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Welcome

Dear Participant,



On behalf of the Board of Directors of Hungarian Medical Association of America, it is with the greatest pleasure that I welcome you to FÜRED2014, the summer conference organized for the sixth year in a row by the Hungary Chapter of our Society. I have no doubt that this year's meeting will be another great success in the tradition of prior conferences. I encourage you to take advantage of this unique program and learn from all the talented and motivated young faculty, residents, and medical students who – possibly like yourself – will present their clinical, translational, and research from our 4 medical schools of the country and beyond.

This is indeed a superb opportunity for networking, building collaborations, and strengthening the connection between Hungarian medical professionals across the Atlantic. We should remember that the origins of FÜRED2014 go back to a small group of devoted alumni who graduated from of the HMAA student exchange at SUNY Buffalo Medical School, a highly appreciated project that is unique in its offerings to foreign medical students in the United States.

I would like to express my sincere thanks to the Hungary Chapter's leadership and all the conference organizers for putting together another great agenda for this year, both for the scientific and the social events. We remain grateful to Dr. István Bóka, the mayor of Balatonfüred, for continually hosting the Füred conferences in one of Hungary's most beautiful cities. Finally, many thanks to Professor Gábor Veress, the physician-in-chief of the Balatonfüred Állami Szívkórház, for providing FÜRED214 again with a historic and noble venue. Enjoy!

With best wishes,



A handwritten signature in blue ink, which appears to read "B. Baffy".

György Baffy, MD, PhD

HMAA President



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ABSTRACTS

Balatonfüred, Hungary 22–23 August, 2014

MULTIDISCIPLINARY SESSION I.

A. Behavioral Sciences

A/1. SATISFACTION WITH THE DOCTOR, COMPLIANCE AND THE USING OF ALTERNATIVE METHODS IN THE TREATMENT OF CHILDREN WITH ALLERGIC RHINITIS

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Keywords: allergic rhinitis, asthma, satisfaction with medical services, alternative method, compliance

Introduction The information related to the illnesses are available for the large majority of patients in the 21st century. The connection of patients and their parents don't end with the guidance of the doctor. **Methods** A survey with questionnaire was made among children who suffer in isolated allergic rhinitis (AR) and allergic rhinitis with asthma (AR+A) and their parents in the capital as well as in the countryside between August and November, 2013 at medical consultations (36%) and in schools (64%). 73 children (48 boys, 25 girls) took part in the survey. 19 of them were under the age of 12, fifty four of them were 12 years old or older. Mean age: 13.6 years $\pm$ 2.7SD. We used GraphPad (Chi-square with Yates' correction) for the elaboration. **Results** In connection with the illness of the child 81% of the parents started an individual research. 73% of them totally keep the medical orders. 88% of them take out all the inscribed medicines.

63% of the parents are totally satisfied with the medical attendance, but half of them complemented the treatment with the alternative therapy and the partially satisfied did the same. Regarding the educational level of the parents, more than half of the college graduate respondents and approximately one third of the secondary or lower graduate respondents use alternative treatments with their children. We didn't find statistically significant correlation between the usage of alternative treatments and the educational level achieved by the participants and the satisfaction with the doctor. **Conclusion** There is a very positive result about the compliance. The satisfaction level with the medical attendance was very high. An alternative treatment was used by approximately the half of participants, it would worth to find the causes of it.

A/2. A WORKING THEORY OF STUDENT SATISFACTION AND MOTIVATION

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Keywords: Motivation, Feedback, Education, University, Model

Background: As a provider, it is essential for the university to have a valid educational quality assurance. The current law and ethical code does not allow us to oblige the students to fill out the feedback questionnaires. The self completion rate is low, to provide a high-enough rate for quality assurance is

troublesome. It was inevitable to create a motivational system to solve this issue. Methods: With the professional help of lawyer, sociologist, educational-organizers we have discussed options to motivate the students. Every option was acceptable by the Hungarian law and ethical norms. We used self completion online questionnaires to analyse how strongly would options motivate the students. Results: Of all alternatives, 70% of the students picked the possibility for earlier exam registration. Those students who give feedback on obligatory subjects within the set deadline, will be awarded a bonus that entitles them to one day earlier registration for exams. Out of 13925 questionnaires from the previous semester, 6848 have been filled out, almost 50%. It is vital that this 49,2% is divided equally between all subjects, which gives us a general view of student satisfaction. The questionnaires were available for 2408 students, of which 1122 students (46,6%) were oblige for early registration. Conclusion: Our newly set up online system has exceeded expectations. The 50% fill out rate, which is a significant rate, that has been a statistical data, now is divided between each subject equally, giving us a general view of the student satisfaction.

A/3. WHAT MAKES A POPULAR LECTURE?

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Keywords: Feedback, Lecture, Student satisfaction, Popularity, Participation

Background With the arrival of the „Z”-generation in higher education, we witness a changing landscape in educational culture, especially considering the lectures. In our previous studies, we explored the factors that influence a practice’s judgement. The goal of

our current study was to analyse what makes a lecture to be attended and to define the factors, which determine the judgement of the lectures. Summary of work 12 997 anonymous questionnaires have been processed. Explorative and confirmative factor analysis has been used to validate the inventory. Forward-stepwise automatic linear modelling was used to explore the underlying connections between the items. Summary of results Satisfying accurate (75,2-79,5%) linear models were made, which have determined, that the most influential factors in a lectures judgement are it’s role in exam-preparation, the dynamism, the well-organized message. The most defying factor in the attendance of a lecture is the semester when it is held with a stunning 98%. Discussion In point of attendance the actual school year is the most important factor, because the seniors do not attend so frequently the lectures as the freshmen, independently from it’s excellence. In point of student satisfaction the usefulness is the most important factor, which means –to a student- the role in exam preparation.

A/4. RELATIONSHIP OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AND SELF-CONCEPT IN HUNGARY AND IN THE USA

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Keywords: ADHD, self-concept, psychiatry, stimulants, non-stimulants

Introduction: Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by difficulties in

paying attention, excessive activity, and impulsivity. Previous studies have contradictory findings on the relationship between ADHD and self-concept: some studies show that self-concept scores are higher in children with ADHD than those without it, others report that scores are lower in children diagnosed with ADHD, while others state that there is not any significant difference in self-concept scores between children with and without ADHD. In this study my first objective was to find out which one these is the proper one in my examined population. Secondly I hypothesized that if the self-concept is impaired in children with ADHD the medication sets back the score to the same value as measured in the normal population. As ADHD is treated with two different type of medication (stimulants and non-stimulants) it requires examination if they effect the self-concept differently. Methods: A slightly modified version of the Piers-Harris Children's Self-Concept Scale (2nd Edition) was used to measure the children's self-concept scores. The children participating in this study were 10-18 years old. The examined population consisted of four sub-populations: ADHD patients in Massachusetts, control group in Massachusetts, ADHD patients in Székesfehérvár and control group in Székesfehérvár. All of the questionnaires were completed in English. Collected data was analyzed using T tests and Principal components factor analysis. Results: Preliminary results show that factors such as family background and social settings in school play an important role in self-concept in children. Conclusion: These results are preliminary and the final picture on self-concept will be reached shortly.

MULTIDISCIPLINARY SESSION II.

B. Pediatrics-Obstetrics & Gynecology

B/1. THE EFFECT OF CALCINEURIN-INHIBITION ON THE RENAL RENIN-ANGIOTENSIN SYSTEM. A NEW PLACE FOR RENIN EXCRETION

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Keywords: renin-angiotensin system, calcineurin inhibitor nephrotoxicity, multiphoton microscopy, collecting duct, renin inhibition

Introduction Tacrolimus (Tac) and CyclosporinA (CyA) are two effective immunosuppressants which are essential therapeutic solutions in the prevention of allograft rejection. However, it is well known that both of them have nephrotoxic potential. The precise mechanism how these drugs act as nephrotoxic agents are still not fully revealed. In this study we investigated in-vivo the effect of calcineurin-inhibitors on the renal renin-angiotensin system. Methods Three weeks old, male C57BL/6 mice (n=15) were divided into five groups: mice treated with vehicle (C) or with 0.075 mg/kg/day of Tac or with 2mg/kg/day of CyA or with 0.075 mg/kg/day of Tac + 25mg/kg/day Aliskiren or with 2mg/kg/day of CyA + 25mg/kg/day Aliskiren. After three weeks of

treatment, the renin content in the collecting duct (CD) was evaluated applying flow cytometry and multi-photon microscopy. The contraction of the vessels was assessed. The consequent fibrosis was determined by Masson staining. Eventually, serum creatinine was measured. Results Flow cytometry showed four times higher CD renin content following the treatment with calcineurin inhibitors. It was further confirmed by multi-photon microscopy: the renin granulation increased remarkably in both localizations. As a result of the local renin activation, vasoconstriction was present in both treated groups. After three weeks of treatment with immunosuppressants, fibrotic islands were found in the kidney tissue. Serum creatinine was significantly elevated in both Tac and CyA groups. Conclusion In summary, our study revealed for the first time, that calcineurin inhibitors possess nephrotoxic effect on the kidney parenchyma due to the enhanced renin activity not only in the juxtaglomerular apparatus but also in the CD-s. Therefore, the inhibition of renin-angiotensin system could be beneficial in the prevention of calcineurin inhibitor nephrotoxicity. Further studies are needed to reveal what kind of inhibitors in which combination could provide the most efficient treatment. Supported: OTKA K-108688, SE-MTA Lendület LP2001-008/2011

B/2. THE CLINICAL DECISION RULE FOR PEDIATRIC HEAD INJURY

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Keywords: head injury, computed tomography, radiation, clinical decision rules, intracranial injury

Introduction: The traumatic head injury is one of the most significant health problems of children, but there is still a controversy about the diagnostic methods, and the indications of Computed Tomography (CT). The aim of this study was to assess the effectiveness of the clinical decision rule used at the Péterfy Sándor Hospital and Traumatology Center and to compare it with three most acknowledged clinical decision rules in Europe. **Methods:** Seven - years retrospective study of children aged 0-18, hospitalized at the Traumatology Center with history of head injury was done. We analyzed the next eight criteria: anamnesis, injury mechanism, loss of consciousness, the level of consciousness, symptoms of cranial fracture, vegetative symptoms, neurology and the age of the child (< 3 years). Based on these criteria we set up three levels of risk of significant intracranial injury. **Results:** 1623 children were enrolled in the study, who were observed between 2002 and 2008. 93% had mild, 4% moderate and 3% had severe head injury. All observed patient had an X-ray, but the CT scan rate was only 12.6%. 100% of children with moderate or severe injury had CT scan and all of them showed abnormality. 5% of children with mild injury underwent CT scan, and 30% showed intracranial pathology. The indication of the CT was any deviation in the 8 diagnostic criteria at the first examination or any change during the observation period. **Conclusion:** Our clinical decision rule is a highly sensitive clinical decision rule for the reasonable use of CT. If the patient is not in the lowest level of risk of intracranial pathology, the patient needs a clinical observation, and depending of the change of the symptoms, a CT scan. The observation may be an effective strategy to reduce unnecessary cranial CT.

B/3. SERUM CORTISOL LEVELS AND HYDROCORTISONE SUPPLEMENTATION IN MULTI-ORGAN FAILURE OF ASPHYXIATED NEWBORNS TREATED WITH HYPOTHERMIA

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Keywords: hypoxic ischemic encephalopathy, hypothermia, hydrocortisone supplementation, low blood pressure, circulatory failure

Introduction: Hypoxic ischemic encephalopathy (HIE) is the leading cause of the mortality and long term morbidity of the term neonate. Recently hypothermia treatment was proved as the only effective treatment to improve the neurological sequelae of HIE. Circulatory failure is often observed as side effect of hypothermia, which may be treated with steroid – in cases of volume and catecholamine resistant hypotension. Previous results suggest that low dose, transient steroid therapy was effective in preterm infants, but has not been tested in asphyxiated newborns. In the present study, initial cortisol levels were registered and short-time effect of hydrocortisone supplementation (HCS) was investigated on low blood pressure in asphyxiated newborns. **Methods:** In this retrospective study we analyzed 115 consecutive term newborns with perinatal asphyxia treated with hypothermia, in the 1st Department of Pediatrics of Semmelweis University, between 2006 and 2012. The HCS was used during hypothermia treatment in 37 patients. Before HCS, 30 patients required volume replacement and inotrope therapy due to hypotension. **Results:** Serum cortisol levels, measured before HCS, was 94

[55,25-132,25] nmol/l which is relative low, particularly compared to the low blood pressure. The median time of HCS initiation was 41. hours of life, the average dose was 0.68 ± 0.35 mg/kg. The median of initial mean arterial pressure was 37 [30-43] mmHg, one hour after HCS it was increased significantly to 42.5 [37-50.5] mmHg, 6 hours later it increased to 47 [44-51.25] mmHg. No short term adverse effect was noted. **Conclusion:** Our results suggest that relative adrenal insufficiency plays a role in hypotension of asphyxiated newborns, therefore hydrocortisone supplementation may be a causal therapy. Further clinical studies needed to determine the safety profile of hydrocortisone supplementation in this patient population.

B/4. TIMING OF THE SURGICAL CORRECTION MAY AFFECT BAROREFLEX-SENSITIVITY IN PATIENTS WITH COMPLEX CONGENITAL HEART DISEASES

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Keywords: baroreflex sensitivity, congenital abnormality, transposition of great arteries (TGA), tetralogy of Fallot (ToF), hypoxia

Introduction: Arrhythmia-related sudden cardiac death is a common long-term complication in tetralogy of Fallot (ToF) and transposition of great arteries (TGA). It was shown that impaired cardiac autonomic function, indicated by reduced baroreflex-sensitivity (BRS), is an independent predictor of sudden cardiac death in various

cardiovascular diseased states. Preoperative chronic hypoxia may lead to reduced BRS in congenital heart diseases. Therefore, we investigated the BRS and the association between BRS and the time till surgical correction in ToF and TGA patients. Methods: 20 ToF- (14 ± 3 years), 23 TGA patients and 20 age- and gender-matched control subjects were examined. BRS was determined by analyzing blood pressure (BP) and heart rate, in spontaneously occurring sequences in which BP and RR-intervals (RRI) concurrently increased and decreased. The slope of the BP-RRI regression line gave us the index of the baroreflex-sensitivity (increasing sequences: BRS+, decreasing sequences: BRS-) Results (mean $\pm$ SD): BRS+ and BRS- were lower in ToF than in TGA patients or in healthy controls (BRS+: 12.0 ± 8.6 , 18.5 ± 11.6 , 18.5 ± 7.2 ms/mmHg, $p < 0.001$; BRS-: 10.7 ± 7.7 , 18.5 ± 12.0 , 16.0 ± 7.3 ms/mmHg, $p < 0.001$). BRS+ and BRS- was not different between TGA patients and healthy subjects. The first surgical correction was earlier in patients with TGA than in patients with ToF (1.0 ± 0.2 vs. 2.5 ± 1.2 years, $p < 0.01$). Conclusion: In patients with TGA BRS is preserved, but BRS of ToF patients is reduced. The explanation for this difference might be the later timing of the first surgical intervention in ToF patients. We assume that prolonged hypoxia in ToF caused the irreversible impairment of the baroreflex function.

B/5. MUTATIONS AND POLYMORFISMS IN BREAST CANCER

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Keywords: Deep infiltrating endometriosis, Nerve sparing surgery, Urinary complications, Quality of life, Pelvic nerves

Introduction: BRCA mutations are the most well-known hereditary risk factors of breast cancer (BC). In our retrospective study we analyzed the incidence of classical mutations and polymorphisms amongst screened patients and their relationship with the pathological features of BCs. Methods: We report on 68 patients in whom BRCA analyses were performed between 2012 and 2013. In case of the manifested BC cancer we determined biological subtypes - based on the hormone and HER2 status and the Ki-67 labelling index. Results: BRCA mutations or polymorphisms were detected in 60 cases. We found five classical mutations. 59 patients had SNPs from which 50 were S1613G (heterozygote:41/homozygote:9). In 20 patients we found a cluster of 4 SNPs (S1613G-K1183R-E1038G-P871L). 14 other SNPs occurred. We identified benign breast lesions (BEN) in 29 patients, 28 of these have SNPs, in 27 cases S1613G. We detected significant correlations between the presence of BEN and SNPs ($p=0.036$), and S1613G ($p=0.01$). 34 patients [44.8 ± 9.5 year] had BC: 31 invasive ductal, 2 lobular, and 3 other carcinoma were detected (grade 2=10, grade 3=24). Biological subtypes: Luminal A=8; B1=8, B2=4; HER2+=1; triple negative=13 patients. Three of these patients had classical mutations, 31 had SNPs. 23 was S1613G (19/4), the four-SNP-cluster was confirmed in 11. We did not find significant correlations between SNP profiles and hormone receptor/HER2 status nor the biological subtypes; however, triple negative tumors prevailed in all cases of polymorphisms or mutations. Conclusions: In our screened population the incidence of SNPs was considerably higher. In the aspect of BC patients, young age and high grade invasive ductal carcinoma were typical. In case of non-classical BRCA mutations none of the biological subtypes prevailed, however, with an increased number of enrolled patients our

results could be refined. Additionally, the role of correlations between SNPs and benign breast lesions need to be clarified.

B/6. VARIATION TREND OF ANTHROPOMETRIC DATA OF SCHOOLCHILDREN LIVING IN GURGHIU VALLEY IN THE LAST SEVEN YEARS

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Keywords: childhood obesity, abdominal obesity, anthropometric reference data, cryptorchidism

Introduction: The prevalence of childhood overweight and obesity has increased worldwide in the last decades. Due to the lack of anthropometric data for Romanian children there are difficulties in evaluating the somatic development, so we used the reference range of other European countries. **Methods:** We collected the anthropometric data (height, weight, waist and hip circumference, body-mass index, weight-height ratio) of schoolchildren living in three villages of Gurghiu valley, Mureş County (95 children, aged: 10.37 ± 2.10 years), and compared them to the results of our similar study made in 2006 in the same region (135 children, aged: 12.05 ± 1.64). All data were processed in Growth Analyser. **Results:** The mean standard deviation (SD) of body weight in the cohort investigated in 2013 was: 0.43 ± 1.50 SD. Based on the BMI the prevalence of overweight was 20%, and that of obesity 4.2%. According to the waist circumference (WaC) and weight-height ratio (WHtR) most of the obese children had central type of fat

distribution. We observed cryptorchidism in two cases out of the 48 boys (4.2%). Compared to the 2006 survey (mean SD of body weight: 0.14 ± 1.15 SD, overweight in 8.1%, obesity in 0.7%) a significant increase in the prevalence of obesity ($p=0.01$) was observed, especially among the 10-14 old children ($p=0.014$). The difference between the mean height in 2006 and 2013 was not significant. **Conclusion:** The prevalence of childhood overweight and obesity in Gurghiu valley has increased significantly in the last seven years, especially among the 10-14-years old children. We observed a dominance of central type of fat distribution among overweight/obese children. The considerable prevalence of cryptorchidism underlines the importance of physical examination.

B/7. Towards Single embryo transfer in IVF: “avoidance of the minivan syndrome”

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Aims: The goal of this presentation is to review the most recent recommendations and options for single embryo transfer in in vitro fertilization and present a pilot study on elective single embryo transfer (eSET). Multiple pregnancies remain the most common cause of maternal, fetal, and perinatal morbidities. While there has been a significant decrease in higher order multiples, the incidence of twins have remained stubbornly stable.

Methods: All women < 38 years old proceeding with IVF, regardless of ovarian reserve status, diagnosis (testicular sperm, PGS, donor egg excluded), single ovary, uterine surgery, prior failed cycles, and

insurance coverage, were consented for participation in a novel program to incentivize them to undergo eSET (blastocyst day 5/6 ET).

Results: ASRM guidelines for SET will be discussed as well as the costs involved with multiples. Despite significant financial incentives and high ongoing pregnancy rates, 37.5% of eligible couples declined to have an eSET, because they desired twins and because they were concerned about lower success rates. A total of 23.8% of couples with insurance coverage declined to participate, not due to financial reasons, rather they preferred a chance at having twins, providing yet another barrier for implementation of eSET.

Conclusion: We were able to increase our eSET rate from <10% to 62.5%. Short of mandating eSET, it appears many couples in the United States will remain reluctant to have an eSET despite an excellent pregnancy rate. Insurance companies should consider incentivizing patients to undergo eSET by covering cryopreservation and allowing those who agree to have eSET to have perhaps additional attempts at lower or no cost.

