally decided to go for invasive testing and no chromosomal abnormality was

diagnosed. The follow-up of pregnancies is still going on. The combined screening in early pregnancy (week 11-13 of gestation) can significantly decrease the invasive procedures and reduce fetal loss rate.

Keywords: prenatal screening, combined test, trisomies, invasive diagnostics, chromosomal aneuploidy

K/6 Health status of pregnant women and infants in Hungary between 1997 and 2012

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Introduction. Monitoring of the populations is essential to good health policy decisions. This is particularly true in maternal and child health where targeted and timely interventions may have long-term consequences. Our objective was to describe changes in the health status of pregnant women and infants at the national and county level during the period of 1997-2012. Methods. Data were extracted from the mandatory annual reports of district nurse responsible for primary maternal and child care. Information on the smoking status of expecting mothers, special care during pregnancy, pregnant women entering into maternity care after 28 weeks of pregnancy, intrauterine retardation were analyzed using Excel and Stata 10. Results. The mean prevalence of smoking was 14% among pregnant women during the investigation period. The ratio of smoking pregnant women was significantly, at least 30% higher ($p<0.000$) in Borsod, Nógrád, Heves, Szabolcs and Somogy counties. The ratio of pregnant women requiring special care was significantly ($p<0.000$), at least 22% higher than the national average in Somogy, Szabolcs, Borsod and Nógrád counties. Almost 20% of the pregnant women were not taken into primary maternity care by district nurse before the 12th week of the pregnancy, and nearly 2% of the pregnant women entered into care only after the

28th week of the pregnancy. The prevalence of premature babies (8.6%) was higher than the EU average in 2010. Conclusions. National data hide significant regional disparities within the country which should be amended by targeted interventions, taking into account the great regional inequalities in the country. „This research was realized in the frames of TÁMOP 4.2.4. A/1-11-1-2012-0001 "National Excellence Program – Elaborating and operating an inland student and researcher personal support system" The project was subsidized by the European Union and co-financed by the European Social Fund.”

Keywords: health status., maternal and child health, pregnant women, inequality, district nurse

K/7 Analysis of the practice of induced abortions in France induced abortion

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Background: Medical abortion is a widespread technique for terminating pregnancy used in about 40 countries. The method was first introduced in 1988 in France where women have the possibility to choose between medical and surgical intervention. Although 25 years' experience is available, in Hungary all the 40000 induced abortions per year are carried out surgically. Objectives: My aim was to get an insight into the everyday practice of induced abortions with special attention to those carried out medically. To get to know the procedure of the intervention, the number of the successful and complication-free ones, the most frequent complications and if there are factors influencing their appearance. To know the preferences of patients regarding the different methods. Methods: I carried out the retrospective analysis of the medical records of those 204 patients who had gone through an induced abortion between January and March 2012 in the Medical and Surgical Center of Obstetrics in Strasbourg, France. Results: 94% of patients decided to

undergo medical abortion. 97% of the interventions were successful, 73% passed off without any complication. Most frequent complications were early expulsion, prolonged or heavy bleeding and intense pain. Late gestational age raised the rate of unsuccessful intervention and complications requiring hospitalization. Early gestational age increased the percentage of heavy bleeding. Young age raised the rate of vomiting, heavy bleeding and severe pain. Primigravidity can be a risk for bleeding and pain. Conclusion: Medical abortion can be considered to be a safe and successful alternative of the surgical method but providing personal information on probable complications is necessary.

Keywords: medical abortion, France, risk factors, pregnancy

MULTIDISCIPLINARY SESSION VI:

L. Physiology-Pathophysiology session

L/1 The role of endogenous PACAP in the kidney during ischaemia-reperfusion

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Introduction: Several diseases, certain surgical interventions and kidney transplantation are accompanied by ischaemia-reperfusion-induced kidney injury. We have previously described the presence of PACAP (pituitary adenylate-cyclase activating polypeptide) in the kidney and demonstrated its changes following renal ischaemia-reperfusion. The aim of the present study is to investigate whether endogenous PACAP influences the extent of ischaemia-reperfusion-induced injury in the kidney. Methods: PACAP knockout (homozygous and heterozygous) and wild-type mice underwent 45

or 60 minutes of renal ischemia followed by a two-week reperfusion. Kidneys were processed for histological analysis. Sections stained with PAS-haematoxylin were graded for histological parameters (dilatation of the Bowman's capsule, tubular dilatation, thyreoidisation-like changes, lymphocyte and macrophage infiltration, damage of the glycocalyx layer) on a three-degree scale. In other sets of experiments, tissue cytokine expression and the level of the endogenous antioxidant superoxide dismutase (SOD) were also determined in wild-type and knockout mice after 60 minutes ischemia and 24 hours reperfusion. Results: No significant difference was observed in postoperative mortality between the investigated groups. PACAP knockout mice showed more severe histological outcome compared to wild-type mice, with significantly higher histological scores for most of the tested parameters. Cytokine profile of the kidney was markedly altered in PACAP knockout mice and the level of SOD was significantly reduced in these mice after ischemia-reperfusion. Conclusion: Both the partial and the total lack of PACAP results in increased susceptibility to renal ischaemia-reperfusion, the developed injuries are more severe, suggesting that endogenous PACAP has a protective effect in the kidney. Grant support: TÁMOP 4.2.4.A/2-11-1-2012-0001.

Keywords: kidney, ischaemia-reperfusion, PACAP, knockout, nephroprotection

L/2 Expression and phosphorylation of LIM-kinase in cancer cells

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Phosphorylation level of the retinoblastoma protein (pRb) has an essential role in cell cycle regulation. It is determined by the activity of kinase and phosphatase enzymes. Despite the elucidated process of the phosphorylation of pRb, we know much less about the dephosphorylating phosphatases. However, elevated level of phosphorylated pRb in cancer cells suggests the importance of endogenous phosphatase inhibitory mechanisms. One of the most

important enzymes among pRb phosphatases is the myosin phosphatase holoenzyme, which belongs to the Protein phosphatase-1 (PP1) family. The phosphorylated form of the 17 kDa weight CPI-17 protein (P-CPI-17) specifically inhibits myosin phosphatase. Our original aim was to investigate the role of CPI-17 in the dephosphorylation of pRb, but during the experiments the CPI-17-like LIM-kinase (LIMK) got into the center of our interest. In cell lysate we identified proteins similar to CPI-17 with anti-P-CPI-17 antibody, using Western blot analysis. In THP-1 cells we identified LIMK via immunoprecipitation. Flag-tagged LIMK was expressed in HeLa cells. We checked the efficiency of the overexpression with the help of immunofluorescence and Western blot. Viability of cells was analysed by MTT-assay. To measure the phosphatase activity, we administered radioactive 32-P-myosin light chain as a substrate. Anti-P-CPI-17 antibody showed cross-reaction with many proteins (35-75kDa), among which one was identified as LIMK. The efficiency of the LIMK overexpression was confirmed by both immunofluorescence and Western blot analysis. After the overexpression the viability of cells did not decrease in a significant manner, but the phosphatase activity showed a significantly decreased level. After caliculyn-A (CLA) treatment we noticed an increased level of phosphorylated LIMK. In parallel with this, the level of phospho-pRb was also elevated. Our results suggest that the disfunction of phosphatase inhibitory proteins resulting in an increased phosphorylation level of them may contribute to elevated level of phospho-pRb in malignantly transformed cells.

Keywords: Retinoblastoma, protein, Protein phosphatase-1 phosphatase, inhibitory proteins, LIM-kinase, overexpression, Calyculin-A treatment

L/3 Long-term hemodynamic effects of complement C5a antagonist treatment after experimental mesenteric hypoperfusion mesenteric hypoperfusion

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Introduction: Mesenteric circulation is sensitive to systemic hemodynamic derangements thus vasoactive treatments targeting circulatory malfunction could have significant therapeutic relevance. Complement activation plays decisive role here. Our objective was to investigate the long-term effects of complement C5a antagonist (AcPepA) treatment on the mesenteric circulatory changes in a reproducible, standardized small animal model of mesenteric hypoperfusion. **Methods:** In groups 1 and 2 of anesthetized rats (n=6, each) the mean arterial pressure (MAP) of the splanchnic area was kept between 40-50mmHg for 60min by partial aortic occlusion (PAO), group 3 (n=6) served as sham-operated control. Group 1 was treated with AcPepA (4 mg/kg iv) 15 min before the end of ischemia, while no AcPepA was administered to groups 2 and 3. After 24 hrs the animals were re-anesthetized and mesenteric artery flow, ileal microcirculation, MAP, heart rate (HR), cardiac output (CO) and total peripheral resistance (TPR) were monitored. **Results:** 24 hrs after PAO MAP was significantly higher (115 ± 21.2 vs 91 ± 2.5 mmHg) than in the control group, HR (401.8 ± 45.4 vs 348 ± 14.8 bpm) and CO (278.9 ± 28.6 vs 215.7 ± 17.3 ml/min/kg) were also elevated, while intramural red blood cell velocity was significantly decreased. AcPepA treatment moderated the CO elevation (195.5 ± 13.9 ml/min/kg), increased the TPR (1.626 ± 0.15 vs 1.082 ± 0.243 mmHg/ml/min) and improved the intramural microcirculation as compared to the PAO group. **Conclusion:** The C5a antagonist AcPepA treatment in this reproducible small animal model can effectively influence the potentially harmful, local and global long-term consequences of acute mesenteric hypoperfusion. Supported by TÁMOP-4.2.2A-11/1/KONV-2012-0035

Keywords: c5 antagonist, ischaemia, reperfusion, microcirculation

L/4 Ghrelin and nicotine directly increase the dopamine release in the rat striatum and amygdala