MULTIDISCIPLINARY SESSION III.

C. Physiology-Pathophysiology

C/1. THE POTENTIAL ROLE OF THE MELANOCORTIN SYSTEM NEUROPEPTIDE Y IN THE REGULATION OF ENERGY HOMEOSTASIS IN SPONTANEOUSLY HYPERTENSIVE RATS.

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Department of Pathophysiology and Gerontology

Keywords: spontaneously hypertensive rats, food intake, body weight, melanocortins, neuropeptide Y

Introduction: Caloric intake and body weight (BW) of spontaneously hypertensive rats (SHR) developed for the study of essential hypertension are lower than those of age-matched normotensive (NT) controls. Their BW does not reach that of controls even on a high-fat diet suggesting a dysregulation of their energy homeostasis. We assumed an enhanced activity of the hypothalamic anorexigenic melanocortins in the background, that has been shown to contribute to their hypertension, as well. A diminished tone of the dominant orexigenic neuropeptide Y (NPY) was also hypothesized. Aim: We analyzed the activity of melanocortins and NPY using in vivo and in vitro methods in SHR rats. Methods: Food intake (FI) of adult male SHR rats and NT Wistar rats was recorded in an automated FeedScale system upon intracerebroventricular injection of NPY (5 µg) or a melanocortin agonist (5 µg alpha-melanocyte-stimulating hormone, alpha-MSH) or central infusion of melanocortin antagonist HS024 (1 µg/h, 7 days). Using immunofluorescent labeling we determined the number of alpha-MSH producing cells and also performed the quantitation of alpha-MSH and NPY specific signal density (SSD) in the arcuate nucleus of the hypothalamus. Results: The alpha-MSH-injection reduced spontaneous night-time FI more efficiently in SHR than in NT rats. HS024 started to increase daily FI and consequently BW in the NT group already from the 1st, in SHR animals only from the 3rd day. In contrast, responsiveness of day-time FI to NPY injection was suppressed in SHR. We did not find difference between SHR and NT rats in terms of alpha-MSH-producing cell counts and NPY SSD in the arcuate nucleus, but the

SSD of alpha-MSH immunosignal was significantly higher in SHR rats. Conclusion: Our in vivo and also in vitro results suggest higher melanocortin-production and -responsiveness and lower NPY-responsiveness in SHR rats, what may contribute to the explanation of their metabolic dysregulation.

C/2. TEMPORAL CHARACTERISTICS OF DYNAMIC RANDOM DOT CORRELOGRAM EVOKED VEPS SUGGEST MULTIPLE MECHANISMS IN STEREOVISION

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Keywords: visual evoked potentials (VEPs), stereovision, visual information processing, Dynamic Random Dot Correlogram (DRDC), steady state VEP

Introduction: Previous research has found that the phase of steady state Visual Evoked Potentials (ssVEPs) is linearly correlated to the frequency of stimulation. The apparent latency (i.e. response time) can be calculated from the steepness of the regression line fit to the phase-frequency data. When ssVEP responses are recorded in a wide frequency range, an apparent change in steepness can be observed in the phase-frequency plots for most visual stimuli (e.g., plaid patterns, checkerboard luminance and chromatic contrast reversals). These studies assume multiple neural processing mechanisms in the background. Our goal was to examine the phase-frequency relationship of Dynamic Random Dot Correlogram evoked responses (DRDC-VEPs) that has never been examined before. Methods: Nine adults with intact binocular vision were included in the study. DRDC-VEP responses were evoked by DRDC stimuli at 15 temporal frequencies.

Stimuli were presented on the red and green channels of the CRT monitor while observers were wearing red-green goggles for dichoptic viewing. Flash and luminance reversing checkerboard pattern VEPs of similar temporal frequencies were used as controls. Reliability of VEP responses were evaluated by T2circ statistics. Significant Fourier components of the fundamental frequencies were plotted and regression lines were fit to the data. Goodness of fit was indicated by R2 values. Apparent latencies were calculated from the steepness of the regression lines. Results: In all cases, including DRDC-VEP data, we found at least two linear fits (i.e., two apparent latencies) during data modeling. These two main apparent latencies were found at around 160 and 100 ms indicating a slower and a faster processing mechanism. Conclusion Based on these results, it is very likely that binocular information is processed by more than one, possibly two parallel mechanisms, each having different temporal characteristics. We propose that they are linked to the classic parvo- and magnocellular visual pathways.

C/3. ROLE OF THE HOMEBOX GENE NKX2-3 IN STROMAL REGULATION OF STRESS HEMATOPOESIS

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Keywords: Nkx2-3, erythropoietin, hematopoiesis, extramedullary, spleen

Introduction: In addition to the immunological role, spleen both in man and rodents can work as a hematopoietic tissue, this activity is limited to the red pulp. The transcription factor Nkx2-3 plays an important role in the development of red pulp, so in our work we investigated the role of Nkx2-3 in extramedullary hematopoiesis

reactivated by acute anemia. Methods: Acute anemia was induced in adult Nkx2-3 KO and wild-type mice with bloodletting. The erythroid cells were identified by their Ter119/CD45 expression and were evaluated by flow cytometry and double immunofluorescence. The extent of tissue reactivity was assessed by AnalySIS software. EPO levels were measured by sandwich ELISA. Results: Before bleeding the frequency of erythroid cells in bone marrow was higher in Nkx2-3 KO mouse than in wild-type mouse, however the frequency of these cells in spleen were significantly lower in KO mouse than in wild-type mouse. Due to bleeding in wild-type mouse the number of erythroid cells increased both in bone marrow and spleen, but in KO mouse only in bone marrow. In the KO spleen the frequency of erythroid cells decreased. After bleeding the levels of EPO in serum raised in both groups, showed parallel rates with activities of bone marrow. Thus lowest level of EPO was measured in wild-type mouse before bleeding, highest level of EPO was found in KO mouse after bleeding. The level of EPO in KO mouse before bleeding was higher than level of EPO in wild-type mouse after bleeding. Conclusion: Our findings indicate that the homeodomain transcription factor Nkx2-3 plays an important role not only in the prenatal erythropoiesis, but lack of this factor cause the failure of reactivation of stress hematopoiesis in adult mouse.

C/4. PROTEIN KINASE C AND EXTRACELLULAR SIGNAL REGULATED KINASE MEDIATE APELIN-INDUCED INOTROPY

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Keywords: Apelin, cardiac contractility, signal transduction, protein kinase C, extracellular signal regulated kinase 1/2

Background: The endogenous peptide apelin is emerging as an important regulator of the cardiovascular homeostasis. We previously demonstrated that apelin augments cardiac contractility; however, its underlying signaling mechanisms remain largely elusive. Here we characterized the contribution of various kinase pathways to the positive inotropic effect of apelin, including protein kinase C (PKC), extracellular signal regulated kinase (ERK) 1/2, and myosin light chain kinase (MLCK). **Methods and Results:** In isolated perfused rat hearts (n=134), infusion of apelin (2 nM) increased contractility (27±3%, P< 0.05), phosphorylation of ERK1/2, and translocation of PKCε, but not PKCα, from the cytosol to the particulate fraction. Suppression of ERK1/2 phosphorylation by U0126 (5 μmol/l) attenuated the inotropic effect of apelin by 56 % (P<0.05). Pharmacological inhibition of PKC reduced apelin-enhanced contractility by 42 % (P<0.05). Although PKC may serve as an upstream regulator of ERK1/2, PKC inhibition had no effect on ERK1/2 phosphorylation under our experimental conditions. In addition, the MLCK inhibitor ML-7 (1 μM) attenuated the apelin-induced positive inotropic response by 53 % (P<0.01). **Conclusions:** Our data demonstrate that ERK1/2 activation is crucial for the inotropic response to apelin. PKCε signaling also contributes to the inotropic effect, and

importantly, ERK1/2 activation is mediated through PKC-independent mechanisms in the adult rat heart. In addition, apelin enhances cardiac contractility via activation of MLCK, a possible way to increase Ca²⁺ sensitivity of the myofilaments. Selective activation of PKC ϵ and ERK1/2 signaling may represent novel means to support cardiac function in disease.

C/5. HOW DOES MATERNAL SMOKING INFLUENCE THE EARLY NEUROBEHAVIORAL DEVELOPMENT OF RAT PUPS?

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Keywords: Prenatal, smoking, neurobehavioral tests

Exposure to tobacco smoke during perinatal life is known to have various deleterious effects. Among others they worsen cognitive functioning, decrease locomotor behavior and present a risk factor for future psychiatric disorders. The aim of our study was to investigate the influence of maternal smoking during pregnancy on the early physical and neurobehavioral development of newborn rats. Wistar rats were exposed to whole-body smoke exposure for 2x40 minutes daily from the mating until delivery. For the treatment, TE2 manual closed-chamber smoking system and 4 research cigarettes per occasion were used. The neurobehavioral development of the pups was monitored by a battery of tests until postnatal day 21. Weight was measured daily until postnatal day 21. On the 4rd week

of life motor coordination tests were carried out. Some parameters appeared earlier, like eyelid and ear twitch reflexes, forelimb and hindlimb placing, forelimb grasp. On the other hand we observed a delay in the appearance of forelimb and hindlimb reflexes. These results suggest that maternal smoking during pregnancy has unfavourable effects on the early neurological development of the rat pups.

C/6. EFFECT OF TWO DIFFERENT TYPES OF ENRICHED ENVIRONMENT PRECONDITIONING ON FUNCTIONAL OUTCOME OF RATS AFTER EXPERIMENTAL HEAD INJURY

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Keywords: traumatic brain injury, enriched environment, open field, beam balance, outcome

Introduction: There is an ongoing debate on the efficacy of enriched environment (EE) in rehabilitation: experimental data are rather controversial. The aim of our present study was to investigate the effects of early post-natal EE and auditory stimuli preconditioning on functional outcome in case of severe TBI. **Methods:** In the 1st experimental setting 15 male Wistar rats were traumatized with

lateral fluid percussion head injury model with 2.6 atm injury severity. Eight animals lived within EE conditions on their first 35 post-natal days. Functional outcome was measured by the open field and beam balance tests on the 1st, 4th and 8th post injury days. In the 2nd experimental setting 31 male Wistar rats were traumatized with impact accelerational head injury model with 450g weight from 1.5m. Pre-injury, 17 of them lived in an enriched auditory stimuli environment which involved listening of 60dB loud music 12h per day. Results: While the early post-natal EE animals performed better at each time points in the beam balance test the number of grooming and rearing in the open field test were increased in case of control animals related to the EE. The difference was significant in case of grooming in the 1st post-injury day ($p=0.047$). Surprisingly, rats that had received the auditory stimuli performed significantly worse in the beam balance test independently from the TBI (even in pre-injury setting). In the open field test we found significantly more rearing activity on the 1st day post-injury of the auditory preconditioned animals $p=0.018$. Conclusions: While we have proven at least partial beneficial effects of early post-natal EE our study revealed controversial effects of auditory stimuli preconditioning most probably due to noise-induced labyrinth-injury.

C/7. AGE RELATED CHANGES IN AT1-RECEPTOR (AT-1R) DEPENDENT VASOCONSTRICTION, AND ITS MEDIATION BY SUBCELLULAR MECHANISMS

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Keywords: Aging, angiotensin II, AT1 receptor, signal transduction, signalling proteins

Introduction, Background: Previous studies revealed that angiotensin II (Ang II) mediated vasoconstriction and arterial AT1R-mRNA and protein expression show an age related function (initially they increase and then decrease). It is likely that a well-regulated genetic program is responsible for these changes. However, until now, the age-related changes of the AT1R induced vascular transducing mechanisms have not yet been elucidated. Thus we hypothesized that the age-related expressions of subcellular signalling proteins show similar pattern. **Methods:** Common carotid arteries were isolated from different age groups of male Wistar rats: New-born (8 day (d)), young (2-6 month (m)) middle aged (8-16m) and old (24-30m). The expression signalling proteins (β -arrestin2, CPI-17, Rock2, p-MYPT) were measured with Western Blotting and assessed by normalized optical density (%). **Statistically Evaluated Results:** The β -arrestin2 expression decreased continuously during aging from 8 day to 24 months (8d: 75 ± 6 ; 2m: 10 ± 4 ; 16m: 12 ± 4 ; 24m: 5 ± 5 ; density %). Rock2 protein expression increased from 8 days to 2 months, then decreased to 24 months (8d: 17 ± 3 ; 2m: 47 ± 5 ; 24m: 14 ± 3 ; density %). CPI-17 expression decreased continuously from 8 days to 24 months (8d: 46 ± 6 ; 2m: 43 ± 5 ; 16m: 16 ± 4 ; 24m: 5 ± 3 ; density %). The p-MYPT level increased from 8 days to 2 months and then, decreased to 24 months (8d: 19 ± 5 ; 2m: 75 ± 7 ; 24h: 3 ± 2 density %). **Conclusion:** These results indicate that the arterial expression of P-MYPT β -arrestin2, CPI-17, Rock2 proteins show age-related patterns; findings, which

could contribute to a better understanding of the physiological aging dependent changes in the magnitude of Ang II-induced vasoconstriction. Support: Hungarian National Science Foundation (OTKA K-108444), 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 "National Excellence Program"

C/8. CHRONIC WHISKY CONSUMPTION CAUSES MITOCHONDRIAL DYSFUNCTION AND INCREASED ENDOGENOUS METHANE PRODUCTION IN RATS

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Keywords: Glycerylphosphorylcholine, whisky, methane, mitochondria, liver

Introduction: We have shown previously that blockade of the mitochondrial cytochrome c oxidase complex can lead to the production of non-bacterial methane in living aerobic systems (Ghyczy 2008, Tuboly, 2013). Chronic alcohol load generates similar intracellular NADH/NAD⁺ imbalance leading to oxido-reductive stress in target organs (Zakhari, 2013). Our aim was to investigate the effects of chronic ethanol consumption on endogenous methane production and mitochondrial function in vivo. In addition, we examined the effects of the potentially membrane protective compound L- α -glycerylphosphorylcholine (GPC) in this scenario. **Methods:** SPRD rat groups were treated with whisky per os (6.6 ml/kg/day for 10 days), which was combined with GPC-enriched diet (0.8% GPC in food) or antibiotics for the reduction of the potentially methanogen intestinal flora (p.o. rifaximin, 10 mg/kg/day), with

accompanying control groups (n=6-6, each). The whole-body emission of methane was detected with diode laser-based photoacoustic spectroscopy, the oxygen consumption of the hippocampal and the liver mitochondria was measured directly with high resolution respirometry (Oroboros O2k). **Results:** Chronic whisky consumption induced significant methane production on the 3rd day, compared to the controls (p<0.05), and this level remarkably decreased by the 5th day in the GPC-treated group (p=0.04). The same tendency was observed after antibiotic treatment but only on the 8th day (p=0.002 vs control). The GPC treatment did not affect the altered mitochondrial oxygen consumption in the hippocampal samples, whereas the mitochondrial dysfunction was significantly decreased (p=0.05) in the liver. **Conclusion:** Non-bacterial methane production might be an indicator of the alcohol-generated dysfunction in the liver and brain mitochondria. GPC treatment partially decreases the potentially destructive consequences of chronic alcohol consumption by the protection of mitochondrial function. Supported by: TÁMOP-4.2.2.A-11/1/KONV-2012-0035; OTKA K104656; TÁMOP-4.2.4.A/2-11/1-2012-0001, National Excellence Program

C/9. SRC FAMILY KINASES IN MONOSODIUM-URATE CRYSTAL-INDUCED NEUTROPHIL ACTIVATION

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Keywords: Neutrophils, Monosodium-urate crystals, Src family kinases, Superoxide, Cytokines

Introduction: Deposition of monosodium-urate (MSU) crystals in the joints or other tissues is a hallmark in the pathogenesis of

gout, which is known to be mediated by immune cells, among others neutrophils. Although MSU crystal-mediated signal transduction is in the focus of recent investigations, the molecular mechanism is only partially characterized. In this study, we investigated the role of Src family kinases in MSU crystal-induced neutrophil activation. Methods: Bone marrow isolated neutrophils from wild type and triple Src family-deficient (Hck-/-Fgr-/-Lyn-/-) mice were stimulated by different concentrations of MSU crystals, followed by the analysis of superoxide production and cytokine release. We also used Fc-receptor γ -chain- and CD18-deficient cells in order to investigate the role of Fc-receptors and β 2-integrins in the above-mentioned processes. Results: MSU crystal-induced superoxide production was increased by a dose dependent manner. Compared to wild type cells, Src family-deficient neutrophils practically failed to produce superoxide. MSU crystal-induced IL-1 β and CXCL2 release were dramatically reduced by Src family-deficient neutrophils compared to wild type cells. In the absence of Fc γ -receptors and β 2-integrins the above-mentioned cell responses showed only a slight damage. Conclusions: Based on our results, the Src family kinases Hck, Fgr and Lyn play an indispensable role in MSU crystal-induced neutrophil activation. Presumably Src family kinases take part at least partially in pathways independent of Fc γ -receptors and β 2-integrins. The outstanding importance of Src family kinases in MSU crystal-mediated inflammatory processes raises the possibility for these tyrosine-kinases to become therapeutic target molecules in the future.

MULTIDISCIPLINARY SESSION IV.

D. Biochemistry-Biophysics-Anatomy

D/1. INCREASED MECHANICAL RESISTANCE OF CLOTS IN THE PRESENCE OF DNA AND HISTONES

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Keywords: Neutrophil extracellular trap, DNA, Histone, Haemostasis, Clot resistance

Neutrophil extracellular traps (NETs) are bactericidal scaffolds composed primarily of DNA+histones released by neutrophils at sites of inflammation. In the surrounding of these structures a fibrin matrix develops. We studied the impact of DNA+histones on fibrin structure and their effects on mechanical properties of clots. Scanning electron microscopy (SEM) images were analysed to study the modulatory effects of DNA+histones on fibrin structure and fibrin fibre diameters. Small angle X-ray scattering (SAXS) was used to define the changes in the

periodicity of fibrin monomers. Alteration of clot pore size was followed with permeability assays. The effects of DNA±histones on thrombin inactivation were measured by coagulometry. Rheometry was used to investigate the changes in mechanical attributes of clots. According to SEM images histone±DNA significantly increase the diameter of fibrin fibres (fibrin clots:~50%, plasma clots:~10% increase). SAXS results show that DNA alters the longitudinal alignment of fibrin protofibrils, while histone interferes with the lateral organization of fibres. Addition of heparin to the clots reverses both effects. In permeability assays DNA reduced pore size of clots. Using histone, the permeability constant increased in fibrin clots, but a ~50% decrease was seen in plasma clots, and DNA reduced these effects. In the coagulometry studies histone inhibited the effect of antithrombin even in the presence of 0.025 U/mL heparin, however DNA partially reversed the inhibition by histones when using 1 U/mL heparin. Rheometry evidenced that addition of DNA causes more than 50% decrease in the critical shear stress necessary to disassemble the clot. Histone and especially histone+DNA together resulted in a mechanically more stable clot. DNA and histones alter the structure and mechanical properties of clots, which can result in a more resistant clot in vivo. Our findings propose a possible therapeutic benefit from agents that degrade DNA and histones as a supplementation of thrombolytic therapy.

D/2. A LINK BETWEEN THE Ca^{2+} BALANCE AND THE REDOX HOMEOSTASIS IN THE ENDOPLASMIC RETICULUM

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Keywords: Endoplasmic reticulum, Ca^{2+} balance, Redox homeostasis, Membrane permeability, Transporters

Introduction: The lumen of the endoplasmic reticulum greatly differs from the cytosol. The most prominent differences are the highly oxidative environment and the magnitudes higher calcium concentration. Both circumstances are needed for proper functioning of the organelle, namely the folding of secretory and membrane proteins. Any disturbance in redox or calcium balance leads to ER stress which can result in cell death. Lately it has been revealed, that decrease in the intraluminal Ca^{2+} content causes a quick reductive shift in the redox balance. The underlying molecular mechanism and physiological significance of this phenomenon are not yet understood. We suppose that the rapid reductive shift upon calcium depletion changes the permeability of the ER membrane, which leads to an increased influx of reductive agents. **Methods:** To verify our conception we monitored two intraluminal redox sensors. We used transfected Hyper, a fluorescent protein to real time measure intraluminal H_2O_2 on single cells; and we established a cell line expressing 11β -hydroxysteroid dehydrogenase, an intraluminal enzyme using NADPH as a co-factor. Ca^{2+} depletion was induced by the inhibition of SERCA, or by the opening of a Ca^{2+} leakage channel. **Results:** We observed that the Ca^{2+} depletion induced reductive shift in Hyper can be inhibited by lowering the cell's GSH pool or the selective permeabilization of the cell membrane. Decreasing intraluminal Ca^{2+} levels also effected cortisone reduction, which was due to the increased availability of the reducing cofactor. **Conclusions:** These

results suggest that depletion of luminal Ca^{2+} pool increases ER membrane permeability, leading to elevated transport of reducing molecules. The permeability change can be due to opening a non-selective pore, which can have essential role in the co-factor supply of luminal processes of this critical organelle.

D/3. COMPONENTS OF NEUTROPHIL EXTRACELLULAR TRAPS (NETS) INCREASE FIBRINOLYTIC RESISTANCE OF FIBRIN- AND PLASMA CLOTS

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Keywords: Neutrophil, Extracellular Trap, DNA, Histone, Haemostasis, Fibrinolysis

NETs are web-like structures with a DNA-histone backbone released by stimulated granulocytes. Appearance of NETs in the circulation triggers activation of cellular and soluble components of the haemostatic system, resulting in clot formation. We investigated the effects of DNA±histones on fibrinolysis in a set of model thrombi. Turbidimetry, confocal microscopy -using fluorescent fibrinogen and tissue-type plasminogen activator (tPA) variants-, and macroscopic time lapse scanning of clots prepared in channels of microslides (IBIDI™) were used to investigate fibrinolysis in fibrin- and plasma clots containing DNA±histones or NETs derived from phorbol-myristate-acetate(PMA)-activated neutrophils. Binding of fibrin degradation products (FDP) of various size (determined with gelelectrophoresis), fibrinogen and plasminogen to DNA was

measured with isotherm titration calorimetry (ITC). Effects of DNA on defibrinogenated plasma-induced inactivation of plasmin were estimated from the residual activity of plasmin monitored with spectrophotometry. According to turbidimetry, DNA±histone prolonged tPA-induced lysis times in fibrin- and plasma clots. Incorporation of PMA-activated granulocytes in plasma clots supported these findings showing a significant increase in 90% lysis time (control: 43 ± 5.7 min; +PMA: 107.2 ± 14.3 min). Confocal microscopy studies reported a decreased velocity of lytic tPA-front movement in plasma clots, and ITC confirmed that DNA binds large (>150 kDa) FDP with high affinity ($K_d \sim 140$ nM), possibly accounting for the delayed disassembly of clots. Time lapse scans of clots in channels of IBIDI plates showed no significant difference in plasmin-induced lysis between pure fibrin clots and those containing DNA±histone, however in plasma clots, DNA slowed down lysis by ~50%. These discordant effects were elucidated by the enhanced inactivation of plasmin in the presence of DNA detected with spectrophotometry. In summary, NETs and their major components, DNA±histones render clots more resistant against enzymatic resolution. Our findings raise the prospect that disruption of DNA-histone matrices of clots (e.g. by DNases) might improve efficiency of current thrombolytic protocols.

D/4. EXAMINATION OF THE ROLE OF ENDOGENOUS PACAP IN DIABETIC NEPHROPATHY

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Keywords: diabetes, nephropathy, kidney, cytokine, histology

Introduction: Hypophysis adenylate cyclase activating polypeptide (PACAP) is a

neuropeptide exerting cell protecting effects by inhibiting several apoptotic and inflammatory processes. All its three receptors (PAC1, VPAC1/2) are expressed in the kidney. Previous studies have proven that the extent of damage is significantly greater in PACAP knockout mice, than in their wild type mates. The aim of the present study was to investigate the role of endogenous PACAP in diabetic nephropathy. Methods: Mice were randomly divided into 4 groups: intact or diabetic PACAP+/+ and intact or diabetic PACAP-/. Diabetes was induced by a single intraperitoneal injection of streptozotocin (200mg/kg). After 10 weeks survival, histological analysis was carried out on the kidneys. Alterations in the expression of cytokines and angiogenetic factors were examined by semiquantitative cytokine and angiogenesis array. Western blot analysis was performed to measure the level of the pro- and antiapoptotic factors. Results: Histological analysis showed changes typical of diabetic nephropathy in kidneys of both PACAP knockout and wild type diabetic animals, however, lesions were significantly more severe in PACAP knockout mice. Increased expression of several cytokines (RANTES, TIMP-1, MCP-1) was observed already in intact knockout kidneys, while others were decreased or remained stable. Diabetes induced the expression of almost all the cytokines, which was further increased in the PACAP knockout animals (IFN γ , TNF α , interleukins). Levels of angiogenetic factors were markedly elevated in diabetic PACAP+/+ animals, while changes observed in diabetic PACAP knockout mice reflects a more progressed disease. Western blot analysis confirmed our previous results. Conclusion: The present study revealed more advanced histological changes, increased expression of proinflammatory cytokines and enhanced apoptosis in PACAP-/- mice compared to the wild type animals. This

raises the possible renoprotective role of PACAP in diabetic nephropathy. Grant support: TÁMOP-4.2.4.A/2-11/1-2012-0001 Nemzeti Kiválóság Program, PD109644, TAMOP 4.2.2.A-11/1/KONV-2012-0024, Arimura Foundation, PTE-MTA "Lendület" Program

D/5. THE ANATOMIC VARIABILITY OF THE RIGHT POSTERIOR HEPATIC ARTERY (RPHA) AND ITS IMPORTANCE IN LIVER SURGERY

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Keywords: liver, RPHA (right posterior hepatic artery), RPHD (right posterior hepatic bile duct), cholangiocarcinoma, RPV (right portal vein)

Introduction: In extended left hepatectomy the rate of postoperative complications is ~40 %. Intraoperative injury to RPHA is considered to be the main cause in patients who underwent left-sided hepatectomy for perihilar cholangiocarcinoma. Furthermore, protection of this artery supplying the right lateral part of the liver is essential in case of safe transplantation of the right lateral sector of the liver. No data are available on the topographical relationships of both the RPHA and right posterior hepatic bile duct (RPHD) to the right portal vein in the same specimen. **Methods:** We injected a special color and CT density coded resin mixture into human livers through the proper hepatic artery, the portal vein and the common bile duct. The parenchyma was corroded, and then we analyzed the topography of the RPHA and the RPHD related to the right branch of the portal vein (RPV) on 43 casts. **Results:** According to Yoshioka's classification, there are 3 variations of the RPHA: infraportal (87,2%), supraportal (5,1%), and combined

type (7,7%). In our series, the normal anatomic variation was also the infraportal course of the RPHA (86,1% - 37/43). The supraportal (2,3% - 1/43) and combined (11,6%-5/43) types could be considered as „variant” anatomic patterns. We found the RPHD being supraportal in 93,5% (29/31), infraportal in 3,25% (1/31) and combined in 3,25% (1/31). We haven't found supraportal RPHA and infraportal RPHD being present together in a cast. Conclusions: Supraportal and combined variants of RPHA are not unusual, with an incidence of 14% (6/43) thus the preoperative CT angiography and cholangiography are essential in surgical planning. The supraportal type of the RPHA running beneath the RPHD can be an unexpected anatomic trap for the surgeon. Negative proximal margin and secure reconstruction is more easily achieved in case of infraportal RPHD. Tutors: Mátyás Kiss MD assistant professor, Semmelweis University, Department of Human Morphology and Developmental Biology Ágnes Nemeskéri MD associate professor Semmelweis University, Department of Human Morphology and Developmental Biology liver - RPHA - RPHD - RPV variation

D/6. APPLICATION OF THE THREE HIT THEORY IN PACAP HETEROZYGOTE MICE: MATERNAL SEPARATION AND CHRONIC STRESS INFLUENCE CRF AND FOSB IN THE BNST

László Ákos Kovács, Tamás Gaszner, Gabriella Bodnár

Department of Anatomy

Keywords: Stress, Mood disorders, Maternal separation, CRF, PACAP

Introduction: According to the three hit theory genetic, epigenetic and stress factors lead to major depressive disorder. The

shortage of pituitary adenylate cyclase-activating polypeptide (PACAP) also leads to depressive-like symptoms in mice. The importance of corticotropin releasing factor (CRF) and hypothalamus-pituitary-adrenal (HPA) axis in stress adaptation response is known, but its supra-hypothalamic regulation (bed nucleus of the stria terminalis [BNST]) is largely elusive. Aims: We hypothesized that mice carrying all risk factors will show mal-adaptation in the HPA axis and CRF systems. Methods: To model the disease, litters from pituitary (PACAP) heterozygote pairs were exposed to different maternal separation (short: daily 15, and long: daily 180 minutes) versus controls for two weeks. Later half of adult offspring was subjected to chronic variable mild stress. The model's validity was determined by the measurement of HPA axis activity. The contribution of CRF producing neurons in the oval and ventral nuclei of BNST (BNSTov, vBNST) was studied by CRF-FosB immune-labeling. Results indicate that chronic variable mild stress most effectively increased adrenal weights in mice suffered from long maternal separation. Maternal separated mice upon chronic variable mild stress had increased CRF-cell counts in the BNSTov and had increased specific signal density in the BNSTov, vBNST. CRF containing cells show increased FosB specific signal density if mice carried both three risk factors. Conclusions: The increased CRF neuronal activity in both regions (BNSTov, vBNST) suggests that the neurons may change their functions if all three risk factors of depression coincide. The three hit theory of depression seems to be applicable in PACAP heterozygote mice to study the pathophysiology of stress-related mood disorders.

D/7. CLINICAL ANATOMY OF THE GASTRODUODENAL ARTERY AND ITS SURGICAL RELEVANCE IN PANCREATIC INTERVENTIONS

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Keywords: gastroduodenal artery, vascular anatomy, pancreatic surgery, complications, prevention

Introduction: the branches of gastroduodenal artery (GDA) play important role in surgery of pancreatic region. Most studies about the vascular anatomy of pancreaticoduodenal groove have focused on the system of pancreatic arcades, but no data are known about the terminal arborization of GDA. Thus, the major objective of our investigation was to explore the variations of these branches. **Methods:** 53 abdominal organ complexes were injected by special resin through the abdominal aorta, and then the soft tissue was corroded. On each corrosion cast, terminal arteries were identified. The observed variations were classified according to the number of branches and supplied regions. Digital photos and CT-images were taken on all complexes, and 3D-reconstructions were made. **Results:** the classical bifurcation [right gastroepiploic artery (RGEA) and anterior superior pancreaticoduodenal artery (ASPDA)] was observed in 23 cases – this variant was the most frequent, however, its rate was less than 50% of the cases. The GDA bifurcated into the RGEA and a common trunk of anterior

and posterior superior pancreaticoduodenal arteries in three other preparations. In trifurcations (20/53), the transverse pancreatic or the lower isthmian incisural or the infrapyloric artery was identified as the third branch. In 6 cases, quadrifurcations were observed supplying large (wide) area. These vessels mostly displayed richly branching small arteries for surrounding organs. In one case, RGEA arose from the anterior inferior pancreaticoduodenal artery, and the GDA divided into ASPDA and PSPDA. **Surgical relevancies:** branching patterns of GDA are highly variable. The interventions of pancreatic region are frequently associated with high morbidity (~40-50%) - complications mainly are due to the poor blood supply of the remnant organs. Detailed preoperative analysis of the vascular anatomy in the area is of primary importance in preventing the pancreatic leakage, gastroparesis or postoperative hemorrhage.

MULTIDISCIPLINARY SESSION V.

G. From cell to clinical sciences:

Immunology-Cell Biology –

Orthopedics session

G/1. THE EXAMINATION OF THE KNEE JOINT'S ALIGNMENT IN CHILDREN

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Keywords: knee joint, 3D reconstruction, EOS, condylus-plateau angle, gender

INTRODUCTION: The changing of the lower limb's alignment in childhood is well known, but can be terrifying for the parents, what makes it a frequent complain in the daily practice. The knowledge of the exact, population and gender specific normal ranges

is essential to make the right clinical decision. The goal of our study is to define the normal range of the normal knee's frontal alignment's parameters in the 4-16-year-old age group. **METHODS:** From the 7108 EOS 2D/3D examination, what was carried out at our department, those pictures were selected, which (1) presented the 4-16-year-old age group, (2) were appropriate for 3D reconstruction, (3) do not typify any disorder, what can influence the biomechanics of the lower limb, (4) the patient had negative lower limb anamnesis. The statistical analysis was carried out using two-sample t-test, spearman correlation and regression analysis. **RESULTS:** The condylar-hip angle (the angle between the femoral condyles' tangent and the femoral mechanical axis) shows mildly increasing tendency (from 2,55° to 3,10° in boys, from 2,42° to 3,27° in girls). The plateau-ankle angle (the angle between the tibia plateau's tangent and the mechanical angle of the tibia) decreases from -1,19° to -3,18° in boys, and 0,36° to -0,78° in girls. The condylus-plateau angle (the angle between the condylar and plateau tangent) does not show any correlation with the age, it's value is around -0,69° in boys and -0,89° in girls. **CONCLUSION:** We could determine the parameters of the knee joint's alignment, which have not been defined in this age-group before. We found that the parameters follow the changing of the lower limb's axial alignment, keep the joint space consistently slightly medially narrowed.

G/2. THE ROLE OF ADENOSINE RECEPTORS IN THE INFLAMMATORY RESPONSES OF HUMAN MACROPHAGES

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Department of Physiology, University of Debrecen

Keywords: Macrophage, adenosine, adenylate-cyclase, TNF α , IL-1 β

Introduction: IL-1 β and TNF α are two main inflammatory cytokines that regulate immune responses. They take part in many pathological cases such as chronic inflammatory diseases, autoimmune diseases and metabolic diseases. One of the main source of these cytokines are the activated macrophages such as LPS-activated GM-macrophages. GM-macrophages are differentiated from monocytes in presence of granulocyte-macrophage colony stimulating factor (GM-CSF) and are described as inflammatory macrophages. GM-macrophages can be regulated by many endogenous and exogenous agents such as adenosine or caffeine. So far four adenosine receptors were described that are involved in the effect of adenosine or caffeine. These adenosine receptors (A1, A2a, A2b, A3) are 7 TM-receptors and regulate intracellular cAMP level by activating or inhibiting adenylate-cyclase enzyme. **Methods:** Human monocytes were separated from human peripheral blood and were cultured for five days in the presence of GMCSF to become inflammatory macrophages (GM-MFs). The macrophages were activated by LPS, and treated with adenosine and adenylate-cyclase inhibitor. The cytokine production was measured by ELISA. **Results:** Our results show that LPS-induced GM-macrophages secrete increasing amount of IL-1 β and decreasing amount of TNF α in the presence of extracellular adenosine. In the presence of adenylate-cyclase inhibitor adenosine-treated LPS-activated cells produce even more IL-1 β , and even less TNF α . As an antagonist caffeine can also effects macrophage function. **Conclusions:** Though both IL-1 β and TNF α function as pro-inflammatory cytokines, their expression is regulated oppositely in GM-macrophages.

G/3. CHONDROGENIC CELLS EXPRESSING CB1 RECEPTORS

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Keywords: Chondrogenesis, cannabinoid receptor 1 (CB1R), endocannabinoid system, chondrocytes, osteoarthritis

Introduction: Recently, more and more countries have legalised the use of cannabis containing products in treatment of various skeletal diseases (osteoarthritis, rheumatoid arthritis), based on their anti-inflammatory and analgesic effect. They mainly act upon the Cannabinoid 1 and Cannabinoid 2 (CB1 & 2) seven transmembrane domain receptors. CB1 receptor is known to be expressed on mature and arthritic chondrocytes; however we have limited information of the receptor's appearance and function on differentiating chondrocytes. **Methods:** During the in vitro part of our work high density chondrogenic cell cultures (HDC) were established from limb buds of 11,5 day-old mouse embryos. The mRNA and protein expression of the members of Endocannabinoid System (ECS) was examined by semiquantitative RT-PCR and immunocytochemistry. For evaluating the effect of CB1 agonist (anandamide; AEA) and inverse agonist (AM251) on chondrogenesis dimethyl-methylene blue (DMMB) staining and RT-PCR techniques were applied, to monitor chondrogenic markers and matrix- constituents. Ex vivo we followed the mRNA expression of ECS members in cartilage samples of different developmental stages and observed the spatiotemporal distribution of the CB1 receptor in mouse embryonic limb buds and in the limbs of young mice. **Results:** Our results show the presence of each receptor and enzyme of the ECS mentioned by the literature at mRNA level in mouse HDC.

CB1 receptor protein is expressed in HDCs, limb buds of a 15-day-old mouse and in the articular cartilage of young animals. Modulation of the function of ECS caused alterations in cartilage formation. **Conclusion:** Our results prove that CB1 is present during in vivo and in vitro chondrogenesis and the applied pharmacons influence chondrogenesis. This research was supported by the European Union and the State of Hungary, co-financed by the European Social Fund in the framework of TÁMOP-4.2.4.A/ 2-11/1-2012-0001 'National Excellence Program'

G/4. THE ROLE OF HEMOKININ-1 AND SUBSTANCE P IN ACUTE PAIN IN MICE

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Keywords: hemokinin-1, substance P, tachykinin, nociception, neurogenic inflammation

INTRODUCTION Hemokinin-1 (HK-1) encoded by the Tac4 gene, is present in the nervous and immune systems. It has similar structural and immunological characteristics to those of substance P (SP) derived from the Tac1 gene. Moreover, these peptides show similar affinity to the neurokinin 1 (NK1) receptors. We studied the roles of these tachykinins in acute somatic and visceral nociception, as well as acute neurogenic inflammation using gene-deleted (Tac4^{-/-}, Tac1^{-/-}, Tac1/4^{-/-}, NK1^{-/-}) mice compared to their C57Bl/6 wildtypes. **METHODS** Acute somatic nocifensive behaviour was evoked by intraplantar formalin injection. Nocifensive reactions arose in two phases

(direct stimulation of sensory nerves between 0–5 min and consequent activation of inflammatory mechanisms between 20–45 min), and were quantitatively evaluated by the duration of paw liftings, lickings and shakings. Visceral nociception was induced by i.p. acetic acid injection to elicit abdominal contractions (writhings), which was counted during the 0–5, 5–20 and 20–30 min time-intervals. Acute neurogenic inflammation was evoked by the ultrapotent Transient Receptor Potential Vanilloid 1 receptor agonist resiniferatoxin (RTX; i.pl.). After control measurements, noxious heat and mechanonociceptive thresholds were measured with increasing temperature hot plate and dynamic plantar aesthesiometer, 5–20 min and 2–24 hours following RTX-administration, respectively. **RESULTS** Formalin-evoked paw liftings and lickings were significantly reduced in Tac1^{-/-} and Tac1/4^{-/-} mice, while acetic acid-induced writhings decreased in all gene-deleted animals compared to their wildtypes. RTX-evoked thermal allodynia was totally diminished in Tac1^{-/-} and Tac1/4^{-/-} mice, and partly reduced in Tac4^{-/-} animals, while mechanical hyperalgesia was significantly decreased in Tac4^{-/-} and NK1^{-/-} mice. **CONCLUSION** SP mediates somatic and visceral nociception and inflammatory thermal allodynia, but NK1 receptors are only involved in these actions in the visceral region. HK-1 plays a predominant role in visceral pain and inflammatory mechanical hyperalgesia, which actions are partly mediated by NK1 receptors. **Consultants:** Dr Zsófia Hajna, Dr Zsuzsanna Helyes

G/5. NOCICEPTIVE ROLE OF HEMOKININ-1, THE NEWEST MEMBER OF THE TACHYKININ FAMILY, IN CHRONIC TRAUMATIC NEUROPATHY MODEL OF THE MOUSE

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Keywords: Neuropathy, pain, tachykinin, hemokinin-1, nerve growth factor

Introduction: Traumatic neuropathy is a chronic pain condition caused by mechanical injury of peripheric nerves. There is no satisfactory therapy and the pathophysiological mechanisms are not completely understood. Although regulatory roles have earlier been proposed for tachykinins, our researches did not verify the role of substance P and its NK-1 receptor in neuropathic pain. The Tac4 gene coded hemokinin-1 has similar immunological and pharmacological properties to substance P. Our goal was to examine the role of hemokinin-1 in a model of neuropathy using gene-deleted mice. **Methods:** We induced traumatic mononeuropathy in male C57Bl/6 (wild-type) and hemokinin-1 gene-deficient (Tac4^{-/-}) mice by 1/2-1/3 ligation of the right sciatic nerve. On the 3rd, 5th and 7th postoperative days we examined the mechanonociceptive threshold with aesthesiometry, cold tolerance with paw withdrawal latency from 0°C water and motor coordination by measuring time spent on accelerating RotaRod wheel. On the 7th day we determined the level of nerve growth factor (NGF) with ELISA from the paw homogenizates. **Results:** By the 5th day the mechanonociceptive threshold of WT mice decreased by 35% (mechanical hyperalgesia), the cold tolerance by 70% (cold hyperalgesia), the motor function didn't change. Compared to WT mice in Tac4^{-/-} group mechanical and cold hyperalgesia was significantly reduced after surgery. Tac4^{-/-} motor function did not change due to operation, but was worse throughout the entire experiment. The control NGF-level in Tac4^{-/-} mice was lower compared to WT

group. After nerve ligation the NGF level didn't change in WT mice, but significantly increased in Tac4-/- mice compared to their own control measurements. Conclusion: We were the first to prove the role of hemokinin-1 in the development of mechanical and cold hyperalgesia in traumatic mononeuropathy, wherein the inhibition of NGF production can be an important factor.