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Introduction: The orexigenic peptide ghrelin plays a prominent role in the regulation of energy balance and in the mediation of reward mechanisms and reinforcement for addictive drugs, such as nicotine. Nicotine activates the mesencephalic dopaminergic neurons via nicotinic acetylcholine receptors (nAChR). Ghrelin stimulates the dopaminergic neurons via growth hormone secretagogue receptors (GHS-R1A) in the ventral tegmental area and the substantia nigra resulting in the release of dopamine in the ventral and dorsal striatum and in the amygdala. Previous studies provide little evidence of the effect of ghrelin on these dopaminergic target areas. Therefore, the aim of the present study was to investigate the direct effects of ghrelin on the striatal and amygdalar dopamine release, in vitro. **Methods:** Male Wistar rats and in vitro superfusion system were used. Incubation of striatal and amygdalar slices was performed with tritium-labelled dopamine, followed by superfusion and electrical stimulation. Ghrelin and/or nicotine were administered 12 minutes before the electrical stimulation. Selective GHS-R1A antagonist GHRP-6 or selective antagonist nAChR antagonist mecamylamine were added 10 minutes before the administration of ghrelin and/or nicotine. **Results:** Ghrelin increased significantly the dopamine release from the striatum and the amygdala following electrical stimulation. These effects were reversed by both mecamylamine and GHRP-6. Nicotine also increased significantly the dopamine release in both nuclei under the same conditions. These effects were antagonized by mecamylamine, but not by GHRP-6. In the striatum, ghrelin enhanced the nicotine-induced dopamine release. In the amygdala ghrelin and nicotine elevated equally the dopamine release. **Conclusion:** Our study demonstrates that ghrelin stimulates the dopamine release directly in the rat striatum and amygdala through GHS-R1A and nAChRs. Additionally, ghrelin can amplify the nicotine-induced dopamine release in the

striatum. It also suggests that ghrelin signaling may serve as a novel pharmacological target for treatment of addictive disorders.

Keywords: ghrelin, nicotine, dopamine, striatum, amygdala

L/5 The effect of systemic PACAP treatment on locomotor activity in male and female rats systemic PACAP treatment

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Introduction: The main research field of our team is the effects of pituitary adenylate cyclase activating polypeptide (PACAP), which is a neuropeptide with a wide range of functions. PACAP has protective effects in animal models of various diseases. Recently, a few human studies have been also published. Therefore, it is important to examine how systemic PACAP treatment affects animal behavior. Some previous studies have revealed that the administration of PACAP in the CNS modifies the locomotor behavior of animals. However, there are no details known about the effect of systemic PACAP treatment on general behavior. Most investigations are carried out in male animals, however, we have shown that certain effects of PACAP treatment are gender-dependent: in a rat model of Parkinson's disease PACAP treatment significantly decreased the behavioral deficit in male, but not in female, rats. The goal of the present experiment was the investigation of behavior of male and female rats after systemic PACAP treatment. **Methods:** Wistar rats were treated intraperitoneally with 50 µg PACAP-38. One day before, one and ten days after PACAP administration, open-field tests were carried out. The behavior of the animals were recorded for 5 minutes, and then the locomotor parameters (distance, time activity, rearing, centrally time spent) were evaluated. **Results:** We found that the systemic treatment in male rats did not cause significant behavioral alteration. In contrast, after PACAP treatment the locomotor activity of female rats significantly decreased and their anxiety increased. This difference in behavior could be

observed both 1 and 10 days after the treatment. **Conclusion:** In conclusion our results show that single systemic PACAP administration causes changes in the behavior of female rats. This study also shows the importance of necessity that both sexes should be tested because there could be significant gender differences. **Support:** OTKA K104984, TAMOP (4.2.1.B-10/2/KONV-2010-002, 4.2.2.B-10/1-2010-0029, 4.2.2.A-11/1/KONV-2012-0024), Arimura Foundation, PTE-MTA "Lendület" Program. **Supervisor:** Dr. Horváth Gábor, Dr. Farkas József, Dr. Reglődi Dóra

Keywords: locomotor, behaviour, gender, dependent changes, open field test, rat

L/6 Methane biogenesis in human organism, is case of oxido-reductive stress conditions

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Introduction Our recent studies have demonstrated significant methane CH₄ production in eukaryotic cells in oxido-reductive stress conditions (Cell Physiol Biochem 2008). Our aim was to investigate the possibility of non-bacterial methanogenesis in humans, and to identify the CH₄-producing capacity in patients exposed to heart surgery, where transient suspension of the cardiac action may be accompanied by acute oxido-reductive stress episode. **Methods** Breath samples were taken from the ventilator or the mechanical pump-oxygenator outputs in 10 patients during heart surgery, the exhaled CH₄ production was analyzed with a newly-developed online gas detection method based on photoacoustic spectroscopy. During surgeries, systemic hemodynamics and blood pO₂, pCO₂ and pH values were regularly monitored. Control breath samples were taken in matching group of 15 healthy individuals. **Results** Right after artificial cardiac arrest the breath CH₄ concentration

elevated promptly (10.75 ± 3.06 ppm) in comparison to the baseline values (8.725 ± 2.71 ppm), independently from blood gases, age, sex, or the cause that required surgery. During identical time frame change in methane output was not detected in healthy control population (baseline: $12,220 \pm 5,720$ ppm; end values: $12,460 \pm 5,717$ ppm). Conclusion Transient myocardial hypoxia, caused by the administration of cardioplegic solution, resulted in increased exhaled CH₄ concentrations. CH₄ release might be indicator of transient mitochondrial dysfunction. Detection of CH₄ may be diagnostic tool in pathological states, where hypoxic stress is involved. Support OTKA K75161, OTKA K104656, TÁMOP 4.2.4.A/2-11-1-2012-0001

Keywords: methane, endogenous heart, surgery, stress

L/7 The effects of urocortin II and urocortin III on the anxiety- and depression-like symptoms in nicotine-treated mice

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Introduction: Urocortin II and Urocortin III are selective agonists of the corticotropin-releasing factor receptor type 2. The aim of the present study was to investigate the effects of these agonists on the anxiety- and depressive-like symptoms and the activity of the hypothalamic-pituitary-adrenal axis in nicotine-treated mice. **Methods:** Male CFLP mice were treated intraperitoneally with saline or nicotine for 7 days, 4 times/day. On the 8th and the 9th day they were treated intracerebroventricularly with saline or Ucn II or Ucn III. 12 and 24 hours after the last intraperitoneally administration plus-maze test and forced swimming test were performed for the determination of anxiety- and depression-like symptoms, respectively. In parallel, plasma corticosterone was measured by chemofluorescent method. **Results:** On the 8th

day, following the chronic nicotine treatment, the activity in the open arms increased. Plasma corticosterone level was elevated. On the 9th day, following the acute nicotine withdrawal, the activity in the open arms decreased (anxiety-like symptom); the time of immobilization in the water increased (depression-like symptom). Plasma corticosterone level was even more elevated. Ucn II and Ucn III ameliorated the anxiety- and depression-like symptoms. In addition, both decreased the plasma corticosterone concentrations measured at 12 and 24 hours after the last administration of nicotine. **Conclusion:** Our experiments demonstrate that both Ucn II and Ucn III inhibit the anxiety- and depression-like symptoms and the hyperactivity of the HPA axis. Our results suggest that the selective agonists of CRFR2 could be useful drugs in the therapy of nicotine addiction or nicotine abstinence.

Keywords: nicotine, CRF, anxiety, depression, corticosterone

L/8 The effects of selective CRF receptor antagonists in alcohol-treated rats

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Introduction: Acute alcohol intake induces dopamine release from the striatum and GABA release from the amygdala. These are mediated through corticotropin-releasing factor (CRF), which is produced by both hypothalamic and extrahypothalamic nuclei. The aim of the present experiments was to determine the effects of selective CRF receptor (CRFR) antagonists on the release of extrahypothalamic neurotransmitters in alcohol-treated rats. **Methods:** Male Wistar rats were treated with ethanol or saline solution (control) intraperitoneally for 5 days, 4 times/day. Antalarmin, a selective CRFR1 antagonist or astressin 2B, a selective CRFR2 antagonist, or saline (control) were administered intracerebroventricularly on the 6th or the 7th day, respectively. In vitro superfusion of tritium-labelled neurotransmitters and liquid scintillation

counting was performed to measure the striatal dopamine and amygdalar GABA levels. Results: On the 6th day (12 hours after the last intraperitoneal administration) the striatal dopamine and the amygdalar GABA release increased in rats treated with alcohol, compared to those treated with saline. These effects were inhibited significantly by antalarmin, but not by astressin 2B. On the 7th day (24 hours after the last intraperitoneal administration) a reduced striatal dopamine level and an enhanced amygdalar GABA level were observed in alcohol-treated rats, compared to the control. Both levels were reversed efficiently by antalarmin, but not by astressin 2B. Conclusion: The present results demonstrate that the changes of the striatal dopamine release and the amygdalar GABA release observed following chronic alcohol treatment and consequent acute alcohol withdrawal are mediated exclusively by CRFR1.

Keywords: alcohol, CRF, CRF receptors, striatal dopamine, amygdalar GABA

L/9 Effects of TRPM4 modulation in vascular tissue

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Effects of TRPM4 modulation in vascular tissue
The transient receptor potential melastatin 4 channel (TRPM4) is a monovalent cation channel, which is expressed in various excitable and nonexcitable cells. It is relatively specific to monovalent cations such as Na⁺ and K⁺ over Ca²⁺. Its activation results in increased intracellular Na⁺ concentration, which depolarizes the plasma membrane, and opens the voltage-dependent Ca²⁺ channel. High intracellular Ca²⁺ concentration may initiate contraction of smooth muscle in the vessels. TRPM4 may play an important role in vascular biology, which can influence the blood pressure. Here we performed carotid artery cannulation in anesthetized rats and measured blood pressure, in vivo. Effects of the proposed TRPM4 activator A23187 and the TRPM4 inhibitor 9-phenanthrol were tested. Application of 9-phenanthrol alone was without significant effects. A23187

treatment resulted in a biphasic response: there was an increase in blood pressure at lower A23187 concentrations, while the blood pressure dropped dramatically at higher doses. The blood pressure was 147/122 Hgmm and the heart rate was 432/min at the beginning of the experiments. 3 microgramm/kg A23187 evoked a significant increase in blood pressure to 169/132 Hgmm without effects on the heart rate (396/min at this dose). In contrast, A23187 evoked a robust dilation when applied at 3 mg/kg dose (75/28 Hgmm) with a significant decrease in heart rate (to 276/min). My data suggest that TRPM4 may be modulated by A23187 at low doses. This observation is in accordance with our findings suggesting that A23187 evokes TRPM4 mediated vasoconstriction at nanomolar concentrations. A23187 may be the first selective, high affinity ligand for TRPM4.