MULTIDISCIPLINARY SESSION VI.

H. Neurology-Ophthalmology

H/1. CONVENTIONAL VS QUANTITATIVE ASSESEMENT OF POST-TRAUMATIC VENTRICULOMEGALY IN SEVERE TRAUMATIC BRAIN INJURY

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Keywords: Neuroimaging, CT, sTBI, ventriculomegaly, outcome prediction

Post-traumatic ventriculomegaly is a known complication of severe traumatic brain injury (sTBI) associated with poor clinical outcome. Subjective assessments leave the relationship of ventriculomegaly and outcome measures elusive. We hypothesized that ventricular volumetric based identification of ventriculomegaly could add to subjective radiologic assessment of ventriculomegaly in predicting outcome. This retrospective analysis was performed on 84 adults with blunt sTBI requiring a ventriculostomy. Serial CTs within 3 hours and an average of 3 additional scans within the first 10 days of sTBI and 6-month outcome data, Disability Rating Scale (DRS) and Glasgow Outcome Scale-Extended (GOS-E), were available for 64 patients. Subjective assessment for

ventriculomegaly and quantified ventricular volumes were determined. Relative enlargement to initial volume was calculated. The relationship to 6-month outcome was assessed between patients without ventricular enlargement and each of the following groups: (A) Subjective radiological diagnosis of ventriculomegaly. (B through E) Quantitative measurement groups: (B) any, (C) overall, (D) bilateral, (E) unilateral enlargement. Mann-Whitney U-test determined significance ($p \leq 0.05$). Ten surviving patients with unilateral enlargement (E) had significantly worse DRS and GOS-E scores than all other 19 surviving patients (mean scores for group E: DRS=10, GOS-E=4; for non-unilateral enlargement group: DRS=4, GOS-E=6). Other groups (A-D) did not differ in outcome from non-enlargement patients. Quantitative approach identified a subgroup of sTBI patients with unilateral ventricle enlargement indicating poor outcome while other types or subjective-diagnosed ventricle enlargement did not.

H/2. IN VITRO MODEL OF SUBARACHNOID HEMORRHAGE INDUCED VASOSPASM: ROLE OF BLOOD COMPONENTS

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Keywords: arteria basilaris, vasomotor dysfunction, subarachnoid hemorrhage, intracellular calcium, stroke

Background: Subarachnoid hemorrhage induces substantial vasospasm causing serious damage to the cerebral circulation. However, the role of various blood

components eliciting vasospasm has not yet been identified. We hypothesized that blood components have different effects on vasoconstriction. Methods: Basilar arteries (BA) were isolated from Wistar rats and placed into an isotonic myograph chamber. Diameters of arteries were measured by videomicroscopy. Hemolysed blood and its components were administrated into the chamber. Statistical analysis was performed by One Way Anova Holm- Sidac method. Results: The active diameter of BA was $233 \pm 11 \mu\text{m}$, while the passive diameter was $361 \pm 10 \mu\text{m}$. Hemoglobin (control : $254 \pm 17 \mu\text{m}$; Hgb 10-12 M: $248 \pm 9 \mu\text{m}$; Hgb 10-6 M: $274 \pm 22 \mu\text{m}$) and platelet concentrate (Pc, control: $188 \pm 11 \mu\text{m}$, Pc $185 \pm 13 \mu\text{m}$) did not cause significant vasoconstriction. However, hemolysed blood (HB, control: $278 \pm 12 \mu\text{m}$, HB: $164 \pm 11 \mu\text{m}$), blood serum (control: $246 \pm 8 \mu\text{m}$, serum: $170 \pm 6 \mu\text{m}$), red blood cell concentrate (RBCc, control : $217 \pm 9 \mu\text{m}$, RBCc: $166 \pm 6 \mu\text{m}$), platelet suspension (Ps, control : $191 \pm 15 \mu\text{m}$, Ps: $165 \pm 16 \mu\text{m}$) and plasma (control : $258 \pm 7 \mu\text{m}$, plasma $226 \pm 7 \mu\text{m}$) caused significant vasoconstriction. Conclusions: These results indicate that extravascular hemoglobin and platelet concentration had no significant vasoconstrictor effect. The greatest constriction was elicited by hemolysed blood. The serum, RBC, Ps, and plasma elicited smaller constrictions (in descending order). These findings may help the development of optimal clinical management of subarachnoid hemorrhage. Support: Hungarian National Scientific Research Found (OTKA) K-108444, and SROP-4.2.2.A-11/1/KONV-2012-0024, and SROP-4.2.2.A-11/1/KONV-2012-0017. TÁMOP 4.2.4. A/2-11-1-2012-0001 "National Excellence Program"

H/3. MANGANESE ENHANCED MRI (MEMRI) IN RAT: IS THE EFFECT OF

THE ENRICHED ENVIRONMENT VISIBLE IN THE BRAIN?

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Keywords: enriched environment, MEMRI, manganese, neuroprotective effect, rat

Introduction. Manganese enhanced MRI (MEMRI) is suited for contrast intensification, tractography, monitoring neuronal activation and detection of hypoxia. It is well known that manganese is a cardio-, hepato- and neurotoxic agent, therefore, it appeared conducive in the in vivo examination of the enriched environment, previously shown by our research group to have neuroprotective effect. The aim of our experiment was to reveal MEMRI detectable effects due to the enriched environment. Methods. Eighteen male, adult Wistar rats were examined. The enriched environment group was held in a larger cage with toys from birth to the fifth postnatal week, while standard conditions were provided for the poor environment and the manganese-free control groups. Isoflurane anaesthesia was used for all procedures and the imaging as well. MR imaging was performed with a Siemens MAGNETOM Tim Trio 3T scanner. Quantitative T1-mapping was calculated before and 48 hours after $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ solution was administered intravenously (v. dorsalis penis: $1 \mu\text{l/ttg}$, 100 mM, pH 7,4 with bicine) to induce contrast enhancement and neurotoxicity. Cerebral T1-time changes were examined with software evaluation (FSL, FMRIB, Oxford), and volumetric analysis was performed in the whole brain, the hippocampi and the lateral ventricles. Results. A decreased T1-time was observed in both treated groups, indicating contrast enhancement (48 hour imaging: treated $752,0 \pm 12,5 \text{ ms}$ vs. control $841,1 \pm 18,5 \text{ ms}$; $p < 0,05$). No difference was found in the

extent, rate and localisation of the decrease in the treated groups. Significantly larger hippocampi and lateral ventricles were found in the enriched environmental group along with similar whole brain volume. Conclusion. The enriched environment did not influence the manganese enhancement, however, it resulted in larger volumes of the hippocampi and the lateral ventricles. Our experiment provides a T1-time determining MEMRI-model adequate for further in vivo examination of various neural damaging effects (hypoxia, neurotoxic agents, etc.) in rats.

H/4. THE SUSCEPTIBILITY WEIGHTED MAGNETIC RESONANCE IMAGING (SWI MRI) IN 3D RECONSTRUCTION REVEALS ATYPICAL MORPHOLOGY WHITE MATTER (WM) LESIONS IN TRAUMATIC BRAIN INJURIES (TBI)

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Keywords: SWI MRI, morphology, TBI, atypical, perivascular

Introductio: SWI MRI is the best imaging technique so far to detect the microscopic bleedings developing in relation to diffuse axonal injuries (DAI). However, the exact clinical relevance of these lesions is unclear. Our original objective was to characterize DAI connected hypointesities (lesions) in different severity TBIs in a follow-up study. During the characterisation we found numerous lesions not fully appropriate to the definitive ones. Our further objectives were the examination of the occurrence and importance of these lesions in an available TBI data base. Methods In our study we examined the TBI related WM SWI lesions in 22 patients with moderate or severe TBI on T1 weighted and SWI images provided by a

Siemens Magnetom Tim Trio 3T device. The control group contained five healthy patients. We performed a linear registration of the T1 and SWI images with software FSL (FMRIB, Oxford), so we were able to localise and coordinate the lesions in the differently weighted images precisely. We also performed the 3D reconstruction of these lesions with another software (3D Slicer), documented the size, the morphology, the localisation and number of them. Results $\Sigma 43$ hypointensities were found in 15 patients. 23 of these were appropriate to the literature definition: WM localisation, 3-10mm diameter, rounded hypointensity (18 subcortical, 11 in the corpus callosum and 4 in the brain stem). We found 10 subcortical, atypical morphology lesions in 7 patients. These lesions were definitive in localization and size, but showed an extension reaching the grey matter or the surface of the brain. Conclusion The atypical lesion visualized by 3D reconstruction can be related to vascular or perivascular pathology. Its clinical relevance surely differs from the “classical” axonal injury related lesions’ but its differentiation from it in traditional horizontal plane, not T1 coregistered SWI images is nearly impossible.

H/5. FEASIBILITY OF STATIC AND DYNAMIC STEREOVISION TESTS IN VISUAL SCREENING OF PRESCHOOL CHILDREN

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Keywords: amblyopia, stereovision, visual acuity, screening, stereotest

Introduction: Lazy eye or amblyopia is a condition accompanied with decreased vision on one eye and lack of stereovision. It is the leading cause of permanent vision loss under the age of 40 in Europe, but screening for the disease is not properly implemented, even though early recognition enables appropriate treatment. **Methods:** We investigated the feasibility of static and dynamic stereovision tests that have been developed for the early detection of amblyopia in preschool children. We examined 403 children between the ages of 4-6 in Trieste (Italy) with the following screening protocol: monocular visual acuity (VA), Lang, static and dynamic stereovision tests, Brückner and cover tests and corneal light reflex examination. **Results:** Out of the 403 examined children, 56 (13.9%) had an uncorrected VA difference of more than 0.2 between the two eyes, and 20 (5% of total) of them failed the dynamic stereotest as well. Altogether 60 (14.9%) failed both static and dynamic stereotests and 68% of those who failed both stereotests showed positivity in other tests as well. Positive cases were advised to see an Ophthalmologist. **Conclusion:** Based on our finding, it is very likely that 5% of children aged 4-6 have a high risk for amblyopia in Trieste, which is compatible with the European average. We have confirmed that the test is easy, efficient and quick to carry out even on a young population and anybody can do it after a short training session. It demonstrated a high efficiency in indicating positivity of any of the other performed tests as well. With its present settings, our stereotest on its own does not provide a substitute for complex vision screening tests. However, with minor adjustments, its sensitivity can be optimized and could serve as an essential part of vision screening for amblyopia.

H/6. THE INHERITANCE OF CORNEAL ENDOTHELIAL CELL DENSITY

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Keywords: endothelial, density, twin study

Purpose: To estimate the genetic influences on the corneal endothelial cell density in monozygotic and dizygotic Hungarian twins.

Methods: Corneal endothelial cell density was investigated in 110 twin subjects (41 monozygotic, MZ and 14 dizygotic DZ pairs; mean age 48±15 years) by Konan Noncon Robo NSP-9900 specular microscopy. For the statistical analysis, structural equation modeling (ACE model) was applied.

Results: Endothelial corneal cell density was highly heritable in both eyes (right eye: 60.2%, 95% CI, 30.0% to 81.0%, left eye: 81.3%, 95% CI, 63.0% to 90.9%), while as the unique environmental contribution was 39.8% (95% CI, 19.0% to 69.9%) and 18.7% (95% CI, 9.1% to 36.9%) in the right and left eyes, respectively. Shared environmental factors had no influence on the endothelial corneal cell density.

Conclusion: In Hungary, in this twin study, we established first that the density of the corneal endothelial cells is strongly heritable. This result highlights the important role of

early screening of several corneal degenerations and dystrophies.

SPECIAL FOCUS SESSION

I. New ways and strategies in neoropharmacology researches

I/1. STRESS AND HERITABILITY FACTORS IN THE BACKGROUND OF DEPRESSION

Prof. Dr. György Bagdy

**Department of Pharmacodynamics,
Semmelweis University, Budapest**

No abstract available.

I/2. NEUROPROTECTIVE MECHANISM OF ESTRADIOL ACTION ON BASAL FOREBRAIN CHOLINERGIC NEURONS

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University of Pécs, Szentágotthai Research
Centrr, Centre for Neuroscience**

Keywords: estradiol, non-classical action,
cholinergic neurons, NMDA, neurotrophin
receptors

It is well-known that estrogen protects cholinergic neurons against neurotoxic insults but the molecular mechanism of this action remains unclear. We identified non-classical estrogen actions on receptors/downstream signalling molecules and explored the role of this non-classical estrogen pathway in estrogen-induced neuroprotection on basal forebrain cholinergic neurons. In the first series of experiments, we measured the diffusion parameters of TrkA receptor and calculated the incidence of downstream signaling on live adult cholinergic neurons using single molecule detection. We have shown that 17 β -estradiol (E2) rapidly increases TrkA molecule activity enhancing the incidence of downstream signaling

processes. We also demonstrated that E2 induces a rapid phosphorylation of downstream signaling molecules such as ERK1/2 and CREB in basal forebrain cholinergic neurons and it was abolished in neuron-specific estrogen receptor α knock-out mice (ER α KO) in vivo. Selective blockade of the MAPK pathway completely prevented estrogen-induced CREB phosphorylation in cholinergic neurons. In the second series of investigation NMDA was injected to elicit cholinergic cell death in basal forebrain and consequent cholinergic fiber loss in the parietal cortex. A single injection of E2 after the NMDA lesion protected the cholinergic fiber density in the cortex in vivo. The estrogen-induced cholinergic fiber protection was absent in ER α KO mice. Selective activation of non-classical estrogen signaling in vivo by estren induced estrogen-like protective actions. Selective blockade of the ERK1/2 activation prevented estrogen's ability to protect cholinergic fibers. These findings demonstrate that estrogen induces rapid ER α dependent non-classical action on CREB phosphorylation via ERK1/2 signaling pathways activation in cholinergic neurons. These observations reveal the critical role of non-classical estrogen signaling via ER α and ERK1/2 pathways in estrogen-induced neuroprotection in the cholinergic system.

I/3. THE ROLE OF PITUITARY ADENYLATE CYCLASE-ACTIVATING POLYPEPTIDE (PACAP) IN PRIMARY HEADACHE DISEASES: PRECLINICAL AND CLINICAL RESULTS

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Brubel 7, Dóra Reglődi 7, Nikolett Szabó
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Keywords: trigeminovascular activation, migraine, interictal/ictal period, PACAP, radioimmunoassay

No English abstract available.

I/4. PITUITARY ADENYLATE CYCLASE-ACTIVATING POLYPEPTIDE (PACAP)-INDUCED RELAXATION IS LESS EFFECTED IN CEREBRAL THAN PERIPHERAL ARTERIES

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Department of Pathophysiology and Gerontology, University of Pécs, Hungary

Keywords: PACAP1-38, Vascular tone, PAC1 receptor, Isolated carotid and basilar arteries, Aging

Introduction: Pituitary adenylate cyclase-activating polypeptide (PACAP) is a well-known neuropeptide, which also has vasomotor effects. Less is regarding its vasomotor effect, especially in that of cerebral arteries. Also, it is known that aging affects the function of arterial vessels. We hypothesized that the vasomotor effects of

PACAP differ in peripheral and cerebral arteries and aging substantially modulates them. **Methods:** Thus, carotid (CA) and basilar arteries (BA) were isolated from young (2 months old), middle age (12 months old), and old (30 months old) rats. Their vasomotor responses were measured with an isometric myograph (DMT610M) in response to cumulative concentrations of PACAP1-38 (10⁻⁹–10⁻⁶ M).

Results: PACAP1-38 induced (1) significantly greater concentration-dependent relaxations in CA compared to that of BA of young, middle age, and old rats; (2) relaxations of CA significantly decreased, whereas they did not change substantially in BA, as a function of age; (3) sodium nitroprusside (SNP)-induced relaxation did not change after PACAP1-38 administration in any conditions; and (4) inhibition of PAC1 receptors by selective PAC1 receptor blocker (PACAP6-38) completely diminished the responses to PACAP in all age groups of BA and CA.

Conclusion: Collectively, these findings suggest that the neuropeptide PACAP elicits greater relaxation in peripheral than in cerebral arteries, and that aging has less effect on the relaxation of cerebral than peripheral arteries, suggesting that the relaxation to PACAP is maintained in cerebral arteries even in older age. These findings could be used to develop therapeutic modalities.

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I/5. MODELS FOR EXAMINING AND REHABILITATING PERINATAL INJURIES OF THE NERVOUS SYSTEM IN RODENTS

Péter Kiss, MD

University of Pecs Medical School, Department of Anatomy

Keywords: perinatal injuries, PACAP, asphyxia, enriched environment, early neurobehavioral development

Perinatal period is crucial for the development of the nervous system both in humans and animals. Any injury in this period can produce long term disabilities, highly influencing the quality of life. Even nowadays perinatal toxic, asphyctic or traumatic injuries are hard to predict or successfully treat. Even with the excessive research in the past few decades, no neuroprotective procedure was proven to be successful except hypothermia. This underlines the importance of animal models to study the pathomechanism of such injuries. In the present lecture a small summary is given about those animal models, which our research group has developed or adapted in our laboratory to examine the short term neurobehavioral outcome of different perinatal injuries in rats. Also some possible methods will be presented to treat these conditions, and improve early neurobehavioral development, and ameliorate the histologic and functional outcome of some specific perinatal injuries.

I/6. CALCIUM IMAGING IN BRAIN SLICES AS A PHARMACOLOGICAL SCREENING METHOD

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Keywords: calcium imaging, brain slice, acetylcholine, muscarinic receptor cochlear, nucleus

Intracellular calcium concentration measurement in brain tissue has a huge potential both in vivo, and in surviving brain slices in vitro. Most neurons possess some kind of high threshold voltage gated calcium channels in their somatic or proximal dendritic membrane. Action potential (AP) firing leads to calcium entry, and this can be seen as a calcium transient with characteristic kinetics during imaging. Thus, calcium imaging is suitable for indirect, simultaneous monitoring of neuronal activity (action potential firing) in multiple cells, and therefore it can be appropriate for the investigation of neuronal network function, and for the functional mapping of synaptically coupled neurons. However, certain biological and technical characteristics of the technique have to be considered when the goal is the precise tracking of network function: the different duration of the AP coupled calcium transients and APs themselves; the maximum frame-rate of the imaging; or the view-field of the given objective. Together with its strengths and weaknesses calcium imaging in brain slices is a robust pharmacological screening method, so long as the aim is to detect differences in AP firing patterns of sparsely firing neurons, as a response for the application of a given pharmacological agent. At the end of my talk I will present an example for such „screening” through our earlier work proving the existence of muscarinic receptors on granule cells of the cochlear nucleus.

J. POSTER SESSION I.

Basic sciences: Physiology- Pathophysiology-Biochemistry- Biophysics

J/1. THE POTENTIAL ROLE OF ALARIN IN THE REGULATION OF ENERGY BALANCE OF RATS

Peter Balla, Bianka Aubrecht, Alexandra Miko, Nora Furedi, Marta Balasko, Erika Petervari

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Keywords: energy balance, alarin, thermoregulation, body weight, food intake

Background: In the background of obesity, regulatory alterations in energy balance affecting peptide systems may also be assumed. Regulation of energy balance does not only involve maintenance of body weight but also that of metabolic rate and core temperature. The contribution of alarin, a new member of the potentially orexigenic galanin peptide family to the regulation of energy metabolism has been recently suggested. Our aim was to analyze the thermoregulatory and orexigenic effects of alarin in rats. Methods: Adult male Wistar rats received full-length alarin, its truncated form (Ala6-25Cys) and scrambled alarin in various doses intracerebroventricularly (ICV) at cool or slightly subthermoneutral ambient temperatures. Oxygen consumption (VO₂, indicating heat production) heat loss (assessed by tail skin temperature) and core temperature (T_c) were recorded in an indirect calorimeter system. The spontaneous and fasting-induced food intake was automatically recorded in FeedScale system. Results: Upon ICV alarin injection, even at cooler ambient temperatures an increase in VO₂ and continuous tail skin vasoconstriction induced a rise in T_c. This

effect was not dose-dependent, however, the administration of Ala6-25Cys prevented this action. Fasting-induced food intake was significantly reduced by alarin. Conclusion: Alarin appears to elicit a hypermetabolic, hyperthermic thermoregulatory response and an anorexigenic effect in rats. Such responses rather characterize catabolic mediators. Ala6-25Cys seems to act as an antagonist to the thermoregulatory effects. Further investigations are needed to clarify the complex role of alarin in energy homeostasis.

J/2. THE BILE ACID, TAUROCHOLIC ACID ACTIVATES RYANODINE RECEPTOR AND INHIBITS SERCA ACTIVITY

Gyula Diszhazi, Nikolett Geyer, Janos Almassy, Istvan Jona

Department of Physiology, University of Debrecen

Keywords: taurocholic acid, ryanodine receptor, SERCA, pancreatitis, calcium

The earliest critical event of pancreatitis is a long lasting high amplitude rise of intracellular Ca²⁺ concentration in the acinar cell, which can be triggered by secretagogue overstimulation or high concentration of bile acids. Although, Ca²⁺-release through ryanodine receptors (RyR) is involved in the process, the significance and the exact mechanism of bile acid's action on RyR has not been fully elucidated yet. Therefore, we aimed to test whether taurocholic acid (TCA) exerts a direct effect on RyR and SERCA pump. We show that TCA enhanced RyR's 3H-ryanodine binding in the pathologically relevant 25-500 µM range. We also found that 500 µM TCA triggered robust Ca²⁺-release from RyR-enriched vesicles, which was prevented by the application of 12 µM dantrolene. Single channel current analysis of RyRs reconstituted into lipid bilayers demonstrated that 200 µM TCA induced a 5-

fold increase in channel open probability ($K_d=180 \mu\text{M}$) Furthermore, we show that TCA suppressed Ca^{2+} -uptake and ATP-ase activity of SERCA- enriched vesicles. Overall, our data strongly suggest that TCA activates RyR and inhibits SERCA with an allosteric mechanism, which might contribute significantly to TCA-induced pathologic Ca^{2+} -leak from the endoplasmic reticulum in pancreatic acinar cells.

J/3. ROLE OF THE TRANSIENT RECEPTOR POTENTIAL ANKYRIN 1 (TRPA1) ION CHANNEL IN THE ACUTE AND CHRONIC INFLAMMATORY PAIN MODELS OF THE MOUSE

Adam Horvath

Department of Pharmacology and Pharmacotherapy, University of Pécs

Keywords: TRPA1 receptor, carrageenan-induced hyperalgesia, CFA-induced inflammatory hyperalgesia, paw edema, myeloperoxidase activity

Introduction: Transient Receptor Potential Ankyrin 1 (TRPA1) is calcium-permeable non-selective cation channel, which is predominantly expressed on capsaicin-sensitive sensory nerve endings. Beside cold temperature ($<17^\circ\text{C}$) TRPA1 is stimulated by many endogenous noxious agents and exogenous irritants like mustard oil, cinnamaldehyde, H_2S and allicin. Since few contradictory data are available on the involvement of this receptor in inflammation and nociception, we aimed to investigate the role of TRPA1 in acute and chronic inflammatory pain models. **Methods:** Experiments were performed with male TRPA1 gene-deficient mice (TRPA1 $^{-/-}$) in comparison with their wildtypes (TRPA1 $^{+/+}$). The acute inflammation was evoked by intraplantarly injection of 3% carrageenan, while the chronic inflammation

was induced by injected Complete Freund's adjuvant (CFA) in the right hindpaw and the root of the tail. The noxious heat and the mechanonociceptive thresholds were measured with increasing-temperature hot plate or dynamic plantar aesthesiometer and the paw volume with plethysmometry. Cold allodynia was determined by the latency decrease of the nocifensive behaviours in icy water. The activity of neutrophil myeloperoxidase was investigated with luminol based luminescent in vivo imaging in the CFA-model. **Results:** In the TRPA1 $^{-/-}$ animals there were no significant difference between the carrageenan-induced inflammatory hyperalgesia as well as the paw volume compared to their wildtypes. In contrast, the mechanical hyperalgesia and paw edema were significantly lower in TRPA1 $^{-/-}$ mice in chronic inflammation model. The myeloperoxidase activity indicating neutrophil activation was not influenced by deficiency of TRPA1. **Conclusion:** The chronic paw edema and mechanical hyperalgesia caused by central sensitization can be mediated by TRPA1. However it is not involved in the neutrophil activation and production of reactive oxygen species. This receptor may not play an important role in acute inflammation. **Support:** SROP-4.2.4.A/2-11-1-2012-0001, SROP-4.2.2/A-11/1/KONV-2012-0024

J/4. CHANGES IN THE CENTRAL ALPHA-MSH SENSITIVITY IN MALE AND FEMALE RATS OF VARIOUS AGES

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Keywords: female rats, alpha-MSH, age-related alterations, estrus cycle, energy balance

Introduction: The obesity of the middle-aged and the anorexia of aged individuals leading to frailty and sarcopenia have wide health-related consequences. The results of our previous studies confirmed that age-related alterations of the regulatory processes of energy balance in male Wistar rats play a basic role in the background of these age-related changes. In humans there are well-known differences in body composition between sexes. Furthermore sarcopenia appears to develop differently in men and women. **Aim:** We intend to compare the changes of efficacy of centrally administered alpha-melanocyte-stimulating hormone (alpha-MSH) on energy metabolism in female and male rats of different age groups. **Methods:** First the neuropeptide sensitivities were compared on each day of the estrus cycle in 3-months old female Wistar rats. The food intake was measured in an Feedscale system. The stage of the estrus cycle was determined by staining of vaginal smear with May-Grünwald Giemsa stain. After that age-dependence of neuropeptide sensitivities were measured in different age groups (2-, 3-, 6-, 12-, 18-, 24-month-old). The anorexigenic effect of alpha-MSH injection was measured upon re-feeding after 48-h food deprivation. **Results:** The spontaneous nighttime food intake of female animals depends on the stages of estrus cycle. Alpha-MSH significantly alter the food intake on various days of the estrus cycle, but we did not find significant estrus cycle-dependent differences to neuropeptide in 3 months old female rats. Age-dependent changes of alpha-MSH sensitivity were similar in female and male rats. **Conclusions:** Our data suggest that age-related changes in the efficacy of alpha-MSH is similar in female and male rats, therefore the role of the sex hormones seems to be more important in the background of age- and sex-related changes in body weight and body composition. (34039/KA-OTKA/13-25)

J/5. AUTOPHAGY AND MTOR PATHWAY IN THE HEART OF HYPERCHOLESTEROLEMIC RATS

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Department of Pharmacology and Pharmacotherapy

Keywords: autophagy, mTOR pathway, hypercholesterolemia, heart, Western-blot

INTRODUCTION: In hypercholesterolemic state the cellular metabolism crashes over. The autophagy plays an important role in maintenance of cellular homeostasis: its function is the degradation of damaged and aged organelles, hereby to maintain physiological cellular metabolism and energy balance. It is proved, that autophagy plays important role in stress adaptation, such as ischemic preconditioning. It is also known, that hypercholesterolemia disturbs the physiology of these mechanisms, but the state of autophagy in hypercholesterolemia and its exact role in such altered conditions is still unclear. **OBJECTIVES:** To test whether autophagy is diminished in hearts of hypercholesterolemic rats. Furthermore, to assess status of the mTOR pathway in hearts of hypercholesterolemic rats. **METHODS:** Male Wistar rats (250-300 g) were fed either normal chow or chow enriched with 2% cholesterol and 0.25% cholic acid for 12 weeks. At 12 weeks animals were anesthetized and heparinized through femoral vein (1000 U/kg). Hearts were excised and perfused with Krebs-Henseleit solution for 5 min. Hearts were freeze-clamped, pulverized and homogenized in a sucrose-based buffer for a latter determination of autophagy and mTOR-related proteins. Statistical analysis of results was done by Student t-test. **RESULTS:** Hypercholesterolemic rats exhibited a 41% increase in plasma total cholesterol level over that of rats fed standard chow (2.89 mmol/L vs. 4.09 mmol/L). Hypercholesterolemia resulted in a

significant decrease in the expression LC3-II and Beclin-1 compared to control ($p<0,05$). In accordance with mTOR activation, the phosphorylation of S6 protein showed a significant increase in hypercholesterolemic group compared to controls ($p=0,021$). **CONCLUSION:** Our results showed that hypercholesterolemia suppresses basal cardiac autophagy. The decrease in autophagy may be a result of an upregulated mTOR pathway. However, the link between hypercholesterolemia and the induction of mTOR pathway is yet to be identified. The decrease in autophagy may be responsible for the loss of cardioprotection in hypercholesterolemia.

J/6. EFFECTS OF EARLY ENVIRONMENTAL ENRICHMENT ON GnRH AND ESTROGEN CONCENTRATION IN SERUM AND HYPOTHALAMUS IN RATS

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Keywords: enriched environment, rats, GnRH, estrogen, ELISA test

Effects of environmental enrichment on the central nervous system are researched for decades. Our team has also published several studies in this field. Earlier studies also proved that the enriched environment is able to improve the memory, increases the plasticity, and it can reduce the negative effects of certain toxic and ischemic injuries. The aim of our present study was to investigate the possible effects of enriched environment on the reproductive endocrine system, including the changes occurring in levels of GnRH and estrogen. Two groups of rats were examined. The control group was kept in a normal laboratory cage during their whole life; the other group was kept in enriched environment from the birth until the

age of 5 weeks. The sampling was performed at the age of nine months. In case of females, cycle diagnostic process was carried out, and the sampling was timed on the day of proestrus. In this way the difference of the hormone levels caused by physiologic reasons could be avoided. Peripheral blood was obtained by cardiocentesis, serum was obtained after clotting, and the hypothalamus of the rats was removed and homogenized. GnRH level of the serum and hypothalamus homogenates was detected by ELISA test in both gender, and the estrogen level was also measured in the serum of the female rats. We found that the serum GnRH level decreased in environmental enrichment in males and females, too. However there was no difference in the hypothalamic GnRH concentrations between the two groups. The serum estrogen level, like the serum GnRH, decreased in enriched environment.

J/7. THE ROLE OF GENETICAL POLYMORPHISMS IN THE DEVELOPMENT OF TOURETTE SYNDROME

Alexandra Riczu

Department of Medical Chemistry, Molecular Biology and Pathobiochemistry

Keywords: Tourette Syndrome, TSGeneSee, TNF-alpha, tic, autoimmune reaction

Introduction: Tourette syndrome (TS) is a neuropsychiatric disorder presenting in childhood characterized by motor and vocal tics. The etiology of TS is unclear, but environmental and complex genetic factors are believed to contribute. The role of inflammation due to Streptococcal infections, as well as autoimmune factors have also been hypothesized in the pathomechanism of the disorder. Methods: Samples from five European countries including $n=298$ TS patients, as well as $n=534$ healthy controls were involved in the present study. DNA

samples were subject to conventional Polymerase Chain Reaction (PCR) followed by agarose gel electrophoresis for genotyping 120 bp duplication, and 48 bp variable number of tandem repeat (VNTR) polymorphism in exon 3 of the dopamine D4 receptor (DRD4) gene, as well as the dopamine active transporter (DAT) intron 8 VNTR, and 40 bp VNTR in monoamine oxidase A (MAO-A). The TNF- α gene promoter -308 polymorphism (rs1800629) was detected by real-time PCR using TaqMan probes. Results: Significant association was found between the G-allele of the TNF- α gene promoter -308 polymorphism and Tourette Syndrome ($p=0.001$). Conclusions: TNF- α is not only produced by leukocytes, but in the CNS also by microglia and its expression is regulated by different promoter polymorphisms including -308 as well. Our findings indicate that this genetic variant of TNF- α may play a role in the development of Tourette syndrome. The effect of this polymorphism may manifest through post-streptococcal inflammation and the modification of autoimmune reactions.

K. POSTER SESSION II. - CLINICAL SCIENCES

Diagnostics: Radiology- Prevention - Pathology-Oncology

K/1. SOFTWARE IN THE WORLD OF RADIOLOGICAL REPORTING

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Keywords: artificial intelligence systems, structured reporting, pre-reporting, RSNA, templates

In radiology training it's a very important moment that specialists learn how to read the acquired images and produce proper medical reports. The resulting readings are of major help in diagnosing pathological cases. My goal is to introduce and develop such software that may help in the process of medical reporting, pre-reporting or may solve the problem of double reporting. To solve this problem, there are few possibilities to choose from, depending on which area we want to search and how we want to ease our work. I would like to approach the solution from two directions of software systems. The AI - artificial intelligence systems are knowledge based expert systems of which task is to suggest solutions for the problems occurring in a certain area. The AI systems would help in setting a diagnosis, and a well-designed software interface can only raise the level of quality of work. The other possibility is the structured reporting. This reporting system helps to extract important information faster. The RSNA radiology reporting initiative is improving reporting practices by creating a library of clear and consistent report templates. (<http://www.radreport.org>). These templates make it possible to integrate all of the evidence collected during the imaging procedure. In practice, the question- answer programming can be solved in all software languages. What appears to be the best available is a web based interface, in which the set of questions allowed are for example: Java/HTML application .Our study can introduce this reports with plus function: in the end you can get synoptical report. It was written in Java, focused RSNA templates. The system is still in development taking „baby steps” on the road of improvement but we should strive to have this system expanded to be available to make structured reporting of the whole body.

K/2. CALCULATION OF TORTUOSITY METRICS IN CORONARIES AMONG TWINS USING CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY: FIRST EXPERIENCE

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Keywords: Tortuosity, Coronary, CT, Angiography, Twins

Introduction: Increased arterial tortuosity is a result of ageing, hypertension and numerous connective tissue diseases. Increased arterial tortuosity may provoke atherogenesis due to its influence on local hemodynamic conditions. Therefore, we aimed to assess the feasibility of measuring different tortuosity parameters using coronary computed tomography angiography (CCTA). **Methods:** Four twin subjects, two monozygotic (MZ) twin pairs were selected, one with tortuous (T), and one pair with non-tortuous (NT) coronary arteries. The images were acquired using a 256-slice CT (Brilliance iCT, Philips Healthcare, Best, The Netherlands). The left anterior descending artery (LAD) and the right coronary artery (RCA) were segmented and the inner-lumen mesh was extracted using a dedicated software (QAngioCT, Medis BV, Leiden, The Netherlands). Vessel curvature, torsion and tortuosity-indices were calculated using an in house developed software. **Results:** Curvature parameters of the RCA showed similar values for both twin pairs (T: 0.12 and 0.17, NT: 0.15 and 0.16 [mm⁻¹], respectively). Torsion values showed slightly greater differences (T: 0.19 and 0.00, NT: 0.02 and -0.10 [mm⁻¹]). A greater difference was observed between the tortuosity-indices of the twin pairs (T: 2.01 and 1.92, NT: 0.99 and 0.95, respectively). The values showed

similar tendencies for the LAD. **Conclusions:** In this pilot study we show that the calculation of tortuosity metrics seems feasible using CCTA images, and that tortuosity-index might be a promising indicator of the degree of coronary artery tortuosity. Further studies are needed to evaluate the possible genetic effects on the tortuosity characteristics of the coronary tree. We intend to evaluate coronary anatomy in larger twin cohort with the application of more in-depth biometrical twin statistics.

K/3. ANALYSIS OF METABOLIC DIFFERENCES IN BRAIN BETWEEN GENDERS OF WILD-TYPE RATS WITH NANOSCANPET/MRI

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Keywords: PET/MRI, 18F-FDG, rat brain metabolism, pharmacokinetic brain map, in vivo imaging

Introduction: 18F-FDG (18F-fluorodeoxyglucose) is a commonly used PET radiotracer characterizing the metabolic changes of the examined organ. It is used both in preclinical and clinical diagnosis. Despite of this fact, we have found little information about the pharmacokinetics of FDG in rat brain. This is one of the reasons why we have decided to investigate the metabolic changes in different regions of the rat brain and also the metabolic differences between genders using the above mentioned biomarker. **Methods:** The tests were performed on n=12 Wistar rats (n=7 female, n=5 male) with nanoScanPET/MRI imaging procedure after the intravenous injection of the FDG (12,07 MBq/rat). The dynamic scan lasted for 60 minutes. Using data from the PET images we were able to describe the

dispersion of the radiotracer in brain tissue, while the concentration of the FDG in blood was examined by multiple arterial blood draws. 9 regions of interests (ROIs) were distinguished as following: cortex, striatum, cerebellum, hippocampus, amygdala, thalamus, hypothalamus, pons and medulla oblongata. The two hemispheres of these regions were analysed separately (except medulla oblongata and pons). Results: Data from PET images were analyzed with 2 compartment pharmacokinetic model, Gjedde-Patlak-, Logan- and RE-plot. This way we managed to build up a wild-type rat brain map and to demonstrate a significant difference in some of the brain regions between genders, but no significant differences were observed between the two hemispheres of the same animals. Conclusion: Our pharmacokinetic map might be used in further preclinical studies that aim to examine the metabolism of the rat brain. Furthermore, our results could contribute to the development of earlier diagnostic methods for different neurological diseases, such as Alzheimer's Disease, Parkinson's Disease or even epilepsy.

K/4. ESTIMATION METHOD FOR THE DETERMINATION OF IMAGE NOISE USING CLINICAL PET DATA

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Keywords: PET-investigation, signal-to-noise ratio, simple measurement, subreconstructions, physical heterogeneity

Introduction: During a PET investigation different parts of the body have various activity distribution and gamma radiation attenuation factors, the signal-to-noise ratio (SNR) of the images will be also different among bed positions. At the reading process of the images the constant SNR would be

preferable, therefore a method would be needed to determine the SNR values for each slice. The most straightforward way for this is repeated scans of the same subject that has mainly limited to phantom scans and cannot be performed at the human clinical case. Methods: We propose a method that uses a special algorithm to assign an SNR value to each voxels of the reconstructed image. These values were calculated from the list-mode files of the 90second PET scans, while performing subreconstructions of identical 7x12 seconds, 6x15 seconds, 5x18 seconds, 4x22 seconds, 3x30 seconds and 3x60 seconds per bed position image sets. Standard deviation (St.Dev.) and mean values for each image voxel were determined for each of these image sets. with a linear regression method. On the other hand, SNR for a 60 seconds/bed position scan was also determined in the conventional way: calculating St.Dev./Mean from the 3 separate 60 seconds.bed position scans. Results: The SNR values gained using the estimation and the conventional method showed a high correlation. We can conclude that the new estimation method can be used for the determination of image SNR in case of PET scans with at least 60 seconds/bed position or more. Although, this time limit could vary for the different scanners using special data collection and reconstruction algorithms. Conclusion: With our method, the noise of individual PET-studies is simply measurable, and the link between the physical heterogeneity and the signal noise ratio in the collected images of each region can be demonstrated.