Keywords: TRPM4, smooth muscle, vascular tone, calcium channel, blood pressure

M. Behaviour sciences session

M/1 The influencing factors of a practice leader's judgement

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Introduction: As our previous studies have shown, the quality of the practical education is the most important factor influencing student satisfaction. Therefore, development in this field can efficiently increase the prestige and marketability of the faculty. The goal of our study was to explore the connection between the personality of the practice leader and the judgement of the subject; to define the factors, which determine the judgement of the practice leaders, and to possibly create descriptive and predictive models to improve the judgement of the practice leaders. Methods: 16581 anonym questionnaires have been processed. Explorative and confirmative factor analysis has been used to validate the inventory. Forward stepwise automatic linear modelling and decision tree modelling (CHAID) were used to explore the

underlying connections between the items. Results: Our developed questionnaire can define the judgement of practice leaders with 94,6% validity and in four components. Satisfying, 65-80% accurate linear models were made, which have determined, that the personality of practice leader is only the sixth most important factor in the judgement of his/her subject. In the judgement of the practices, the personality of practice leader is the second most important, right after the usefulness of the practice. External factors do not influence the judgement of practice leader, each of the ten important influencing factors are connected to his/her personality. Excellent, 75-80% accurate CHAID models have shown, that in the first year the wide intellectual horizon of the teacher, in the second year the helpfulness, in the third year the fascination, in the fourth year the demonstration and in the fifth year the systematization is utmost important. For the English and Hungarian students the wide intellectual horizon, while for the German students the systematization are the dominant factors. Conclusion: Our inventory can define the influencing factors of the practice leader's judgement with excellent validity, hence we could make satisfyingly accurate models. Although the practice is the most important in the judgement of the subject, but it's usefulness is more important, than the personality of practice leader. External factors do not influence the judgement of practice leaders, but different factors depend on the year and the nationality.

Keywords: education, quality, feedback, practice, leader

M/2 The philosophical anthropological and psychopathological aspects of the jungian thesis of synchronicity

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Carl Gustav Jung was one of the psychologists with greatest influence whose theories about the collective unconscious and archetypes affected not only modern psychiatry but philosophical anthropology too. One of his most important ideas is the theory of synchronicity – assuming an

organizing principle (considered to be chance in everyday life) besides causality. Jung makes references to the theory of synchronicity in more of his works but summarizes it as an individual book only when approaching the end of his life. This work was co-written by the well-known quantum physicist Wolfgang Pauli, presenting modern physical arguments supporting the Jungian theory. In my lecture I summarize the original Jungian thesis system of synchronicity together with the most important secondary literature and I briefly touch the metaphysical and quantum physical aspects of synchronicity. Besides theoretical research I performed psychological examination of reception, showing short stories describing synchronistic phenomena to psychotic patients during the course of interviewing them. In the case of four, acute psychotic patients I found their interpreting the stories from the perspectives of their misperceptioned world. In one case where the patient was in remission, his correct interpretation was detected, moreover he was able to define his own past psychotic experiences within the framework of the synchronistic theory. By phenomenological differentiation of confusion and delusion, conclusion can be drawn that synchronicity as an explaining principle can be seen as a parallel to the „confusion” type of psychotic experience.

Keywords: C.G.Jung, synchronicity, chance, collective, unconscious, psychosis

M/3 A comparative study of coping strategies and parental attitudes of parents with a child conceived with assisted reproductive technology and parents with a naturally conceived child

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Introduction: Infertility has become a world-wide public health problem. At the same time, with the advanced infertility treatments specialists can help almost every infertile couple to become parents. However, both infertility and infertility treatments impose a serious physical and psychological burden on sterile couples. Our objective was to explore coping strategies and

parental attitudes of couples who have undergone successful assisted reproduction (specifically in vitro fertilization, IVF), and compare these factors to those couples' coping strategies and parental attitudes who conceived their children naturally. Methods: Altogether 168 people took part in our research. The research group consisted of 42 infertile couples treated at the Kaali Institute in Debrecen, while the control group consisted of parents of naturally conceived children (also 42 couples). We applied the Ways of Coping Inventory, the Psychological Immune System Inventory and the Parental Attitude Research Instrument. Results: Contrary to the control group, couples who were treated successfully with IVF prefer seeking emotional balance and withdrawal as coping strategies to emotional and impulsive behaviour. The IVF couples feel a higher sense of coherence and creative self-concept, and they have more democratic parental attitudes than the members of the control group. Mothers apply support-seeking coping and withdrawal coping more frequently than fathers in both groups. Conclusion: Our research and the previous studies confirm the psychological factors' role in the development and treatment of infertility.

Keywords: infertility, assisted reproduction, IVF, coping strategies, parental attitudes

M/4 The role of school performance in terms of problem behaviours among adolescents school performance

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Adolescence is a critical life period in terms of several problem behaviours such as alcohol drinking and smoking. Both of them cause abundant social and public health problems. The early use of them predicts the late substance use in adulthood. The school performance may have an effect on alcohol drinking and smoking. Poor performance has a connection with learning difficulties, school problems which are associated

with higher risk of substance use. The purpose of the present study was to obtain the effect of school performance on smoking and alcohol drinking. Our sample consisted of 2072 students from elementary and secondary schools. The study was performed in Mako and the villages in its area in Hungary. Self-administered questionnaires were applied that measured sociodemographic variables, lifetime and monthly prevalence of smoking and alcohol consumption, beliefs and attitudes related to substance use. Cross tabulations and chi square test were used to test these relationships with SPSS MS 19.0 statistical program. We found strong relationships between poor school performance and higher risk of substance use both in case of smoking and alcohol drinking. Strong associations were revealed with heavy smoking, problem drinking and drunkenness. According to our results the poor school performance is a key factor predicting smoking and excessive alcohol drinking. We should pay attention to this factor during planning prevention programmes because due to this fact we are able to identify some subpopulations at high risk.

Keywords: problem behaviour, smoking, alcohol, drinking, adolescents

M/5 The development of children's pretend play

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Introduction Play has an important role in the human development. This activity supports the development of the children's social-, cognitive-, physical-, emotional- and communicative skills. Children can practice and consolidate the desired patterns of action and social rules during their play activities. Furthermore object play gives the opportunity to know more about our environment and culture. In this way, objects can be regarded as the mediators of socialization. Although the focus of the Wing's triad, the basis of the classical diagnostic system, connects to the deficiencies of the previous areas, problems of object use can be also observed in autism spectrum disorder (ASD). Methods The aim of my study was to compare the developmental

patterns of pretend play in typical development (TD) and in ASD with each others. So in my investigation I studied videotapes of child-mother dyads' play activities. Children ranged in age from 4-5.5 years. I analyzed the recordings by Observer XT 8.0 program software and SPSS 15.0 for Windows Evaluation Version. Results I found more spontaneous and creative play activities with varied forms of object use in TD. In contrast, ASD-children rather had a tendency to present at most conventional object use and rigid forms of imitation. ASD-children's parents were more dominant in the dyads than mothers with TD-children, which tendency was also characteristic in connection with the analysis of object use and verbal instructions. Conclusion My results support that while children with TD are able to explore the various affordances of the objects and – driven by their imagination – use these objects in many different ways, this is almost unthinkable for the ASD-group. But explicit information, better structured tasks and visual aid can be effective methods for stimulated symbolic play and early intervention. In my case study I would like to present you two dyads' play activities and demonstrate the differences of the development of pretend play through more semi-structured sets of several objects were made available by the investigator.

Keywords: case study, autism, spectrum disorder, typical development, pretend play, socialization

M/6 The patterns of play activities in autism

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Introduction Autism is a neurodevelopmental disorder. It is characterized by (1) abnormal or impaired development before the age of 3 years (2) qualitative impairment is social interaction and communication, furthermore (3) restricted, repetitive, and stereotyped and restricted patterns of interest. The clinical picture is different from the other kinds of pervasive developmental disorders. Although there are a lot of studies in connection with the cognitive aspects of autism, disease of sensory-perceptual

experiences and atypical play patterns can be also found in the disorder. **Methods** In our investigation we studied videotapes of child-mother dyads' semi-structured play activities. We analyzed the recordings by Observer XT 8.0 software. Half of the children were diagnosed as having autism spectrum disorder (ASD). The others were children with typical development (TD). All of the children were preschool-aged and we recorded the interactions in the homes of the consenting families. **Results** Based on our results, it was demonstrated that more flexible, creative forms of play and imitation had been explored in typical development. Members of the group of children with autism more often used stereotyped and repetitive types of object play. While TD-children's mother rather let their son/daughter to unfold in his/ her spontaneous play, ASD-children were intensively influenced by his/ her mother how to play with the available objects. **Conclusion** In summary, our results confirmed that different patterns of play activities can be explored in autism. Further studies are needed to know more about these characteristics, which can open the door to new options of intervention.

Keywords: autism, spectrum disorder, typical development, object use, play activity, child-mother diad

N. Pathology-oncology session

N/1 Possible anti-tumorigenic usage of angiostatin in oncotherapy

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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.

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

N/2 Examination of the protective effects of PACAP in rat diabetic nephropathy

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Introduction: Diabetic nephropathy is the leading cause of end-stage renal failure and accounts for 30-40% of patients entering renal transplant programmes. Pituitary adenylate cyclase activating polypeptide (PACAP) is a neuropeptide consisting of 38 amino acids. Its nephroprotective effect was proved in numerous in vivo and in vitro studies. The aim of our study was to investigate the effect of PACAP in diabetic nephropathy. Methods: Diabetes was induced by a single intravenous injection of streptozotocin (65mg/kg) in male Wistar rats. PACAP-treated animals were administered intraperitoneally

20ug PACAP every second day. Body weight and blood sugar levels were monitored weekly. Kidneys were removed after 8-weeks survival. Besides the complex histological analysis (glomerular PAS positive area/glomerulus area, tubular damage, arteriolar hyalinosis), expression of several cytokines was evaluated by cytokine array. Results: Histological analysis revealed severe diabetic nephropathy in kidneys of control diabetic animals (glomerular PAS-positive area expansion, tubular damage, Armanni-Ebstein phenomenon, vascular hyalinosis). PACAP-treatment significantly diminished the damage. Diabetic kidneys showed strong cytokine activation compared to their healthy controls. PACAP was effective in downregulation of several cytokines including CINC-1 (cytokine induced neutrophil chemokine), TIMP-1 (tissue inhibitor of metalloproteinase 1), LIX (lipopolysaccharide-induced CXC chemokine), L-selectin. Conclusion: To conclude, PACAP is effective in ameliorating diabetic nephropathy. These results raise the opportunity for the use of PACAP as a possible therapeutic or preventive method in treating renal complications of diabetes. Supported by PTE-MTA "Lendület" Program, Arimura Foundation, OTKA K104984, TAMOP 4.2.1.B-10/2/KONV-2010-002, 4.2.2.B-10/1-2010-0029, 4.2.2.A-11/1/KONV-2012-0024.

Keywords: PACAP, diabetes, kidney, cytokine, protective

N/3 Measuring impact of various clinical parameters and postoperative therapy on survival of glioblastoma patients

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Introduction: Treatment of glioblastoma patient has undergone major development in the last 7

years. Introduction of routine concomitant chemoradiotherapy using temozolomide has improved survival rates. Efficacy of bevacizumab monotherapy, however, has not been fully proven. In this research we studied survival rates of glioblastoma patients in the Department of Neurosurgery, UD MHSC, examining effects of different treatment modalities and various clinical parameters on survival. **Methods:** Significance of clinical parameters (age, gender, Karnofsky performance Score, extension of surgical excision, tumor location, -size, -side) were tested versus different postoperative treatment methods (radiotherapy alone, concomitant radio-chemotherapy, concomitant radio-chemotherapy + bevacizumab) and survival data was analyzed in case of 104 glioblastoma patient in our institue. **Results:** We couldn't prove any significant influence of the tested clinical parameters on survival. Radiotherapy+temozolomide resulted in significant longer survival compared to radiotherapy ($p[RT \text{ vs. } RT+TMZ]=0,0098$), while post-progression bevacizumab treatment after concomitant chemo-radiotherapy has also lengthened survival ($p[RT+TMZ \text{ vs. } BVC]=0,0232$). **Conclusion:** Age and gender of the patient, location, size and size of the tumor showed no effect on survival rates. KPS defined postoperative treatment but had no further effect on survival. Surgical radicality seemingly has positive effect on survival but its role cannot be fully cleared statistically. Clinical parameters have an important role in helping the clinican to choose the treatment method but they cannot be used as prognostic factors. Postoperative KPS has a more important role than surgical radicality. Improving oncotherapy clearly had a positive effect on patient survival, concurring chemoradiotherapy plus bevacizumab monotherapy after progression providing the best survival rates.

Keywords: glioblastoma, radiotherapy, temozolomide, bevacizumab, prognostic factors

N/4 The effect of copy number variation on prognosis in glioblastoma multiforme

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Introduction: Glioblastoma multiforme (GBM) is the most common and most malignant primary brain tumor. The expected median survival of the patients is merely 12-14 months. Despite the expanding therapeutic options, the overall response is still low, so it is extremely important to identify prognostic and predictive biomarkers. During tumorigenesis genetic errors accumulate in oncogenic pathways. One type of these errors is the copy number variation (CNV): gene amplifications and deletions. Recent studies revealed the import role of CNVs in GBM. **Methods:** We acquired CNV, clinical and methylation data of 577 patients suffering from GBM from the TCGA database with the cgdsr R package. To identify significant CNVs for each gene we compared the prognosis (overall and progression free survival) of patients with and without a certain copy number alteration. The comparison was made with Kaplan-Meier analysis using the survival R package. **Results:** After p-value corrections was made we identified 2 genes with homozygous deletion (CDKN2A, CDKN2B), 157 genes with heterozygous deletion (e.g., DKK1 MBL2), and 41 genes with amplification (e.g., VSTM2A, SEC61G, EGFR IQCE) that significantly linked to prognosis. All of these genes were altered at least in the 25% of the samples. **Conclusion:** With in silico analysis several genes were identified, which may be related to the survival of GBM patients, and may be useful biomarkers for prognosis. To validate our results we collected 251 paraffin embedded samples from the patients of the OITI (National Institute of Neurosciences). Currently, the isolations of DNA is in progress. **Support:** TÁMOP 4.2.4.A/1-11-1-2012-0001

Keywords: glioblastome multiforme, R copy, number variation, TCGA, biomarker

N/5 MicroRNAs: regulation of gene expression in carcinogenesis, clinical applications in haematological malignant diseases

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MicroRNAs (miRNAs) are a class of non-coding RNAs that regulate gene expression at posttranscriptional level. The 19-24nt mature form is the result of a processing process consisting of several sequential steps in both the cell nucleus and the cytoplasm. Emerging amount of evidence confirms the role of miRNAs in carcinogenesis. Among their target genes, numerous regulators of cell cycle, cell proliferation, DNA repair and apoptosis can be found, therefore miRNAs are implicated in the initiation and progression of cancer, in tissue invasion and in metastasis formation as well. They can act as oncogenes (oncomiRs) and tumorsuppressors (anti-oncomiRs) by targeting tumorsuppressor genes and oncogenes, respectively. MiRNA profiles supply information about the origin and differentiation state of tumours, moreover, their altered levels often can be detected in premalignant conditions. MiRNAs have key role in fine-tuning diverse cell functions. Many of them are involved in the regulation of haemopoiesis. Altered miRNA expression levels were observed in different types of leukemia, but their exact role in the pathogenesis has not been elucidated. However, there are successful attempts to apply miRNAs in the diagnosis and prognosis of acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). Measurement of the expression levels may help clinicians to choose the most suitable therapy, or even to predict the success of administering different kinds of chemotherapeutic drugs. MiRNAs are also regarded as promising therapeutic targets: antitumour effect can be achieved by increasing or decreasing the level of them, which may also improve the results of other therapeutic strategies. All in all, application of miRNAs in the diagnosis, prognosis and therapy of leukemia can contribute to a more personalized therapeutic approach in haemato-oncology.

Keywords: microRNA, leukemia, diagnosis, prognosis, therapy

N/6 Adjustment of the quantitative morphometric measurement of cell proliferation in squamous cell carcinoma

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Introduction: The Ki-67 nuclear protein expression is used as a prognostic factor in malignant tumours. Exact measurement of the Ki-67 positive nuclei is long-drawn. Morphometric methods are used in the measurement but most of them require the pathologist's valuation. The digital method is more precise than the appraisal, or the semi-quantitative measurement. **Objective:** Elaboration of a method for the automatic recognition and measurement of the Ki-67 protein expression. **Methods:** -Detection of the Ki-67 protein, by immunohistochemistry (Benchmark XT automaton), on squamous cell carcinoma samples. -Digitalized slides, evaluated by an automatic quantitative morphometric programme (PanoramicViewer, NuclearQuant module: NQ), by manual counting of nuclei (MAN) and by an area-based morphometric method (Leica Qwin quantification module: QW). -6 cases were studied, choosing 3-3 representative fields of vision per slide. -Evaluation of the same fields of vision with the three methods. **Results:** On average there were 434 nuclei per field of vision. The NQ recognised 74,3% of the nuclei (SD:9,38). The NQ detected 26,1±21,5% nuclear Ki-67 positivity, the MAN detected 22,5±18,8%. By the MAN, we divided the 6 cases into a high and a low Ki-67 protein expressing group (8,3±4,6% versus 36,8±16,6%), the difference between the two groups were significant with the three methods (NQ, MAN, QW), (Mann-Whitney, p<0,05). Spearman's correlation shows significant correlation between the data obtained by the three methods. **Conclusion:** The NQ module can be a good solution for the automatic measurement of the Ki-67 protein expression. Recognition of all nuclei isn't required for determining the percentage of positive nuclei.

Keywords: Ki-67, automatic detection, measurement, exact

O. Lunch symposium

O/1 Medical field socialisation

Levente Láncki M.D.

MULTIDISCIPLINARY SESSION VII.

P. Internal medicine-Family medicine session

P/1 Clinical features of cancer associated myositis

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Polymyositis (PM) and dermatomyositis (DM) are systemic autoimmune diseases classified as idiopathic inflammatory myopathies. Their main characteristics are symmetric proximal muscle atonia and typical skin symptoms in dermatomyositis. The frequency of the association of myositis and tumorous diseases (CAM=cancer associated myositis) is variable, the relative risk of malignancy in DM is 3-fold and 1,3-fold in PM. Our aim is to compare the clinical features, symptoms characteristics and laboratory findings in CAM and not tumor associated cases. We enrolled 78 PM/DM patients from the Clinical Immunology Department in our study. We created two patient groups: cancer-associated dermato- and polymyositis (CAM DM: n=20, age: 53,8+-15,4 years, CAM PM: n=6, 55,1+-9,5 years) and two control groups: (DM: n=30, 49,7+-14,3 years, PM: n=22, 43,5+-12,1 years). The inclusion criteria in the CAM group were the appearance of the malignancy within a one year window of the myositis diagnosis. Group-wise differences in quantitative parameters were evaluated with Student's t-test, for the relationship between continuous parameters we used Pearson correlation coefficient. In cases of CAM DM, the muscle atonia was more severe and the prevalence of distal muscle atonia was significantly higher (25% vs. 3,3%). Similarly, severe skin symptoms were more frequent, the largest deviation was shown for the periungal teleangiectasia (30% vs. 3,3%). In tumor associated DM, elevated We was noticed (55% vs. 23,3%). In CAM DM patients we discovered that the number of muscle groups affected and the age were inversely correlated (Pearson: -0.695,

p=0.001). Most of the presented findings can be attributed to the presence of a tumor, although many differences cannot be explained by the effect of the tumor; we assume the interaction between the autoimmune disease and the malignancy. „This research was realized in the frames of TÁMOP 4.2.4. A/1-11-1-2012-0001 „National Excellence Program – Elaborating and operating an inland student and researcher personal support system” The project was subsidized by the European Union and co-financed by the European Social Fund.”