K/5. ANTIOXIDANT PHENOLICS OF LINGONBERRY AND BILBERRY

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Keywords: berry, antioxidant, polyphenol, ascorbic acid, free radicals

Introduction: Free radicals are released in basic metabolic processes and they support the immune system and participate in metabolism, however, excessive amount of them can be harmful. The abnormally increased free radicals can be eliminated by the antioxidant system where phenoloids and vitamins have crucial a role, directly through scavenger effects and indirectly through affecting signal transduction pathways. Nowadays consumption of polyphenols is gaining attention, because of their beneficial effects and positive influence on the cardiovascular and immune system. Berries, with most of the species adapted to colder and arid climate, are antioxidant-rich foods. As a result of their notable content on bioactive components, they can help to protect the human organism from oxidative stress, while their protective feature against diabetic complications, cardiovascular diseases and cancer are widely studied. Our aim was to compare the vitamin C and antioxidant, especially flavonoid content of two well-known berries: bilberry (*Vaccinium myrtillus* L.) and lingonberry (*Vaccinium vitis-idaea* L.). **Methods:** Reducing power of the samples was determined according to the method of Oyaizu, and expressed in ascorbic acid unit. The vitamin C and the total polyphenol contents of berries were measured according to the VII. and VIII. Hungarian Pharmacopoeia. The total polyphenol contents were expressed in gallic acid units. Polyphenol composition of the samples was evaluated by LC-MS/MS.

Results: Polyphenol and ascorbic acid content of bilberry was higher compared to lingonberries. While remarkable differences regarding phenolic composition of the two species were observed. **Conclusion:** The experiments confirmed that bilberries and lingonberries contain high amounts of antioxidants: polyphenols and ascorbic acid, however, flavonoid composition showed remarkable differences and may result in different therapeutic effects. Consumption of berries are recommended, especially because of their antitumor, anti-inflammatory and beneficial effects on the cardiovascular system, but in vivo studies are needed to confirm their whole palette of protective properties.

K/6. POSSIBLE ANTI-TUMORIGENIC USAGE OF ANGIOSTATIN IN ONCOTHERAPY

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Keywords: Angiostatin, angiogenesis, chimera protein, recombinant plasmid, anti-cancer activity

Introduction: Angiostatin, a cleavage product of N-terminal kringle domains of plasminogen, is an endogenous angiogenesis

inhibitor which decreases tumorous growth. However, the instability makes it hard to use in therapy. Our goal was to design a molecule which produces angiostatin *in situ* and *in vivo*. The construction, an angiostatin-protease chimera cleaves angiostatin in the extracellular space after its activation. Methods: PCR amplified protease and angiostatin cDNA were ligated into an adequate vector in the same reading frame. The vector was used to transfect *E. coli*, mice and human cells to achieve angiostatin production. Aortic ring assay served for monitoring endothelial proliferation of VEGF-induced aortic rings in the presence of transfected cells. BALB/c mice were injected separately with transfected and wild type 4T1 and C26 cancer cells to quantify tumor growth. Results: The chimera was purified from *E. coli*. Its autocatalysis was observed using SDS-PAGE: we got the full size chimera if protease inhibitor mix was used during isolation, otherwise we only detected the cleaved fragments. Endothelial proliferation in hanging drop cultures stopped when transfected cells were propagated at the bottom. The aortic ring assay was negative on transfected cells. *In vivo* tumor progression was tested using 20 independent clones. Progression started after 10 days in mice injected with transfected 4T1 cells, whereas animals treated with transfected C26 cells started growing cancerous tissue 21 days after infection as opposed to control animals. We already had tumor-associated death in the control group while this was absent in the other one. Later, tumor growth was also detected in mice injected with transfected cells but at slower rates. Metastases occurring in these mice showed smaller diameters. Conclusion: Our construction is able to cleave active angiostatin. The anti-tumorigenic effect of the molecule was demonstrated in experiments. Patent application for the chimera is in process.

K/7. THE ROLE OF SOCIAL MEDIA IN MEDICINE AND HEALTHCARE

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Keywords: social media, medical education, medicine, healthcare, web 2.0

Introduction: Social media has made it possible for patients to share information about their diseases, to get in touch with patients having similar disorders: they are the so called e-patients. Medical professionals do not know how to deal with the growing mass of e-patients. In order to make the role of internet in medicine known, I launched a course for medical students in the September of 2013. I demonstrated the current and prospective connection between social media and healthcare through five topics: medical education and collaboration, being up-to-date, online practice, e-patients and the future of medicine. Methods: I presented how foreign medical schools use the new possibilities given by web 2.0 in the education of medicine. I presented the simplest ways of gathering medical/health information. I demonstrated the main points of view of a professional online medical service. I showed how a patient-doctor relationship will look like in the future. I talked about the technological improvements that will appear in future hospitals and will be used by future doctors. Results: In spite of the fact that people are spending more and more time being online, the number of medical professionals who know how to be professionally updated is still low, whereas e-patients show greater and greater interest in their own health management. Conclusion: Digital literacy should be integrated in the medical curriculum. Social media and web 2.0 – used with proper strategy – can be great aids in medical education and in the health care system as well.

MULTIDISCIPLINARY SESSION VII.

L. Surgery

L/1. THE COST-EFFECTIVENESS ANALYSIS OF HEART TRANSPLANTATION AND LEFT VENTRICLE ASSIST DEVICE THERAPY

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Keywords: cost-effectiveness analysis, heart transplantation, left ventricle assist device, incremental cost effectiveness ratio, Heartmate II

Introduction A single center pilot study was conducted from 2011 December to 2013 March to evaluate a cost- effectiveness analysis of the enhanced second -generation LVAD Heartmate II and heart transplantatation. The aim of the study was to assess the economic applicability of the assist device therapy and heart transplantation. **Methods** We created two homologous patient populations from heart transplanted and LVAD implanted patients to compare our cohorts. In the first group two LVAD- patients were enrolled (n=2), in the second group patients were assigned who received allograft (n=15) without any contraindication of LVAD implantation. In both patient cohorts the perioperative material utilization and the postoperative and chronic sustentative drug

costs were estimated. Resource use data were also gathered for all adverse events. In the transplantation group the expenditures in relation to the the donor organ transportation were considered cost elements (ambulance, helicopter, Eurotransplant- airtransport). The transportation values were weighted in weekend/ weekday relation, with regard to the distances. Two decision tree models were established and incremental cost-effectiveness ratio was estimated based on the collected expenditures and the calculated health gain data. **Results** Values were analyzed on a cost-effectiveness plan. Based on our results LVAD destination therapy is not cost effective in comparison to heart transplantation in out patient groups. In case two basic agents: drastic improvement of the survival and 50% reduction of Heartmate II price occurs, the cost-effectivity threshold may be approached. **Conclusions** We have to emphasize the limitations of our study, and the fact that the incremetal cost effectivity ratio alone is not appropriate to decide about the introduction of a health technology. If the trend of falling device cost continues, increased survival benefits and fewer adverse events will impact positively on the cost-effectivity profile.

L/2. ISCHEMIC POSTCONDITIONING AS AN ALTERNATIVE AGAINST LIVER ISCHEMIC-REPERFUSION INJURY

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Keywords: ischemic postconditioning, ischemic-reperfusion injury, liver, rat model, long-term ischaemia

Introduction: Ischemic postconditioning is a useful method to decrease tissue damage in cases of ischemic-reperfusion injury. However, the suitability of this procedure following long-term ischemic periods still needs to be evaluated. Thus the purpose of this study was to examine and compare the protective effect of postconditioning applied after short- and long-term liver ischemia on a rat model. **Material and Methods:** 25 Wistar male rats were randomized in five groups (A-E). Group-A: sham operated animals; Group-B: 45 minutes of ischaemia followed by 6 hours reperfusion; Group-C: after 45 minutes ischemia, postconditioning was applied with 6 alternating cycles of 10-10 seconds reperfusion-reocclusion followed by 6 hours reperfusion; Group-D: 90 minutes ischemia followed by 6 hours reperfusion; Group-E: postconditioning was performed after 90 minutes ischemia accompanied by 6 hours of reperfusion. Hepatic microcirculation was monitored by laser Doppler flowmeter. Biliary epithelial cell damage was assessed by the constant measure of bile glucose and GGT concentrations. Histological alterations of the liver, lung and serum necroenzyme levels were also examined. **Results:** Ischemic postconditioning significantly decreased functional and morphological injuries after 45 minutes of ischemia. Group-C had significantly ($p<0.05$) higher flow rates during reperfusion (plateau maximum: 63% vs. 92%; reperfusion area: 57.4% vs. 99%) and significantly lower serum ALT levels (870 ± 56 vs. 484 ± 48 U/l). Bile glucose and GGT levels also decreased significantly ($p<0.05$) in Group-C. This protective effect was not detected in the long-term ischemic group except for the histological sections where postconditioning reduced the injury

level (7.4 ± 2.12 vs. 9.4 ± 1.6). No significant difference was found between the results of Group-D and -E regarding the microcirculation of the liver or the bile glucose and GGT concentrations. **Conclusion:** The use of postconditioning greatly decreased the hepatic injury in case of short-term ischemia. However, this technique was not able to prevent major damage after long-term ischemia.

L/3. EFFECT OF POSTCONDITIONING ON MICROCIRCULAR CHANGES OF THE SMALL INTESTINE AFTER LOWER LIMB ISCHAEMIA INDUCED BY INFRARENAL AORTIC OCCLUSION

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Keywords: Postconditioning, ischaemia, reperfusion, small intestine, infrarenal aortic occlusion,

Background: Major vascular surgeries on large vessels involving the circulation of the lower limb may result in ischaemic-reperfusion injury with severe systemic complications. The injury of the small intestine is an important component of the postoperative complications. The aim of the present study is to prove that postconditioning is able to reduce gastrointestinal complications by improving macro- and microhaemodynamic parameters. **Methods:** Male Wistar rats ($n=72$) underwent 3 hours of infrarenal aortic occlusion followed by 4 hours of reperfusion. In one group of the animals postconditioning was applied. During the experiment blood

pressure, superior mesenteric artery flow (MSA) and mucosal microcirculation of duodenum, jejunum and ileum were assessed. At the end of the experiment, samples were taken from each intestinal segment for histological examinations. Results: Superior mesenteric artery flow, as well as microcirculation of the duodenum, jejunum and ileum showed significant impairment in the IR group compared to the sham operated group, (MSA flow: $3,41 \pm 1,61$ vs. $9,22 \pm 2,04$ ml/min, $p=0,012$; LDF duodenum: $90,42 \pm 4,73$ vs. $99,83 \pm 2,55$, $p=0,012$; jejunum: $73,40 \pm 5,06$ vs. $98,05 \pm 6,18$, $p=0,008$; ileum: $40,56 \pm 4,19$ vs. $96,01 \pm 5,87$, $p=0,002$), while histological damage was significantly elevated. Strong negative correlation was found between microcirculatory values and histological damage. ($r=-0,911$, $r^2=0,847$, $p<0,001$). Postconditioning was able to limit flow reduction in all three small bowel segments and in the superior mesenteric artery (MSA flow: $9,0 \pm 2,14$, $p=0,009$; LDF : duodenum: $102,03 \pm 4,02$, $p=0,009$; jejunum: $87,36 \pm 3,13$, $p<0,001$; ileum: $82,58 \pm 6,26$, $p<0,001$), and was able to significantly reduce histological damage. Conclusion: After infrarenal aortic occlusion, the extent of small bowel damage showed close correlation with microcirculatory impairment. Postconditioning was able to reduce this remote intestinal damage, possibly through limiting flow deterioration.

L/4. THE PRECONDITIONING EFFECT OF LEVOSIMENDAN AGAINST ISCHEMIA-REPERFUSION INJURY OF THE LIVER

Andras Mihaly Geczi, Andras Fülöp, Peter Onody, Gabor Lotz, Laszlo Harsanyi, Attila Szijarto

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Keywords: Liver, ischemia, reperfusion, precondition, hepatectomy

The Preconditioning Effect of Levosimendan Against Ischemia-Reperfusion Injury of the Liver András Mihály Géczi, András Fülöp, Péter Ónody, Gábor Lotz, László Harsányi, Attila Szijártó During hepatectomy the occlusion of the hepatoduodenal ligament leads to an unpleasant state of the liver, and it suffers ischemic-reperfusion injury. The calcium sensitizer levosimendan, which is often used to support congestive heart failure, proved to be suitable to induce preconditioning-like adaptive mechanisms. The aim of our research was to examine and characterise of the efficiency of the protective function of levosimendan in a hepatic IR rat model. In two subgroups – earlier or later subgroup –, male Wistar rats underwent levosimendan pre-treatment before a 60-minute-long segmental liver ischemia. The microcirculation of the liver was monitored by laser Doppler flow meter. Liver and blood samples, after 24 hours of reperfusion were taken for histology, immuno- and enzyme-histochemistry (TUNEL; PARP; NADH-TR) and laboratory tests. Beside liver antioxidant state and HSP72 expression were measured. In both of the levosimendan pre-treatment groups significant improvement ($p<0.05$) of hepatic microcirculation was observed compared to the analogous IR groups. The measured histological damage was also reduced. The observation was also supported by the significantly lower level of serum AST (Pearly= 0.02; Plate=0.004), ALT (Pearly=0.02; Plate=0.005) and by the moderate DNA damage indicating TUNEL (Pearly=0.05; Plate = 0.034) and PAR positivity (Pearly = 0.02; Plate=0.04). Levosimendan caused a significant improvement of liver redox homeostasis. Apart from this, even the mitochondrial function was significantly better by the animals pre-treated later.

($p=0.003$) The liver defender effect of levosimendan proved to be true; which hopefully can be used before extensive liver resections in the practice in the near future

L/5. MORPHOLOGICAL AND FUNCTIONAL CHANGES IN SPVL INDUCED LIVER REGENERATION

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Keywords: portal vein ligation, liver regeneration, morphology, liver function, animal model

The selective portal vein ligation (sPVL) is a clinically available and commonly used method to induce selective hypertrophy of the nonligated liver lobes. Nevertheless, the knowledge concerning the definite course of events and changes in liver function is still insufficient. Purpose of the current study is to acquire better cognition of the effects of sPVL on liver tissue hypertrophy and on liver function. Male Wistar rats ($n=84$) were subjected to 80% sPVL, resulting in exclusion of lobes III-VII from portal flow. Changes in liver morphology were assessed by the regeneration rate, lobule territory, mitotic and apoptotic activity (Ki-67 and caspase-3 immunohistochemical staining). To evaluate liver function indocyanine green (ICG) clearance tests were used, measuring the plasma disappearance rate (PDR) and retention rate at 15 minutes (R15). The hourly bile production was determined via bile duct cannulation of each liver lobe selectively. The samples were taken before sPVL (0. hour) and at the 12., 24., 48., 72., 120., 168. hours after the operation. SPVL caused atrophy of the lobes excluded from portal flow characterized by necrotic and apoptotic tissue reactions. The hypertrophy of

the hyper-perfused lobes was accompanied by increased mitotic activity of hepatocytes ($20,6\pm3,6$ versus $142,3\pm18,9$), which lead to a significant accretion of lobule territory ($300502,4\pm15402,4$ μm^2 versus $714514,3\pm30490,9$ μm^2). According to ICG clearance test and measurement of bile production the functional capacity of the liver is transitionally impaired, but recuperates by the 168. hour after sPVL. The results indicate, that the regenerating lobes show a likewise significant increase in lobe volume and function as well.

L/6. COMPARISON OF ENDOVASCULAR AND OPEN SURGICAL REPAIR FOR ABDOMINAL AORTIC ANEURYSM – EARLY RESULTS OF THE ENDOVASCULAR ANEURYSM REPAIR – THE LEARNING CURVE AT THE DEPARTMENT OF SURGERY UNIVERSITY OF SZEGED

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Keywords: abdominal aortic aneurism, Endovascular Aneurysm Repair, EVAR, ruptured aneurysm, open surgical repair

Background Endovascular aneurysm repair (EVAR) is an important advance in the treatment of abdominal aortic aneurism (AAA). Both open and endovascular techniques can be successfully employed in the treatment of AAA. The goal of this study is to compare the short and middle term outcomes of the two techniques and also to analyze the cost effectiveness of them. Methods At the University of Szeged Surgery Department endovascular technique was introduced in the year of 2012. A retrospective analysis was conducted of 58 patients repaired with AAA between January

of 2012 and June 2013. Type of repair was chose depending of the patient's health status, fitness, medical co morbidities and the morphology of the aneurysm. Results Despite the technical disturbances (lack of storage of appropriate graft) patients with high risk were more often selected for EVAR (21 versus 31). Even so EVAR was associated with significantly shorter procedure times (2.4 versus 3.1 hours), shorter intensive care unit stay (0, 04 versus 3, 06 days), shorter hospital length (9 versus 11, 5 days), and lower transfusion requirements (0,1 versus 1,9 units). The 30-day operative mortality was 0 percent in the endovascular group and 9,67 percent (three patients) in the total (elective and ruptured) open-repair group. Conclusion Increased interest can be seen in evaluating the effectiveness of treatment options for patients with AAA. The early results of the endovascular aneurysm repair have been encouraging, with reduced 30-day operative mortality compared with open repair. According to the guidelines from European and American surgical societies, an individualized approach is needed when choosing the type of AAA repair. It's difficult to assess the financial implications of the procedures in Hungary, because the human resources are taken less into consideration, so we can rely on the hospital and intensive care unit stay of the patients.

L/7. ROLE OF PRECONDITIONING TO AVOID NOXIOUS OXIDATIVE STRESS INDUCED BY PNEUMOPERITONEUM

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Keywords: Preconditioning, pneumoperitoneum, ischemia-reperfusion, oxidative stress, laparoscopy

Introduction: Pneumoperitoneum, widely used in laparoscopic surgery, increases the intraabdominal pressure. This leads to hypoperfusion of the abdominal organs, and promotes the buildup of reactive oxygen species and inflammatory cytokines, which in turn impair the body postoperatively and slow down the recovery. The aim of our investigation was to evaluate the potential protective effects of short ischemic episodes at low pressure on ischemic damages. **Methods:** The experiments were conducted on 50 Wistar rats. Pneumoperitoneum was created with Veres needle, inserted transumbilically into the abdominal cavity. Rats were divided into 5 groups (n=10/group, each): Group I. sham, Group II. pneumoperitoneum at 5 mmHg, Group III. preconditioning (insufflation and desufflation for 5 minutes), then pneumoperitoneum at 5 mmHg, Group IV. pneumoperitoneum at 10 mmHg; Group V. preconditioning, then pneumoperitoneum at 10 mmHg. Blood samples were taken 2 hours after the procedure. Oxidative stress parameters: malondialdehyde (MDA), reduced glutathione (GSH), sulfhydryl group (-SH) concentrations, superoxide-dismutase enzyme (SOD) activity and inflammatory cytokines: TNF- α and IL-6 levels were measured. **Results:** MDA concentrations were significantly increased and GSH concentrations were significantly decreased in all groups compared to the sham group. In -SH levels there were no differences between groups. SOD: 10 mmHg pressure elicited significantly greater damage than 5 mmHg. SOD activity was significantly increased in 10 mmHg preconditioned group compared to 10 mmHg pneumoperitoneum group. TNF- α and IL-6: the concentrations were significantly higher in each group compared to the control group. In the 10 mmHg preconditioned group the concentrations were

significantly decreased compared to the 10 mmHg pneumoperitoneum group. Conclusion: Based on our results the elevated intraabdominal pressure due to pneumoperitoneum induces oxidative stress, which is dependent on the applied pressure. Preconditioning even at low pressure reduces surgical stress following laparoscopic procedures, but to explore its mechanism requires further investigations.

L/8. MONITORING OF HLA ANTIBODIES AFTER KIDNEY TRANSPLANTATION

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Keywords: kidney transplantation, antibody monitoring, HLA antibodies, Single antigen bead, graft outcome,

Introduction The introduction of the solid phase immunoassay (SPI) technology radically changed the practice of HLA antibody monitoring in organ transplantation. Identification of antibody specificities in complex sera of sensitized patients and monitoring of low levels of donor-specific HLA antibodies in the posttransplant phase became possible. **Methods** We investigated 64 patients with failed kidney transplants for a possible association of the posttransplant presence, de novo development, or persistence of pre-existing donor-specific antibodies (DSA) with graft failure. Patients with successful grafts served as controls. Single Antigen Bead (SAB) assay-detected DSA and non-DSA antibodies were compared between patients with graft loss and matched controls with functioning grafts. We used the C1q linked SAB test for the detection of complement fixing antibodies. **Results** Patients with graft loss had a higher incidence of SAB-detected posttransplant antibodies at cut-off MFI (mean fluorescent

intensity) $\square$ 5,000 in their prefailure serum (total antibodies: 59% vs. 36%; $P=0.013$). However, if de novo antibodies were analyzed, even the incidence of weak DSA or non-DSA at MFI $\square$ 500 was higher in the graft loss group than in the non-rejector group (88% vs. 55%, $P=0.003$). Interestingly, when C1q binding ability in sera of rejectors and non-rejectors with DSA was compared, none of the non-rejectors demonstrated C1q positivity whereas 43% of rejectors showed C1q positive antibodies, although not necessarily donor-specific ($P=0.005$). **Conclusions** Our data show that the posttransplant presence of HLA antibodies, especially if C1q-binding and/or de novo, is associated with graft loss, even if the antibodies are not specific for mismatched donor HLA. Our findings suggest that when DSA are detected in the absence of C1q positivity, additional parameters should be taken into consideration before initiating rejection therapy. We also provide a summary of the recommendations formulated by The Transplantation Society (TTS) as an international effort on antibody monitoring in organ transplantation.

L/9. RESUSCITATION AND EMERGENCY CARE IN 2014 - LET'S DO SOME CPR!

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Semmelweis University, Department of Anaesthesia and Intensive Care, Division of Emergency Medicine and Oxyology

Keywords: cardiac arrest, no flow state, cardiopulmonary resuscitation, chest compression, secure airways

This presentation focuses on the guidelines of the 2010 guidelines of the European resuscitation Council still in force, emphasizing the importance of early recognition, early CPR and early post-resuscitative actions in cardiac and

respiratory arrest. It will also cover the latest controversies regarding the airway management and administration of drugs during CPR. The practical session will offer hands on experience in basic CPR by means of simulation real life situations.

MULTIDISCIPLINARY SESSION VIII.

M. Cardiology-Internal medicine-Family medicine

M/1. EFFECTS OF ACENOCOUMAROL ON ARTERIAL CALCIFICATION

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Keywords: anticoagulation, acenocoumarol, calcification, Agatston-score, atrial fibrillation

Acenocoumarol (Syncumar) is the most commonly used drug in Hungary for anticoagulation. The effect of Syncumar therapy on arterial calcification is not clear, increased arterial wall calcification was reported. Our aim was to determine, whether long-term Syncumar therapy has an influence on arterial calcification in cardiac patients. We compared the amount of calcium (Ca) in mitral and aortic valves, coronary arteries, and the thoracic aorta. Our cohorts consist of patients suffering from chronic atrial fibrillation (AF) treated or not treated with Syncumar. We also added a control group, these patients were neither suffering from AF, nor treated with Syncumar and were matched for age and gender. We used coronary CT examinations for calculating Agatston-score based on the amount of Ca in the arteries and valves. In the group with AF and Syncumar therapy (n=121) the average age was 60 (± 11) years, it was 58 (± 11) years in the group with AF

and without Syncumar therapy (n=73). The control group (n=97) had an average age of 59 (± 10) years. There was no significant difference between the groups in terms of average age and distribution of genders. Presence of diabetes mellitus, uremia, hyperlipidemia, hepatic diseases and smoking in the anamnesis did not show significant difference. We found higher Ca-scores in patients treated with Syncumar at all anatomical localizations. We noticed significant differences in Agatston-scores of the aortic valve ($p < 0.01$) and mitral valve ($p < 0.01$), while the differences in terms of thoracic aorta ($p = 0.68$) and coronary arteries ($p = 0.37$) were not significant. Our results show that long-term acenocoumarol treatment increases arterial calcification in many anatomical localizations. This fact has to be considered in case of anticoagulant treatment in patients with increased risk for atherosclerosis. To prove the exact significance of our results, it is necessary to examine larger cohorts with different causes of Syncumar treatment.

M/2. DEVELOPMENT AND COMPLETE MORPHOLOGICAL AND FUNCTIONAL REVERSIBILITY OF ATHLETE'S HEART IN A RAT MODEL

Dalma Kellermayer, Attila Oláh, Árpád Lux, Csaba Mátyás, Balázs Tamás Németh, Mihály Ruppert, Lilla Szabó, Marianna Török, Ede Birtalan, László Hidi, Anna Meltzer, Gergő Merkely, Béla Merkely, Tamás Radovits

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Keywords: athlete's heart, rat model, detraining, pressure-volume analysis, contractility

Introduction: Long-term exercise training is associated with characteristic structural and functional cardiac adaptation termed athlete's

heart. However the effect of discontinuation of the training (detraining) on left ventricular (LV) function is unclear. Our aim was to evaluate the development characteristics of athlete's heart and the reversibility of morphological and functional changes during detraining. Methods: Rats were divided into trained (n=15) and control (n=17) groups. Trained rats swam 200 min/day for 12 weeks. Detrained rats remained sedentary for 8 weeks after completion of the training protocol. We regularly performed echocardiographic measurements to investigate the development and regression of exercise-induced cardiac changes. LV pressure-volume analysis was performed to calculate cardiac functional parameters. LV samples were harvested for histological examination and myocardial gene expression analysis was performed using qRT-PCR. Results: Echocardiographic examinations showed rapidly developing LV hypertrophy in the trained group according to wall thickness values (LV mass index: 2.45 ± 0.09 vs. 2.07 ± 0.07 g/BW). This adaptation regressed after detraining (LV mass index: 1.94 ± 0.02 vs. 2.05 ± 0.05 g/BW), which was confirmed by post-mortem measured heart weight and histological morphometry. Unchanged myocardial expression of TGF- β and β -MHC and unaltered amount of LV collagen confirmed the physiologic nature of the observed cardiac hypertrophy. Hemodynamic measurements indicated decreased LV end-systolic volume (LVESV) (75 ± 5 vs. 100 ± 7 μ l) along with increased stroke volume (SV), improved systolic function and contractility (dP/dtmax-end-diastolic volume (dP/dtmax-EDV): 35.9 ± 2.6 vs. 25.8 ± 2.8 Hgmm/s/ μ l), ameliorated active relaxation and mechanoenergetics after long-term exercise training. After the detraining period regression of exercise-induced cardiac functional changes were observed: LVESV (117 ± 5 vs. 115 ± 6 μ l), SV, LV contractility

(dP/dtmax-EDV: 30.5 ± 1.7 vs. 28.4 ± 4.3 Hgmm/s/ μ l), active relaxation and mechanoenergetic enhancement reverted completely to control values. Training and detraining did not affect myocardial stiffness. Conclusions: Our results confirm that the morphological and functional adaptation of exercise-induced physiologic LV hypertrophy completely regressed after 8 weeks of detraining.

M/3. THE ROLE OF ECG PARAMETERS IN THE RESYNCHRONIZATION THERAPY OF HEART FAILURE PATIENTS

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Keywords: Heart failure, Cardiac resynchronization therapy (CRT), ECG analysis, Prediction of response, Mortality prediction

Introduction Cardiac resynchronization therapy (CRT) improves the mortality of heart failure, however, some patients do not respond adequately. We aimed to investigate the possibility to predict this response and the 2-year survival of patients by means of ECG analysis. **Methods** We examined the 12-lead ECG records of 136 heart failure patients (38 non-responders and 98 responders) retrospectively with a digital caliper before CRT and 1 and 6 months after implantation. We measured the QRS size and QT time in all leads one by one and then averaged them. We defined the clinical responsiveness as 15% improvement of the ejection fraction. For statistics we used ANOVA or t-test to compare means, Fischer's exact test for categorical variables, ROC analysis for cut-off values, log rank test and Cox regression for survival analysis. **Results** We found that responders had

wider QRS as compared to non-responders at baseline (164.8 [147.8-180.1] vs 151.7 [138.7-170.5] ms, $p=0.04$) and the 6 months reduction was higher in responders (51.9 [36.8-65.5] vs 35.4 [23.3-53.8] ms, $p=0.02$). Patients with longer QT as 404.9 ms 6 months after CRT implantation had lower survival rates after 2 years (log-rank $p=0.005$, HR=5.13 [1.65-17.29], AUC=0.73 [0.59-0.87], $p=0.009$, Sens.: 75% and Spec.: 64%). We verified the independent effect of 6 months QT time on mortality with adjusted multivariable Cox regression analysis (HR=1.99 [1.02-3.87], Wald=4.18, $p=0.04$). **Conclusions** In conclusion, basic ECG parameters were able to predict the mortality of heart failure patients with CRT as well as their response to the treatment.

M/4. HERITABILITY OF VOLUME OF EPICARDIAL ADIPOSE TISSUE IN A CLASSICAL TWIN STUDY

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Keywords: CT, obesity, cardiology, atherosclerosis, coronary

Introduction: Obesity is associated with an increased risk of coronary artery disease. It has been suggested that epicardial fat volume is also associated with coronary artery disease. Whether the epicardial adiposity depends on environmental influences or is determined by genetic factors is not clear. The aim of the study was to evaluate the

genetic influence on the size of epicardial adipose tissue within a sample of twin pairs. **Methods:** In this study, 68 adult twin pairs (37 monozygotic [MZ] pairs, with a mean age of 55.9 ± 9.7 years and 31 dizygotic [DZ], with a mean age of 58.2 ± 8.8 years) were evaluated. The twin pairs were investigated with a 256-slice CT-scanner (Brilliance iCT, Philips Healthcare, Best, The Netherlands). For each patient BMI, CT-based waist circumference (WC) and epicardial fat volume (EFV) were assessed. To quantify phenotypic similarity, intra-pair correlations were calculated. Then these correlations were broken down to additive genetic (A), common (C) and unique (E) environmental correlation components. Both correlation analyses and ACE decompositions were carried out by using maximum likelihood estimation-based methods. The mean EFV of the MZ and DZ pairs was 91.2 ± 41.8 and 91.1 ± 36.6 cm³, the mean BMI was 27.6 ± 4.8 and 27.1 ± 5.0 kg/m², while the mean WC was 95.9 ± 11.6 and 95.1 ± 11.3 cm. The additive genetic effects had a relatively high impact on the EFV (A=70%) and the BMI (A=74%), and a moderate impact on waist circumference (A=51%). **Conclusion:** In this classical twin study we were able to show that both EFV and BMI have a relatively strong heritability. The potential role of EFV in the pathomechanism of coronary artery disease needs further investigation. The study was supported by the New Horizons Programme from the EFSD.

M/5. THE ROLE OF BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) IN DIABETES ASSOCIATED NEPHROPATHY AND COMORBID DEPRESSION

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Keywords: Diabetes, depression,
comorbidity, brain-derived neurotrophic factor
(BDNF), RAAS inhibitors

Introduction: Comorbid depression is common in diabetes (DM) and chronic kidney disease (CKD) increasing the risk of mortality. The level of brain-derived neurotrophic factor decreases in depression and the same phenomenon is observed in DM and CKD. A BDNF-mediated pathway may play an important role in linking depression, DM and CKD, however this pathway has not yet been investigated in the kidney. Recent research suggests that telmisartan improves not only diabetic nephropathy, but also cognitive function suggesting the potential role of renin-angiotensin-aldosterone-system (RAAS) blockers in the treatment of depression. In our experiments we analyzed the effect of RAAS inhibitors on depression, on kidney damage and on the alteration of BDNF levels in diabetic rats. **Methods:** After 5 weeks of streptozotocin induced diabetes male Wistar rats (n=8/group) were treated p.o. with non-pressor doses of ramipril (RAM), losartan (LOS), spironolactone (SPI) and eplerenone (EPL). Untreated healthy rats served as controls. Blood pressure and renal parameters were

measured, moreover depressive behaviour and BDNF level of the kidney were evaluated. **Results:** Neither DM nor RAAS inhibitors influenced the blood pressure. Impairment of renal function and depressive behaviour were observed in DM, which was improved by RAAS-blockers. BDNF was detected in the rat kidney. The expression of precursor and mature forms were different in various organs. In the kidney mature BDNF increased, while the precursor form remained unchanged in DM. RAAS inhibitors reduced the amount of mature BDNF. **Conclusion:** These results suggest the potential role of a RAAS regulated BDNF pathway in the development of DM – CKD- comorbid depression opening new perspectives in the therapy of depression in DM.

M/6. GENETIC EFFECTS ON THE DISTRIBUTION OF ABDOMINAL ADIPOSE TISSUE COMPARTMENTS AND THE PRESENCE OF NON- ALCOHOLIC FATTY LIVER DISEASE: A TWIN STUDY

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Keywords: twin study, non alcoholic fatty
liver disease, abdominal adipose tissue
compartments, CT, heritability

In patients with diabetes and/or obesity, accumulation of abdominal adipose tissue and non-alcoholic fatty liver disease (NAFLD) are linked to increased cardiometabolic risk. Little is known about the genetic and environmental effects on the distribution of the abdominal adipose tissue compartments and those of NAFLD. The aim of the study was to assess the magnitude of genetic impact on the size of various abdominal adipose tissue compartments and the presence of NAFLD within a sample of twin pairs. In this classical twin study, 136 twin subjects (37 monozygotic [MZ] pairs with age of 55.9 ± 9.7 years and 31 dizygotic [DZ] pairs with age of 58.2 ± 8.8 years) were involved. The twin pairs were investigated with a 256-slice CT-scanner (Brilliance iCT, Philips Healthcare, Best, The Netherlands). For each patient CT-based waist circumference, abdominal subcutaneous (SAT) and visceral adipose tissue (VAT) quantification was performed. Liver and spleen attenuation was determined by calculating the average of three 300 mm² areas. NAFLD was characterized by attenuation ratios (CTL/S) and liver-to-spleen attenuation differences (CTL-S). To quantify phenotypic similarity, intra-pair correlations were calculated. Then these correlations were broken down to additive genetic (A), common (C) and unique (E) environmental correlation components. Both correlation analyses and ACE decompositions were carried out by using maximum likelihood estimation-based methods. The median SAT was 207.4 [IQR: 152.3-256.6] cm², whereas median VAT was 146.1 [IQR: 83.2-196.3] cm². Relatively high heritability was found in SAT (A=74%) and VAT (A=59%), while the derived parameters regarding NAFLD showed lower genetic dependency (A=30%). In this classical twin study we were able to show that the distribution of abdominal fat compartments has relatively

strong heritability, while the presence of NAFLD is less influenced by genetic effects. The study was supported by the New Horizons Programme from the EFSD.

M/7. HERITABILITY OF THE CORONARY ARTERY CALCIUM SCORE AND ITS RELATIONSHIP WITH CENTRAL BLOOD PRESSURE, ARTERIAL STIFFNESS AND CAROTID INTIMA-MEDIA THICKNESS

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Keywords: Coronary artery calcium score, Twin study, Heritability, Cardiovascular risk factors, Carotid intima-media thickness

Background and aim: Calcifications in the coronary arteries are an early sign of coronary heart disease. Our aim was to assess the heritable affects on the coronary artery calcium score and its relationship with other cardiovascular risk factors, such as central hemodynamics and carotid intima-media thickness. Methods and Materials: 76 Hungarian (37 monozygotic /MZ/ and 39 dizygotic /DZ/) healthy twin pairs (mean age 56 ± 9 years) recruited from the Hungarian Twin Registry underwent computed tomography (Brilliance iCT, Philips Healthcare, Best, The Netherlands) coronarography, oscillometry (Arteriograph) and B-mode ultrasonography of common and internal carotid arteries (ACC, ACI). Carotid intima-media thickness (IMT) was measured by QLAB software. Age and sex-adjusted partial correlations were calculated with SPSS software. Concordance between MZ and DZ pairs were assessed by Pearson

correlations. Rough heritability was calculated according to the Falconer's formula.

Results: No significant heritability of coronary calcium score was found. Age and sex adjusted partial correlations between calcium score and systolic blood pressure (SBPao), aortic pulse wave velocity (PWV), common carotid artery intima-media thickness (ACC IMT), internal carotid artery intima-media thickness (ACI IMT) indicated 0.097, 0.020, 0.002, 0.094, respectively.

Conclusions: Coronary calcium score is not significantly determined by genetic factors which calls the attention to the lifestyle prevention. Coronary calcium score shows a moderate correlation with ACI IMT and SBPao and no correlation with ACC IMT and PWVao.

M/8. INFECTIONS OF SEVERELY BURNT PATIENTS, CAUSED EXPECIALLY BY MULTIDRUG-RESISTANS (MDR) PATHOGENS

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Keywords: burn infection, multidrug-resistant bacteria, severe burn, microbiology, surveillance

In Hungary, 40-50.000 burns happen each year and 300-400 cases are considered severe. Infection is the leading cause of death among severely burnt patients, as multidrug-resistant pathogens are common in this patient group. Our goal was to assess the colonizing and infecting microbial flora in burn victims by reviewing the results of separate microbiological samples. We retrospectively analyzed cases and culture results of samples gathered in case of infection suspicion (hemoculture, bronchoalveolar lavage) and surveillance (wound whipe, cannula blood, nasal and

pharyngeal swab, collected urine and perianal whipe) samples of adult patients who were treated in the Burns Ward of Saint Stephan Hospital (Budapest, Hungary) between january 1 and december 31, 2013. Significance was set at 95% confidence interval ($p=0,05$). 74 patiens were treated, mean age was 59,1 years. Mortality rate was 39,1% (29 victims). Risk factors of intrahospital mortality: age, end-stage chronic heart failure, in-hospital cardiogen shock. Lenght of stay was highest if patient Baux score was 90. *S. aureus* grew from 25,2% of all the positive samples, followed by MDR *A. baumannii* (23,7%), *P. aeruginosa* (15,2%), *Candida*, *Klebsiella* and *Enterobacter* species (each 9%). *S. aureus* was the dominant pathogen in hemocultures, bronchoalveolar, nasal, pharyngeal and wound cultures. The incidence of MDR *A. baumannii* was high in all of the samples. *Enterobactes* species dominantly grew from urine samples, whereas *Klebsiella* species were isolated from bronchoalveolar lavage and perianal whipe samples in high frequency. *P. aeruginosa* and *Candida* species were the main isolates in wound cultures. The probability of hemoculture positivity was highest if the burnt surface was between 21 and 40% of total body area (70%), and if fourth degree burn were present (49%). The mortality of burn wound infections is high. MDR pathogens, especially *A. baumannii*, *P. aeruginosa* and *S. aureus* mean a serious threat to the victims.

M/9. EPIDEMIOLOGY OF CARDIOVASCULAR IMPLANTABLE ELECTRONIC DEVICE INFECTIONS IN HUNGARY

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Keywords: CIED infection, intracardial device, epidemiology, Hungarian Institute of Cardiology, incidence

Introduction Although cardiovascular implantable electronic device (CIED) infections are rare, the incidence is increasing worldwide. Our goal was to estimate the epidemiologic parameters of CIED infections among Hungarian CIED implanted patients. **Methods** We retrospectively analyzed cases of adult patients who were diagnosed with CIED infections at the Hungarian Institute of Cardiology between January 1, 2011 and December 31, 2013. Pearson's chi-squared test was used for qualitative parameters, significance was set at 95% confidence interval ($p=0.05$). **Results** 62 independent cases of 53 patients were identified. The incidence of CIED infection was 21 ± 4 cases per year which is 3.32% of the yearly average of CIED implantations. 2.15 out of 100 implanted CIEDs became infected per year on average. Infections were stratified whether they occurred <3 months (early) or ≥ 3 months (late) since CIED implantation. The relative incidence of pocket infections and bacteraemias were higher in early cases. Endocarditis and sepsis were more common in the late group. Early pocket infections were more likely to present with erythema, swelling and pus. Late pocket infections more likely appeared with decubitus and pain. Risk factors of early infection include device manipulation within the last 3 months, pocket haematoma and atrial fibrillation before disease onset. Risk factors of late infection were device manipulation beyond the last 3 months and previous CIED infection. Intrahospital mortality was 17% during 3 years. 66% of cases were late infections. Mortality was higher among patients with septic pulmonary metastases.

Risk factors of intrahospital mortality: ≥ 3 device manipulations, previous myocardial infarction and coronary bypass surgery, end-stage heart failure. **Conclusions** CIED infections are emerging in Hungary. The heterogeneous group of infections can be divided into early and late cases according to clinical parameters. Mortality is high among high risk patients.

M/10. TOTAL AORTIC ARCH REPLACEMENT TO A DECELLULARIZED ALLOGRAFT

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Keywords: aortic arch, decellularized allografts, vascular impedance spectrum, ventriculo arterial coupling, replacement

Background: Diseases of the aortic arch often require its replacement by synthetic prostheses, however, their implantation may be unfavourable for several reasons (suboptimal biomechanics, thrombogenicity, toxicity). In this study we investigated in vitro and in vivo properties of conventional prostheses and decellularized aortic arch allografts.