Keywords: myositis, cancer associated myositis, systemic autoimmune disease, tumor, myopathy

P/2 Clinical features of patients with juvenile and adult dermatomyositis

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Juvenile and adult dermatomyositis are chronic, immune-mediated myopathies characterized by progressive proximal muscle weakness and typical skin symptoms. The main aim of our research project was to compare children and adult patients by examining the symptoms, laboratory and immune-serology findings in the two groups. We carried out our research at the University of Debrecen, Medical and Health Science Center, Internal Medicine Department, Clinical Immunology Department where we analyzed data of 57 patients. We set up two patients groups: one with 27 people (average age: 8,7 +/- 4,2years) who suffered from juvenile dermatomyositis (JDM) and 30 persons (average age: 50,3 +/- 16,2years) having adult dermatomyositis. Group comparisons were done with Fisher's exact test and Pearson's chi-squared tests. During the analysis, p values equal or smaller than 5% were accepted as significant. We found statistically significant differences between the juvenile and adult patients in some clinical symptoms, muscle enzymes and inflammatory parameters (CK,LDH,GOT,CRP,We) at the

beginning of the disease. Regarding the symptoms, the incidence of the calcinosis ($p=0,008$) and muscle atrophy ($p=0,011$) were higher in juvenile dermatomyositis. In the case of the adults the V-sign ($p=0,001$), mechanic hand ($p=0,012$), poikiloderma ($p=0,005$) and the Raynaud-phenomena ($p=0,054$) were more frequent. The laboratory findings revealed that the CK ($p=0,005$), LDH ($p=0,000$), GOT ($p=0,054$), We ($p=0,044$) and CRP ($p=0,001$) levels were higher in adult patients at the beginning of the disease. Regarding the immune-serology parameters, we did not find significant differences between the two patient groups. The explanation of this result can be the low number of patients and the small positive cases. Conclusion: our research project supported the data from the literature. Furthermore, despite the small number of patients we could show significant differences in patients with juvenile and adult dermatomyositis.

Keywords: juvenile dermatomyositis, calcinosis, myopathies, serology

P/3 Method for the examination of urinary and tear orosomucoid

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Introduction: Orosomucoid (alpha-1 acid glycoprotein, AGP) is a positive acute-phase serum protein. It is acid-soluble and its molecular mass is 43 kDa. It has been identified in urine and tear of healthy persons, however its pathophysiological and laboratory diagnostical benefit is hardly known in these samples. In our presentation we would like to demonstrate the elaboration of a sensitive method which enables the examination of orosomucoid in urine and tear samples. Furthermore, our aim was to determine the information value of this parameter in different inflammatory states. **Materials and methods:** Samples were obtained from outpatients with Crohn's disease and from septic patients of ICU. The control group consisted of healthy individuals. For each person serum and urine samples (occasionally also tear samples) were obtained at the same time point. Serum AGP

was determined by routine immune turbidimetry. To measure urinary and tear AGP, we elaborated a Western blot method, by enhanced chemiluminescence (ECL) detection. To verify the validity of the quantitative ECL method, we used acid extracts of sera and the obtained ECL data were compared with the directly measured AGP content of sera. Results: Good correlation was found between automatically measured serum AGP data and the corresponding acid extract ECL values ($r^2=0,763$). In the urine samples of Crohn's disease patients the elevation of AGP levels were 4-fold, while in the tear samples it appeared 7-8 times higher compared to data of controls. In septic patients urinary AGP data showed an extremely high elevation (15-20 times vs. controls) related to the severity of disease. Conclusion: We developed a sensitive method for detection of AGP in urine and tear. Urinary and tear orosomucoid undoubtedly shows informational value in diseases conditions we have studied. A further elaboration of a routine automated method by manufacturers would be desirable.

Keywords: orosomucoid, method, Western-blot, Crohn, sepsis

P/4 Analysis of thrombin generation after platelet activation

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Introduction: During activation of the hemostatic system, the platelet and plasma components are usually separately analysed. The activation of platelets can be characterized by measuring cell surface and soluble platelet markers, while the acceleration of the coagulation system is reflected in enhanced thrombin generation. The aim of this study was to simultaneously investigate platelet activation and thrombin generation and their modulation in an experimental setting, that mimics the in vivo circumstances. **Methods:** Platelet rich plasma (PRP) was prepared from peripheral whole blood samples, which was incubated with a protein phosphatase inhibitor, calyculin A (CLA). Platelets were activated by thrombin-receptor activating peptide (TRAP) to

elicit maximal activation. Surface expressions of P-selectin, phosphatidil-serine (PS) expression and platelet-derived microparticle (PMP) formation were examined by flow cytometry. Thrombin generation test was carried out by activation of PRP samples with low concentration of tissue factor. Samples were measured in a fluorimeter and the results were analysed by the thrombinoscope software. Results: In non-activated samples platelet P-selectin expression mean value was 3,6%, which slightly increased upon CLA preincubation to 13,3%. TRAP-induced P-selectin surface expression (58%) decreased to 16,8% by CLA preincubation. Similarly, CLA decreased TRAP-induced PMP formation in the microparticle region also (23,6% vs. 3,1%). In non-activated samples CLA did not have alter PS-expression (2,3% vs. 2,4%), but TRAP-elicited PS-expression was completely blocked (17,9% vs. 3,9%) by CLA. In TRAP activated samples CLA preincubation prevented the TRAP-induced thrombin generation (peak thrombin) and delayed the formation of thrombin (lagtime, time to peak, slope). Conclusion: TRAP activation of platelets increases thrombin generation in PRP. CLA generated a slight increased degranulation on non-activated samples, but completely blocked the TRAP-induced platelet activation and thrombin generation.

Keywords: platelet, activation, calyculin, inhibition, thrombin generation

P/5 Analysis of data of plasma exchange treatment in the last 30 years (1983 - 2012) at the University of Debrecen, Medical and Health Science Center, Department of Internal Medicine, Intensive care unit

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Introduction: Pheresis is a Greek word, in case of plasma removal the process is called plasmapheresis. The first patient who underwent plasmapheresis had Waldenström macroglobulinaemia, after the plasma exchange the patient condition significantly improved. In 1983 Hungary's 2nd apheresis center was founded at the Intensive Care Unit, Department of

Internal Medicine, University of Debrecen Medical and Health Science Center. 5921 treatments were carried out in the last 30 years. Methods: We collected the informations from the patients charts and informatical registry system of the patients (MedSolution system). We analyzed 1184 patients' 5921 treatments data. Results: More than half of the indications were neuroimmunological (myasthenia gravis, Guillain-Barré syndrome, Devic syndrome, sclerosis multiplex and CIDP). We did fairly high number of treatment in systematic lupus erythematosus and in vasculitis as well. In SLE the indication has changed in the last 30 years. Nowadays the main indications are cerebral lupus, secondary antiphospholipid syndrome and diffuse alveolar haemorrhage. In the therapy of progressive systemic sclerosis the role of plasmapheresis was taken over by photopheresis. The clinical manifestations of hyperviscosity can also be cured efficiently with plasma exchange, therefore we can see a relatively high number of treatment because of hyperviscosity. In our practice hypertriglyceridaemia induced pancreatitis retains his role as one of the main indications of therapeutic plasmapheresis in the last 30 years. Among intoxications, the mushroom intoxication's apheresis treatment was the predominant. Conclusion: During the analysis we have found that the indications changed during the 30 years. More than half of the indications are neuroimmunological, which correspond to the international data. In the treatment of crisis situations of systemic autoimmune diseases plasma exchange preserved its main position, but the indications changed.

Keywords: plasmapheresis, neuroimmunology, indication, hypertriglyceridaemia, intoxication

P/6 Investigation of the transport processes of heme, met-heme and hemoglobine in blood serum by ionchromatography and atomic absorption spectrometry

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In the etiology of vascular diseases the heme stress has a dominant role. Red blood cells contain a lot of heme, but escaping from hemoglobine they have a damaging effect on the wall of the vessels. The blood plasma contains some hemoglobine- and heme- binding proteins, which can provide protection for the resident cells of the vessel against these damaging effects. The haptoglobine is able to bind the hemoglobine while the hemopexin binds the heme. The aim of our work was to find other proteins which are similarly able to bind heme and hemoglobine. For separation and fractionation of the components of the human blood serum ion exchange chromatography was used. Up to the top of ion exchange column 2.5 mL native serum sample was stratified. The absorbance of the fractions was measured by UV spectrophotometer. In the collected nearly 70 fractions we determined the iron content by graphite furnace atomic absorption spectrometry. In the studied concentration range a significant albumine binding can be seen. Furthermore, the heme changed the ion exchange capacity of albumine. It was a surprise that, at the IgG peak iron accumulation appeared, which shows dose dependence. With our method at 1 μ M added heme we found the natural level of iron concentration. Whereas, at higher heme concentration a significant dose-dependent heme-binding was detected at the range of IgG peak. Both the oxidized and reduced hemoglobine at their least added concentrations can be eluted with Immunoglobuline G. On the basis of our studies the IgG can have a heme-binding capability which contributes to the defending mechanism of the blood serum. This new function of immunoglobuline can have significance in etiopathogenesis of vascular diseases.

Keywords: heme stress, ion exchange, chromatography, atomic absorption spectrometry, field-flow-fractionation, Immunoglobuline G

R. Anesthesiology-intensive therapy – Neurology-Psychiatry session

R/1 AGING INCREASES THE CONTRACTILE RESPONSES OF ISOLATED ARTERIES TO POTASSIUM CHLORIDE (KCL)

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Introduction: Aging greatly affects the vasomotor function of the blood vessels in order to adapt - among others - to the changes in the hemodynamic environment. Previous studies demonstrated that the magnitude of angiotensin 1 receptor (AT1R) mediated responses of isolated vessels to angiotensin II (Ang II) exhibits a bell shape curve (increases in young and decreases in old vessels). Hypothesis: We hypothesized that this phenomenon is not due to change in the contractile ability of smooth muscle. It is known that KCl-induced response of arteries is mediated without receptor effecting directly the smooth muscle cells allowing testing our hypothesis. Thus, we investigated the responses to KCl of rat carotid arteries isolated from young and old rats. Methods: Carotid arteries were isolated from newborn (8 days: 8d), young (1 month: 1m), adult (12 months: 12m) and senescent (30 months: 30m) rats and their vasomotor responses were measured after repeated administration (after 20 minutes) of KCl (60mM) with an isometric myograph (DMT-610M). Results: Contractions to the first administration of KCl increased from 8d to 30m (8d: 2.4 ± 0.5 mN, 1m: 5 ± 0.7 mN, 12m: 6.1 ± 0.3 mN, 30m: 11 ± 0.7 mN, respectively, $p < 0.05$). Following second administration of KCL also increased from 8 d to 30m (8d: 2.8 ± 0.4 mN, 1m: 5.4 ± 0.3 mN, 12m: 6.3 ± 0.4 mN, 30m: 10 ± 0.5 mN, respectively, $p < 0.05$). There were no differences in the magnitude of vasomotor responses between the first and second administration to KCl (8d: 0.4 ± 0.1 mN, 1m: 0.5 ± 0.3 mN, 12m: 0.2 ± 0.9 mN,

30m: $1 \pm 0.3 \text{ mN}$, respectively, $p > 0.05$).
Conclusions: The data suggest that the previously observed decreases in Ang II-induced contractions in old and senescence arteries were not due to the limited vasomotor capacity of smooth muscle, rather due to changes in AT1-receptor signaling, because the contractile capacity of arteries increases with aging. (Support: SROP-4.2.2.A-11/1/KONV-2012-0024, SROP-4.2.2.A-11/1/KONV-2012-0017, TÁMOP 4.2.4.A/2-11-1-2012-0001, Hungarian Society of Hypertension 2010/2011, Hungarian Scientific Research Fund, OTKA K-71591)."

Keywords: Aging, KCl, Isolate, vessel, hypertension, contraction

R/2 The Effect of Sevoflurane on Cerebral Vasoreactivity and Systemic Arteries

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Introduction: Sevoflurane (SEV) is a widely used volatile anesthetic, although some of its effects are not completely known in details, therefore we investigated how different CO₂ concentrations affect cerebral vasoreactivity and systemic arteries during SEV anesthesia. Patients and methods: The study involved 24 ASA I patients. Cerebral circulation was assessed with transcranial Doppler ultrasound, while SphygmoCor was used to obtain information about systemic arteries. The examination was repeated four times: at first preoperatively, then 20 minutes after induction at 40 mmHg end-tidal CO₂ (ETCO₂) and 5-5 minutes after reaching 35 and 30 mmHg ETCO₂. The minimal alveolar concentration of SEV was adjusted to 1.0. Results: The MAP and its central diastolic component reduced significantly after induction, the augmentation pressure and the heart rate corrected augmentation index (Alx75) were significantly higher and at 40 and 30 mmHg ETCO₂ the subendocardial viability ratio was significantly reduced compared to preoperative values. Mean blood flow velocity has reduced while pulsatility index has elevated significantly

each time after ETCO₂ was altered. Conclusion: An intensified CO₂ reactivity of the cerebral vessels was registered, which highlights that intraoperative CO₂ changes have a more potent effect on intracranial pressure and blood flow than it was previously presumed. SEV dilates systemic resistance vessels, which reduces diastolic blood pressure. Meanwhile, the nearly constant systolic blood pressure and the elevated Alx75 indicate an increased arterial stiffness. Cardiac afterload remains unchanged, while the fall in diastolic blood pressure may decrease coronary artery perfusion causing an imbalance between myocardial oxygen supply and demand.

Keywords: Sevoflurane, Transcranial Doppler, SphygmoCor, Cerebral vasoreactivity, Arterial stiffness

R/3 Rare epileptical seizure phenomena

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According to general knowledge and the statistical data of patients registered and treated in medical practice, the most common seizure types in adulthood are tonic-clonic grand mal and temporal complex partial seizures. Drawing the conclusion we can see that tonic stiffness followed by unintentional, rapid muscle twitching and aura followed by disturbance of consciousness accompanied by munching, rummaging automatism are the two seizure phenomena known the best. These two seizure types do not include though all the elements of the wide spectrum of symptoms in this disease. In the course of my work I examined the seizure phenomena with a more rare occurrence, which – originating from their colorfulness – can mean serious differential diagnostic problems not only for neurologist but also for experts of other medical specialties. I performed semiological examinations on patients from the Department of Neurology, University of Pécs diagnosed with epilepsy according to comprehensive investigation of neurological and neuroanatomical literature. In the course of my lecture I analyze rare seizure phenomena: seizure phenomena accompanied by visual (palinopsia,

ictal blindness), auditorial (musical hallucinations), affective (orgasmic aura, euphoric laughter), cognitive (forced thinking, running thoughts), vegetative (asystolia) and motoric (unusual, rare automatism) symptoms. Briefly touching on the subject of reflex epilepsies in which the seizure is provoked by an environmental factor or by a patient's concrete course of action (light, music, reading, writing, hot water or even brushing teeth). So as to the demonstration of some rare seizure phenomena I present some video recordings.

Keywords: epilepsy, reflex, seizures, gelastic seizures, rare seizure, phenomena, semiology

R/4 The role of medical imaging in planning and choosing the appropriate minimal invasive spine surgery

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Introduction Significant development of minimal invasive procedures has been witnessed in spine surgery recently to avoid biomechanical complications that occurred following some traditional destructive methods. As an additional merit the effectiveness of these operations were improved by the new techniques that prevent damage to crucial posterior stabilizers and preserving structural integrity and stability of the spine. **Methods** The wide variety of reported minimal invasive methods for different pathologies necessitates systematic definition. A classification system is introduced according to the relational localisation of pathologic lesions. The right localisation was determined by medical imaging modalities. **Results** The presented classification system helps the surgeon to select and apply the appropriate minimal invasive procedure depending on relational localisation of

the pathology and process in the spinal canal. The classification system can be recommended and suitable for application in the daily routine of spine surgery. **Conclusion** Medical imaging plays a crucial role in the right localisation of different pathologies and helps to classify the minimal invasive procedures.

Keywords: minimal invasive spine surgery, surgical approach, medical imaging, classification system

R/5 The effect of hypnosis on decision making

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Introduction: Hypnosis has been used for thousands of years, but still up to this day it is a very undiscovered field of the medicine. Hypnosis is an altered state of awareness, consciousness and perception. By the help of it we are able to use our minds more powerfully. The main objective of this study was to determine whether the hypnotic state of consciousness could affect the efficacy of decisions in a situation modelling real life. **Methods:** 48 healthy voluntary students of the medical university (28 of them were females and 20 of them were males) carried out a reward and a punishment form of the computerized version of the Iowa Gambling Task. This is a game with cards where the purpose is to win money as much as they can. They had to perform the tasks both in alert and in hypnotically altered state. **Results:** The first main result of this study is in case of hypnosis the overall performance is significantly higher than in case of alert state. The second result is in this experimental situation the punishment has a more significant influence on the efficacy of decisions than the reward. The third result is that we can observe a learning process within one task in every case. **Conclusion:** These observations may support our hypothesis, that hypnosis as a complex altered state of

consciousness could affect the efficiency of our decisions positively.

Keywords: hypnosis, decision making, Iowa Gambling Task

R/6 Aneurysm of the sinus Valsalva, with recidiv stroke- case report

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We report a case of a 52 years old woman, who suffered an ischemic stroke with right sided hemiplegia in 2010, which was successfully thrombolysed. During the clinical examination, transesophageal echocardiogram (TEE) showed a 15mm x 16mm structure in the myocardium, just behind the anterolateral papillary muscle. TEE could detect a flow in the abnormality, and also showed a moderate aortic regurgitation. To gather more information on this structure, a cardiac magnetic resonance imaging (CMRI) study was suggested. Since the patient did not have any symptoms, no further investigation was performed. In 2012 she suffered a stroke again with left sided hemiplegia and left central facial paresis. Because of early recognition, another successful thrombolysis was performed. After the second stroke the patient was referred to our clinic, where she underwent a cardiac MRI exam. The CMRI showed a 20 x 20 mm round shaped structure in the anterior segments of the basal and in the mid thirds of the left ventricle. The structure was located just below the aortic valve, reaching the anterolateral papillary muscle. There was another 13 x 12 mm structure detected, which showed a connection with the bigger one. On the perfusion scan we could measure a flow in the abnormalities. On delayed images we could identify delayed enhancement in the wall of the structures. To gather more information about the anatomic relation to the aortic root we performed a gated CT angiography (CTA) of the chest. The CTA described a pinhole-like connection between the bottom of left sinus Valsalva and the multiple aneurysm system.

There were signs of mild calcification in wall of the smaller abnormality. After discussing the case with heart surgeons an elective surgery was planned because of the putative aneurysm of the left sinus Valsalva. During the surgical procedure, the neck of the possible aneurysm (3x3 mm) was closed in the left sinus of Valsalva using direct suture. The aneurysm of left sinus Valsalva is an extremely rare condition, can cause life threatening complications such as rupture, stroke and myocardial infarction. Prompt diagnosis, and early treatment is quite important to avoid adverse outcome.

Keywords: sinus Valsalva, aneurysm, cardiac MRI, cardiac surgery, stroke

S. Poster session: Clinical sciences II.: Cognitive (anest, neuro, prev. behaviour, other)

S/1 Extracorporeal circulation during heart surgery can lead to detectable hemodynamic dysfunction of the brain

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Postoperative cognitive dysfunction (POCD) frequently occurs after heart surgery, i.e. when the non-pulsatile extracorporeal heart pump (NP-CPB) is used. The altered range of cerebral autoregulation in the elderly patients – owing to their passive cerebrovascular system – can contribute to POCD. Cerebral hypoxia is often seen during NP-CPB in the prefrontal cortex and indicates impaired cerebral autoregulation (CA). Our goal was to explore the underlying correlation pattern of hemoglobin compartments (HbO, HbR), and to clarify to what extent it is influenced by changes in cerebrovascular reactivity. Patients (63±7 years, 5 female and 5 male) underwent non-pulsatile heart-lung pump assisted (NP-CPB: 2.4 L/min/m², 96±28 minute pump time, 50-70 mmHg MAP – mean arterial

pressure) elective cardiac surgery at Semmelweis University, Heart Surgery Department. With NIRS, the relative change in HbO and HbR compartments were continuously recorded. Vascular reactivity index (rVRI) – correlation coefficient between the low frequency fluctuation of blood pressure and blood volume (HbO+HbR) – and the correlation coefficient of HbO and HbR (rHb) were calculated for 15 minute steady state periods in control (C), before (*M), on (M) and after (M*) heart pump. Our results show that before anesthesia rHb was anticorrelated ($rHb(C) = -0.54 \pm 0.32$) and rVRI was random ($rVRI(K) = 0.02 \pm 0.17$). Switching to heart pump has made both rHb ($rHb(*M) = -0.44 \pm 0.3$), $rHb(M) = 0.11 \pm 0.15$, $rHb(M*) = -0.48 \pm 0.17$, $p < 0.01$) and rVRI ($rVRI(*M) = 0.03 \pm 0.14$, $rVRI(M) = 0.2 \pm 0.25$, $rVRI(M*) = 0.04 \pm 0.09$, $p < 0.01$; repeated measures ANOVA) more correlated. We conclude that CA in our elderly patients – as shown by correlated rVRI on heart pump – was insufficient to cope with MAP of 50-70 mmHg. This results in tissue hypoxia and impaired oxygenation, putatively contributing to POCD. Increase in rHb indicates that the demand-regulated distribution of oxygen in the monitored regions becomes supply-regulated on heart pump. The coordinated changes seen in rVRI and rHb offer the basis for future customization of NP-CPB protocol for an optimal target MAP. Angol / English

Keywords: cardiopulmonary bypass, near-infrared spectroscopy, postoperative cognitive dysfunction, cerebral autoregulation, cerebral oxygenation

S/2 MUSICAL ENVIRONMENTAL ENRICHMENT – A NEW TOOL FOR NEUROREHABILITATION?

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Introduction: The positive effects of enriched environment in neurorehabilitation are well-known. Among others, enrichment reduces the extent of ischemic and traumatic injuries. Previously, we have shown that exposing rats to

environmental enrichment can reduce the extent of retinal toxic or ischemic damage. The effects of musical enrichment are much less known and there are no data about the effects of musical enrichment on early neurobehavioral development. Therefore, our aim was to investigate whether musical enriched environment has any effects on the neurobehavioral development of newborn rats. **Methods:** We used two types of musical enrichment: classic and heavy-metal music from 6PM till 6AM daily. Animals were tested daily for their neurobehavioral development: eye opening, incisor eruption, negative geotaxis, and some reflex performances: placing, grasping, crossed extensor, sensory reflexes. **Results:** Our results show that musical enriched environment has slight effects on the normal development. We found slight differences between the two music groups: the heavy-metal group showed appearance of some reflexes earlier than the classic one. This finding could show that metal music could be a stress factor, accelerating somatic and reflex development. However, as shown with other stressors, this accelerated development has harmful consequences on brain morphology and biochemistry. In our preliminary histological examination of the brain we found differences in myelination and number of oligodendrocytes of the corpus callosum. **Conclusions:** These results show that musical environmental factors only slightly influence the early somatic and reflex development. Our preliminary results show that it can affect the myelination of the brain. We plan to make further examination with CNS injuries to investigate whether it has similar positive effects we previously found in complex enriched environment after CNS injury. We hope that our results could be bridge between the rehabilitation, clinical practice and basic science in the future. **Support:** Lendület Program, Arimura Foundation, OTKAK104984, TAMOP4.2.1.B-10/2/KONV-2010-002, 4.2.2.B-10/1-2010-0029, 4.2.2.A-11/1/KONV-2012-0024.

Keywords: music, environmental enrichment, rat, development, myelination

S/3 Relation of haemorheological parameters to fatigue, vital exhaustion and psychomotor speed in patients with cardiovascular disease

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Vital exhaustion and chronic fatigue are highly predictive psychological risk-factors of myocardial infarction and sudden cardiac death. The pathophysiological mechanisms are not yet well understood, but fatigue might be increased by disrupted rheological processes as well-known independent biological risk-factors for cardiovascular diseases. The current study was aimed to investigate the relationship between various haemorheological and fatigue-related psychological parameters in a group of cardiovascular patients because very little is known about their relations so far. Methods. Patients (N = 79; age between 50-83, with a mean of 65.38) with cardiovascular disease completed the Shortened 9-item Vital Exhaustion Questionnaire, FIS Fatigue Questionnaire, SF-36 Health Survey as well as they performed a Psychomotor Vigilance Test (PVT). In addition, blood samples were collected from each of the participants. Results and Conclusions. The results indicate strong associations between the haemorheological and psychological factors. More specifically, red blood cell deformability, aggregability, aggregation time, haemoglobin content and fibrinogen level showed significant associations with fatigue-related psychological parameters.

Keywords: cardiovascular disease, vital exhaustion, fatigue, psychomotor speed, haemorheology

S/4 Online health management in chronic illness

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Nowadays we use unforced online health-related information in order to preserve our health. Chronic patients and their caregivers actively updated using the Internet, communicate with other patients, create Websites as well as blogs and take decisions, manage their own and their family's health. This phenomenon is widely known as e-Health. The term was created in the late 90's and includes information and communication technologies especially in the field of online health care. Medical specialists find that the number of patients who would like to discuss the information from the computer sources have increased dramatically in recent years. According to a 2005 survey, 57% of adults discuss their doctors online health information at least once. 75% of british family doctor tell about their patients indicated that online health information is consumed their health management. The e-Health, used properly, can help chronic patients the health management, the doctor-patient collaboration, improve the communication and the compliance.

Keywords: chronic illness, e-Health, health management, e-patient, compliance

S/5 How does cherry-treatment modify the transmethylation ability in alimentary induced fatty liver of rats?

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Introduction: Obesity is a main problem in western countries. Excessive energy influences

redox homeostasis, and modifies transmethylation. Transmethylation processes proceed via formaldehyde, and take part in epigenetic and posttranslational modifications. Transmethylation capacity can be detected by the measurement of endogen formaldehyde concentration. Our aim was to demonstrate the effectiveness of sour cherry (*Prunus cerasus* L.) treatment in alimentary induced fatty liver. Methods: Wistar rats in 1st and 4th group were fed with normal diet, but the 2nd and 3rd group's diet was enriched with 1% cholesterol, 0.3% cholic acid and 11% sunflower oil. The 2nd and the 4th group were treated with lyophilized sour cherry extract mixed into the standard rat diet. After 10 day treatment, animals were exsanguinated in deep narcosis (ketamine/xilazine:75/7,5mg/bwkg), their livers were homogenized and standardized to bovine serum albumin. Hydrogen-donating ability and the free sulphhydryl-groups were determined by spectrophotometry and the methyl-pool was measured with OPLC. Results: The fat rich diet increased the hydrogen-donating ability by disturbing the NADH/NAD⁺ balance, and lowered the free sulphhydryl-group concentration and the methyl-pool. Cherry treatment has increased the antioxidant parameters and the endogen formaldehyde concentration. Conclusion: Our results draw attention to the relationship between redox homeostasis and the transmethylation and the increased obesity related diseases such as carcinogenesis. The study also showed that sour cherry can be a good supplement for a healthier diet. Support: OTKA K 84290; 2/1 PhD Program of Semmelweis University

Keywords: sour cherry, redox homeostasis, transmethylationobesity, diet

S/6 Evaluation of the relations between structure and cytotoxic effects and paracellular transport enhancer effect of different α -cyclodextrin derivatives

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Introduction Poor water solubility of drugs is an emerging problem in today's pharmacotherapy. Enhancing bioavailability can be achieved by increasing water solubility. It can be reached by complex-forming molecules, such as cyclodextrins (CDs). α -CDs are cyclic (α - 1,4-linked) oligosaccharides, built up from 6 α -D-glucopyranose units. They possess hydrophilic outer and lipophilic inner surface. CDs are always in higher concentration in the products than stoichiometrically required, thus evaluation of their effects on the living organism is indispensable. The aim of our study was to investigate the cytotoxic properties of newly developed α -CD derivatives. Methods MTT cell viability assay and hemolysis test were performed. MTT assay was done on Caco-2 human colon adenocarcinoma cell line as it was a model of per os administration. The hemolysis test was done on human red blood cells as it refers to parenteral use. IC₅₀ and HC₅₀ concentration values were defined. The kinetics of toxic effect was examined by Real Time Cell Electronic Sensing method. Furthermore we also studied the effects of α -CDs on paracellular permeability. Lucifer Yellow was used as a paracellular marker on Caco-2 transport model. CDs also have effects on the tight junction proteins. The structural changes of proteins (ZO-1, Claudin-4, -5, etc.) can be evaluated by immunohistochemistry. Results α -CDs showed concentration dependent cytotoxicity and hemolytic activity. Based on the IC₅₀ and HC₅₀ values we could set up a row of cytotoxicity. Correlation has been found between the chemical structure and the cytotoxicity. RT-CES results verified the reliability of colorimetric methods and it also provided new information about the

kinetics of cytotoxicity. The studies performed on Caco-2 transport model verified our expectations about the enhanced rate of paracellular transport. Conclusion It has been concluded that our results with α -CD derivatives can facilitate the investigation of better tolerated medicines with better bioavailability.

Keywords: cyclodextrin, permeability, solubility, inclusion complex, cytotoxicity

T. Poster session: Clinical sciences III. (rheuma, pediatrics, surgery, pathology, internal med)

T/1 Survival of patients with systemic sclerosis

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Introduction: Systemic sclerosis (SSc) is usually divided into two subgroups: the diffuse form (dcSSc) characterized by rapid organ fibrosis and the limited form (lcSSc) described with slower deterioration. The disease has no commonly accepted therapy. The early recognition and treatment of certain organ changes is essential in the treatment. Objective: Our aim was to process the data of a single center's large number of patients and determine the survival features. We wanted to examine how affected the changes in the follow-up the survival. Methods: The subgroups of patients followed-up from the foundation of the center (1995.) were compared with the Kaplan-Meier method. The prognostic factors were analyzed by Cox-analysis. Results: Data of 338 patients were processed. The mean follow-up time was 7.5 years until 2012. In the last 17 years 66 patient were deceased. Patients with dcSSc have significantly worse survival than patients with lcSSc (5 year survival rate 77% and 92%). Those patients whose follow-up started in the last 9 years of the existence of the center have significantly better survival than those whose follow up started between 1995 and 2004 (5 year survival rate 93% and 85%). In patients whose follow-up started earlier had a higher death rate compared to those patients whose follow-up started later either in subgroup lcSSc (11.5% and

2.9%) and in dcSSc (26.5% and 10%) as well. Among the risk factors the most efficient effects are renal involvement (Exp.b=7.33), decreased stroke volume (Exp.b=6.99) and less than 50% diffusing capacity (Exp.b=6.23). The female sex is a good prognostic factor (Exp.b=0.16). Conclusion: Due to our follow-up the survival of patients with SSc shows an improving tendency in both subgroups but survival in the subgroup of patients with dcSSc is still poor

Keywords: Hungarian, Survival, Systemic sclerosis, Prognostic factor, Cause of death

T/2 Genetic risk factors of anthracycline cardiotoxicity – relevant polymorphisms identified in enzymes and transporters of anthracycline pharmacokinetics

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Introduction: The main dose limiting side-effect of anthracyclines is late cardiotoxicity. Survivors of anticancer therapy have increased risk for cardiovascular problems and have higher such mortality. Subclinical changes may become crucial in case of later accompanying diseases affecting the cardiovascular system, or these changes can precede severe late onset cardiac failure. Identifying patients with altered tolerance to anthracyclines would provide great clinical benefit. Methods: We studied 164 paediatric acute lymphoblastic leukaemia (ALL) patients who had been treated with ALL BFM protocols. They had cardiac ultrasound scans with a mean follow up of 6.4 years after anthracycline therapy. Left ventricular function was assessed as fractional shortening (LVSF). Germline genotypes of 19 single nucleotide polymorphisms (SNPs) in

the ABCC1, CBR1, CBR3 and AKR1A1 genes were measured. Multifactorial general linear model was used to test for associations. Results: Patients with ABCC1 rs246221CT/TT genotype had lower LVFS at the time of the latest echocardiography compared to CC patients (38.4% and 40.7% respectively, $p=0.027$). Those with AKR1A1 rs2088102CC genotype had lower LVFS than those harbouring at least one T allele (36.9% and 39.1% respectively, $p=0.013$). Further SNPs showed no association with left ventricular function. **Conclusions:** Our results suggest that the ABCC1 rs246221 and the AKR1A1 rs2088102 variations are associated with altered left ventricular function in late survivors of childhood acute lymphoblastic leukaemia. The identified early subclinical changes may contribute to a polygenic disorder that evolves over a longer time and manifests in congestive heart disease later.

Keywords: cardiotoxicity, acute leukemia, anthracycline, pharmacogenetics, late-onset side effect

T/3 A life threatening situation

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Az Országos Mentőszolgálat szállított egy 17 éves fiúgyermeket a Balassa János Kórház Gyermekosztályára két napja fennálló csillapíthatatlan lázzal, súlyos általános állapotban, test szerte hirtelen kialakult bőrvérzésekkel, septicus shock klinikai tüneteivel, meningococcus fertőzés gyanújával. Az osztályon megkezdett akut ellátását -mely magában foglalta az első adag parenterális antibiotikum beadását is- követően a gyermek áthelyezésre került a kórház Intenzív Terápiás Részlegére, ahol állapotstabilizálás, a sokszervi elégtelenség megszüntetése, valamint négy napon

át gépi lélegeztetés történt. A gyermek klinikai állapota és laboratóriumi leletei fokozatosan javultak, az időközben elindított szerológiai mintavétel eredménye Meningococcus C fertőzést igazolt. A hetedik ápolási naptól további kezelését a Gyermekosztály folytatta, mely idő alatt a kiterjedt bőrnekrózisok folyamatos sebészeti ellenőrzés mellett történő eltávolítása, speciális sebkezelés, valamint fizikoterápia zajlott. A szerzők lezárásként röviden összefoglalják a Meningococcus infekció járványtani jelentőségét és a prevenció lehetőségét.

Keywords: meningococcal sepsis, Waterhouse-Fridericksen syndrome, Time is life, Threatening protocol, Late complication

T/4 A probable etiological role of Merkel cell polyomavirus in Merkel cell carcinoma - clinicopathological and virological observations

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Introduction: Contagious viral agents were shown to play an etiological role in the 20% of human tumors. Merkel cell carcinoma (MCC) is a rare, highly aggressive, fast metastasizing skin tumor. Its incidence increases rapidly, and often causes differential diagnostic difficulties. In 2008, a DNA tumor virus integrating into the genome of the host cell, named Merkel cell polyomavirus (MC) was identified in MCCs that shed light on the etiology of the tumor. We aimed to detect MC virus and reveal its contribution to clinicopathological features. Methods: We investigated eight MCC cases (altogether 15 samples) diagnosed in the Department of Pathology, University of Pécs, between 2007 and 2012. The presence of MC was tested in native and formalin embedded samples collected from the primary skin lesions, lymph nodes and cutaneous metastases and MCC neighboring basal or squamous cell carcinomas, by PCR method. Clinicopathological characteristics as age, histological pattern, lymphovascular invasion and comorbidities of MC+ and MC- cases were

investigated. Results: MC was detected in three (37.5%) out of eight patients' primary tumor or metastasis. Histological pattern was found different between the two groups. Virus positive cases were associated with better clinical outcomes. In one case, the entire, 5392 nucleotide long genome of the MC (GenBank: KC202810) was determined from a 70-year-old patient's lymph node metastasis that differed in 10 nucleotides (0.19%) from the prototype MC. A truncated mutation was found at nucleotide position 1461 (timin from citozin) of the large T antigen of the viral genome, which causes stop codon and is thought to abandon viral replication and play an important role in abnormal cell proliferation. Conclusion: MCC is a novel clinical entity with a supposedly oncogenic microbial background. The contagious etiology of this aggressive carcinoma results in a paradigm shift concerning its pathogenesis, diagnostics, therapy and prevention as well.

Keywords: Merkel cell carcinoma, polyomavirus, skin cancer, truncated mutation, oncogenic virus

T/5 Short-term prophylaxis in a patient with acquired C1-INH deficiency

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In acquired C1-INH deficiency, limited experience is available with short-term prophylaxis, which we used with success in a 66-year old female patient. She has been receiving ACE inhibitors for hypertension since 15 years. In 2009, she started to experience gastrointestinal symptoms recurring every other week – on four occasions

with limb edema. Abdominal US and CT imaging detected free peritoneal fluid and edema of the intestinal wall. The complement screen confirmed acquired angioedema due to C1-INH deficiency, without anti-C1-INH antibodies. As the known trigger factors of angioedema attacks include ACEIs, we replaced enalapril with bisoprolol. The patient had a single, mild abdominal attack during the next 6 months. Iliac crest biopsy, performed to investigate pancytopenia, confirmed Non-Hodgkin lymphoma of the splenic marginal zone type. In 2010, splenectomy was performed after pre-treatment with erythropoietin, as the patient rejected blood transfusions for religious reasons. Notwithstanding this, plasma-derived pdC1-INH concentrate was at hand, but surgery and the postoperative course were uneventful. The patient's hematological parameters have been checked regularly since then. A monoclonal protein of the IgG λ type, which has not been detectable in 2009, appeared in the serum (3.34 g/L). Edematous attacks have not recurred during the last two years. Two dental procedures have been performed. Pre-treatment with pdC1-INH one hour before the event prevented edema formation both during and after the interventions. In 2013, she had cataract surgery. By this time, rhC1-INH had become available and was used upon the patient's request with similar success. Short-term prophylaxis would be justified in acquired C1-INH deficiency, just as it is in the hereditary form, because invasive procedures may provoke edema-formation also in the former. Both pdC1-INH and rhC1-INH proved effective: the invasive procedures and postoperative wound healing were all uneventful.

Keywords: C1-INH, C1-INH deficiency, acquired C1-INH deficiency, angioedema, splenectomy

EDITOR'S NOTE

All abstracts available to the Editorial Office as of August 9, 2013 are included in this edition of the Archives of the Hungarian Medical Association of America.

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

Thank you,

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