Methods: After preparing decellularized aortic arch allografts, their mechanical, histological and biochemical properties were evaluated and compared to native aortic arches and conventional prostheses in vitro. Total aortic arch replacement was performed with conventional prostheses and compared to decellularized allografts ($n=5/\text{group}$). Aortic blood flow and pressure were recorded continuously, left ventricular pressure-volume relations were measured by using a pressure-conductance catheter. From the hemodynamic variables end-systolic

elastance (Ees), arterial elastance (Ea) and ventriculo arterial coupling (VAC) were calculated. Vascular impedance spectrum and characteristic impedance (Z) were assessed by Fourier analysis.

Results: Decellularized allografts showed lack of cells and DNA, intact extracellular matrix and normal collagen/elastin content. Their mechanical properties did not differ from native aortic arches and were superior to prostheses. While Ees did not differ between the groups and over time (4.10 ± 1.19 vs. 4.58 ± 1.39 mmHg/mL and 3.21 ± 0.97 vs. 3.96 ± 1.16 mmHg/mL), Ea showed a higher increase in the prosthesis group (4.01 ± 0.67 vs. 6.18 ± 0.20 mmHg/mL, $P < 0.05$) in comparison to decellularized allografts (5.03 ± 0.35 vs. 5.99 ± 1.09 mmHg/mL). This led to impaired VAC in the prosthesis group (+62.5%), while it remained unchanged in the allograft group (+3.9%). Z showed a strong increasing tendency in the prosthesis group and it was markedly higher after replacement when compared to decellularized allografts (44.6 ± 8.3 dyn•sec•cm⁻⁵ vs. 32.4 ± 2.0 dyn•sec•cm⁻⁵, $P < 0.05$).

Conclusion: Total aortic arch replacement leads to contractility-afterload mismatch by means of increased impedance and invert VAC ratio after implantation of conventional prostheses. Implantation of decellularized allografts preserves vascular impedance thereby improving ventriculoarterial mechanoenergetics after aortic arch replacement. Tissue-engineered aortic arch allografts might serve as an alternative for prostheses.

M/11. RHEUMATOID ARTHRITIS: NOT JUST A "RHEUMA" BUT MUCH MORE

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Keywords: rheumatoid arthritis, atherosclerosis, cardiovascular disease, cancer, osteoporosis

Rheumatoid arthritis (RA) is a chronic inflammatory disease that leads to joint damage, functional impairment. RA has been associated with multiple comorbidities, including cardiovascular (CV) disease, secondary malignancies, osteoporosis, amyloidosis and others. Due to these comorbidities, RA will result in much shorter life expectancy compared to the general population. In this talk, the pathogenesis, clinical features and management of these comorbidities will be discussed.

MULTIDISCIPLINARY SESSION IX.

N. Radiology

N/1. MONITORING OF THE METABOLIC ALTERATIONS CAUSED BY PORTAL BRANCH LIGATION USING MULTI-MODAL PET/MRI MEASUREMENTS

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Keywords: PVL, Liver regeneration, Hepatocyte, Hepatectomy, PET/MRI

Introduction: The conventional imaging methods diagnostic precision can be highly enhanced with PET/MRI during two-stage hepatectomies combined with portal branch ligation. Also the metabolic changes caused by the portal occlusion may cause diagnostic difficulties. **Methods:** Male Wistar rats

(n=30) underwent selective portal vein ligation (sPVL): 80% of the liver parenchyma was excluded from the portal circulation (ligated lobes). Before the sPVL and after on the 1-,2-,3- and 7 days multimodal PET/MRI measurement were performed using 18-fluoro-desoxy-glucose tracer. Histological sampling and analysis were done. The standardized uptake value (SUV) of the ligated and non-ligated lobes were calculated and they were compared to the whole liver's (SUVVOI/SUVliver) and the left ventricle's (SUVVOI/SUVCLV) average SUV respectively. The volumetric reconstruction and measurement was done with OSEM 3D algorithm. Results: Large scale cell death phenomena can be observed in the ligated lobes and high level regeneration in the non-ligated. In parallel with the morphological changes the lobes both ligated and non-ligated shown significantly altered FDG uptake and accumulation kinetics. The SUVVOI/SUVCLV was significantly increased in both groups, reaching its maximum value on the 2nd day after sPVL and it returned to its original value by the 7th day after the branch ligation. The tracer uptake was significantly elevated 1-,2- and 3 days after sPVL in the ligated lobes compared to the non-ligated. 7 days after the sPVL the homogenous tracer dispersion has been returned in both groups. Conclusions: The metabolic changes caused by the sPVL can make the judgment of the tumor progression more difficult because of the elevated tracer uptake, especially at the beginning of the regeneration of the non-ligated and atrophy of the ligated lobes.

N/2. MULTIMODAL QUANTITATIVE CHARACTERIZATION OF INTRACRANIAL EPIDERMOID CYSTS: PRELIMINARY RESULTS

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Keywords: MRI, epidermoid cyst, quantitative, T1 mapping, HASTE

Introduction: The differentiation of epidermoid cysts from other intracranial lesions by means of CT and conventional MR imaging is challenging. The risk of residual and recurrent disease is high and multimodal imaging should therefore promote a precise differential diagnosis. Since epidermoid cysts are histologically identical to middle ear cholesteatomas, MRI methods have proved useful in the diagnosis of cholesteatoma; specifically EPI DWI and a non-EPI diffusion subtype (HASTE DWI) may possibly be applicable to epidermoid cysts. Besides testing the diagnostic utility of these methods on epidermoid cysts, we planned to quantify the T1 and T2 relaxation times, the ADC values and the magnetization transfer ratios in order to acquire objective, characteristic information about their structure and contents. Finally, our goal was to provide the physician with a reliable, multimodal diagnostic tool that supports accurate surgical planning. **Methods:** Two patients with epidermoid cysts were examined. Besides the conventional MR scans EPI DWI, HASTE DWI, quantitative T1, T2 and magnetization transfer

measurements were performed with a 3T MR scanner. After image registration, T1, T2 relaxation times and the magnetization transfer ratio inside a ROI were determined according to the lesion location on HASTE DWI. Mean ADC values inside the epidermoid cysts were also calculated by both mono- exponential and bi-exponential diffusion models. Results: Our results revealed relatively high T1 and T2 relaxation times and ADC values, and low magnetization transfer ratios in both subjects. Conclusion: HASTE-DW MRI provides accurate morphological information on epidermoid cysts, while T1, T2, ADC and magnetization transfer ratio maps are quantitative techniques. Thus the combination of these methods results in a confident preoperative diagnosis and aids to determine the indication of retreatment in the event of recurrence.

N/3. COMPARISON OF THREE DIFFERENT ADIPOSE TISSUE SEGMENTATION METHODS AT CT SCANS

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Keywords: CT, segmentation, adipose tissue

Introduction: The numerical characterization of the subcutaneous and visceral adipose tissue volume can be very useful at CT studies. In recent years, three independent segmentation algorithms have been introduced which employ specific but different Hounsfield unit (HU) ranges. One of the workgroups has also developed an algorithm to estimate the patient's BMI index along with their fat-tissue segmentation. We aimed to examine and compare the reliability of these methods. **Methods:** CT scans were performed on 98 patients on Philips Brilliance 64 system and two ROIs were drawn on three axial slices (L1 vertebra; hilus

region of the right and the left kidney) for each series. One ROI was placed on the body contour and one in the abdominal cavity to separate the subcutaneous white adipose tissues (SWAT) from the viscera ones (vWAT). We used the following ranges for the segmentations: [window level, window width] = [-110,160], [-95,110], [-120,150]. We also estimated the BMI values (BMIest) based on the calculated WAT areas and calculated the real BMI. Furthermore, we investigated the resulted segmentation at two different X-ray tube-current. Results: The three different segmented WAT areas showed good correlations with each other, both in the subcutaneous (($y=0.9937 \cdot x+351.01$, $r=0.9996$, $p<0.001$ and $y=0.9946 \cdot x-233.7$, $r=0.999$, $p<0.001$) and in the visceral case ($y=0.958 \cdot x-741.95$, $r=0.9987$, $p<0.001$ and $y=0.9525 \cdot x-376.3$, $r=0.9976$, $p<0.001$). We also found that the correlation of the vWAT area to the mass and BMI were weaker than the corresponding SWAT correlations. The calculated BMIest values were in good agreement with the real BMIs. Additionally, we found that the reliability of the segmentations was largely depended on the adjusted tube-current. Conclusion: The segmentation threshold does not affect significantly the estimated WAT and BMI values at standard tube-current, but decreasing the current the reliability of the segmentations are reduced as well.

N/4. GENETIC OR ENVIRONMENTAL FACTORS INFLUENCE FEMORAL ARTERY ATHEROSCLEROSIS?

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Keywords: femoral artery, atherosclerosis, twins study, heritability, environment

Background and purpose: Peripheral artery disease is a common atherosclerotic disorder with serious complications. Our aim was to assess the effects of heritable factors on the formation of atherosclerotic plaques in the femoral arteries. Methods and materials: 75 Hungarian (39 monozygotic /MZ/ and 36 same-sex dizygotic /DZ/) sets of twins (mean age 56±9 years) were recruited from the Hungarian Twin Registry. We performed B-mode and Doppler ultrasound examination of the common and superficial femoral artery (CFA, SFA), and the origin of the deep femoral artery (DFA) on both sides. We assessed concordance between MZ and DZ pairs by Pearson correlation analysis. Rough heritability was calculated according to the Falconer formula. Results: We identified plaques on CFA, DFA and SFA in 22%, 6% and 9% of patients, respectively. The presence of plaques in the SFA showed high rough heritability (60%). However, CFA showed low genetic dependency, with a rough heritability of 23%. We could not establish any genetic influence on the formation of plaques in the DFA (rough heritability of 0%). Conclusions: Atherosclerotic plaque formation is strongly determined by genetic factors in the superficial femoral artery, and moderately so in the common femoral artery. In contrast, plaque formation in the deep femoral artery is mainly influenced by environmental factors. Families with high risk for superficial femoral artery atherosclerosis may benefit from early ultrasound screening. In addition, our results suggest that atherosclerosis of the common and deep femoral arteries can be prevented by a healthy lifestyle.

N/5. CORONARY PLAQUE QUANTIFICATION WITHOUT TRAINING: DOES ITERATIVE RECONSTRUCTION HELP?

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Keywords: Iterative, Plaque, Reconstruction, Coronary, Plaque quantification

Introduction: We aimed to evaluate the effect of experience with coronary computed tomography angiography (CCTA) on the plaque quantification using a semiautomatic software tool and different image reconstruction algorithms. Methods: 25 patients with significant coronary artery disease on CCTA were randomly selected. CCTA images were acquired on a 256-slice scanner and reconstructed with standard filtered-back projection (FBP) and iterative reconstruction (iDOSE) techniques. Proximal 40 mm of the left anterior descending (LAD) artery of all patients were analyzed by two readers: Reader 1 (R1) a medical student with minimal experience in CCTA, Reader 2 (R2) with 5 years of experience in CCTA. Plaque quantification was performed by using a semiautomatic software tool. Coronary segmentation, lumen and vessel wall delineation was performed automatically, and corrected manually, if necessary. Time for automated segmentation of the coronaries and segmented length of the LAD was registered. Results: Coronary segmentation was faster with iDOSE as compared to FBP

(54.9 vs. 58.6 sec, $p < 0.0001$). Importantly, automatic segmentation could not be performed in 5/25 cases with FBP and in 1/25 case using iDOSE. Longer path of the LAD was segmented automatically with iDOSE, than with FBP (144.7 vs. 121.9 mm, $p < 0.05$). Mean plaque burden by Reader 1 versus Reader 2 in FBR were: 44% vs. 40% ($p < 0.004$); in iDOSE: 41% vs. 39% ($p = 0.152$). Non-calcified plaque volumes by R1 versus R2 in FBR were: 78.7 vs. 67.5 mm³ ($p < 0.019$); in iDOSE: 64.0 vs. 59.6 mm³ ($p = 0.197$). Calcified plaque volumes by R1 versus R2 in FBP were: 45.4 vs. 33.8 mm³ ($p < 0.003$); in iDOSE: 40.8 vs. 36.0 mm³ ($p < 0.030$). Conclusions: Coronary segmentation was more robust using iDOSE, than with FBP. The medical student has systematically overestimated the plaque burden and plaque components on CCTA. Importantly, the overestimation was smaller using iDOSE as compared to FBP.

N/6. INVESTIGATION OF GADOLINIUM BASED CONTRAST AGENTS IN IN VITRO CELL CULTURES

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Keywords: Gadolinium, contrast agents, gliomas, in vitro, NMR

The use of gadolinium based contrast agents has been integrated in the protocol of MRI examinations. It has an importance in diagnosing tumour related mutations. Tumours of different types and sizes may store contrast agents in differing degree, this also helps differential diagnostics. In the course of our research we have been examining to what extent complexes used in MR diagnostics would distribute in in vitro cell cultures. We have been conducting our

researches on two types of cell lines, including three gadolinium based contrast agents being of different chemical structures. While Dotarem is macrocyclic and negatively charged, Omniscan and Optimark are open-chain complexes carrying no molecular charges. Cell lines 'SK-BR-3' deriving from breast tumour and 'A172' deriving from astrocytoma have been placed in breeding vessels. Following the insertion, contrast agents of a quantity of 1. were added to the media, which had no impact on the growth of cells. This cell culture without contrast agent served as control. After the removal of the medium, a reading was prepared of the cells showing relaxation times of T1 and T2. The drop of relaxation time correlating to the control suggests the contrast media having been taken up by the cells. Our results show that Dotarem samples differ 10% from the control, meaning that Dotarem accumulates at a relatively low level in the cells. In the case of Omniscan, the difference was above 20%, consequently, the agent accumulated at a higher level. The stack of Optimark is 26% on cell line 'SK-BR-3' and is 12% on 'A172', thus the transport mechanisms of different cells may also differ.

N/7. THE ROLE OF THE FDG PET/CT IN THE PREOPERATIVE STAGING OF AXILLARY LYMPH NODE REGION IN PRIMARY BREAST CANCER

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Keywords: breast cancer, FDG PET/CT, lymph node metastasis, sentinel lymph node biopsy, conventional imaging

Introduction: The prognosis of early stage breast cancer (BC) is favorable. Accurate staging of the disease is necessary. FDG-PET/CT is highly sensitive in detection of distant metastases; however, its accuracy in

the axillary lymph node region (AL) is controversial. The purpose of this retrospective study was to evaluate the diagnostic performance of FDG-PET/CT in the detection of AL metastases. Materials and methods: We report on 43 patients treated with primary BC between 2009 and 2012. For clinical staging, X-ray mammography, breast and axillary ultrasonography and FDG-PET/CT were performed. Clinical TNM (cTNM) were determined by PET/CT and compared with the result of conventional imaging modalities. The results of diagnostic FNAB/core-biopsies and final surgical histological reports were also analyzed. The biological subtypes were determined. Pathological TNM (pTNM) and cTNM staging were compared. Results: PET/CT defined cT and cN correlated well with pT ($R=0.62$ $p<0.001$) and pN ($R=0.74$ $p<0.001$) stages. PET/CT inaccurately determined T stage in case of ILC or DCIS and - as regards cN - the same inaccuracy occurred by pNmi and pN1a. In two cases conventional imaging performed better than PET/CT in the determination of cT. In one patient both modalities were overestimated cT stage. One patient did not give her consent for the surgical treatment of the axilla. Otherwise, 31 axillary lymph node dissections (ALD) and 11 sentinel lymph node biopsies (SLNB) were performed. All of the SLNB patients were classified as cN0 with PET/CT. Final histology confirmed N0 in 10 patients; only one patient had lymph node micrometastasis (pNmi). Conclusion: In our patient group cTNM - measured by FDG-PET/CT - and pTNM staging were congruent. PET/CT results were fairly predictive for the final histology of AL. In the daily practice, ALD could be spared on the basis of cN0 PET/CT result; however, SLNB is still necessary to perform

N/8. PREDICTORS OF RADIATION DOSE ASSOCIATED WITH CORONARY CT ANGIOGRAPHY

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Keywords: CCTA, Radiation dose, Dose reduction, Iterative reconstruction, Cardiovascular imaging

Introduction: Since the exposure to unnecessary ionizing radiation can be harmful, monitoring the radiation exposure that is received during coronary CT angiography (CCTA) in daily practice is of vital importance for the development of dose reduction strategies. Our goal was to estimate the radiation dose of CCTA in routine clinical practice. Furthermore, we sought to assess the effect of iterative reconstruction technique on dose reduction and identify independent clinical predictors of effective radiation dose. **Materials and methods:** We enrolled 1092 patients in our study, who underwent 256-slice CCTA at the Heart and Vascular Center, Semmelweis University (mean age 58 years, 58.8% men). Radiation dose parameters were extracted from the dose exposure records. Differences in continuous variables were assessed using Student paired t test or Mann-Whitney U test as appropriate. Categorical variables are presented by frequency counts, and intergroup comparisons were performed by a χ^2 test. Linear regression was used to identify the independent factors. **Results:** The median Dose Length Product was 378 mGy*cm. The mean BMI was 28.6 kg/cm². Independent

factors associated with radiation dose were ($p<0.01$) age, gender, heart rate during the scan, BMI, bypass surgery in medical history, mode of gating and reconstruction. Significantly lower radiation dose is achieved by the implementation of the iterative reconstruction technique (397.1 ± 199.5 vs. 458.4 ± 243.7 mGy*cm). Conclusion: Our data suggest that 256-slice CCTA can be performed with low radiation dose (effective dose 4.8 mSv) in routine clinical practice. Independent factors associated with radiation dose were heart rate, BMI, age, gender, the mode of gating and reconstruction.

N/9. HERITABILITY OF LEFT ATRIAL DIMENSIONS: A CLASSICAL TWIN STUDY

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Keywords: twin study, left atrium, cardiac CT, angiography, heritability

Aims and objectives: Recently it has been described that left atrial size is associated with cardiovascular mortality and morbidity. Whether the atrial anatomy depends on environmental influences or determined by genetic factors is unclear. We sought to determine the heritability of left atrial dimensions in a classical twin study.

Methods and materials: We studied 50 asymptomatic twin subjects (14

monozygotic [MZ] and 11 dizygotic [DZ] twin pairs) with no history of coronary artery disease. All participants underwent coronary CT angiography (CCTA) exam using a 256-slice CT-scanner (Brilliance iCT, Philips Healthcare, Best, The Netherlands). Atrial measurements were performed using a dedicated software (EP-planning, EBW, Philips Healthcare, Best, The Netherlands). We measured the left atrial volume (LAV) and the average area of the pulmonary venous ostia (PVOA). We calculated the correlation between MZ and DZ twins with maximum likelihood estimation.

Results: The average age of the MZ and DZ twins was 55.6 ± 9.2 vs. 61.0 ± 7.9 years, $p=0.161$, the average height was 164 ± 9 vs. 167 ± 8 cm, $p=0.284$, the average weight was 72.1 ± 20.4 vs. 77.1 ± 18.1 kg, $p=0.506$. The mean LAV was 60.6 ± 17.9 cm³ and the mean PVOA was 194.0 ± 52.9 mm² after correction to the body surface area. The correlations within each MZ and DZ pairs were the following, LAV: 0.51 (95%CI:-0.02-0.77) vs. 0.29 (95%CI:-0.40-0.79); PVOA: 0.60 (95%CI:-0.35-0.87) vs. 0.14 (95%CI:-0.72-0.83), respectively.

Conclusion: The current rMZ/rDZ ratio suggests that atrial geometry is driven by genetic effects rather than environmental influences.

MULTIDISCIPLINARY SESSION X.

O. Pathology-Oncology- Anesthesiology-Intensive care medicine

O/1. MUTATIONS AND POLYMORPHISMS IN BREAST CANCER

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Keywords: Mutation, breast cancer, hormon
receptor state, SNP, triple negative,

Introduction: BRCA mutations are the most well-known hereditary risk factors of breast cancer (BC). In our retrospective study we analyzed the incidence of classical mutations and polymorphisms amongst screened patients and their relationship with the pathological features of BCs. Methods: We report on 68 patients in whom BRCA analyses were performed between 2012 and 2013. In case of the manifested BC cancer we determined biological subtypes - based on the hormone and HER2 status and the Ki-67 labelling index. Results: BRCA mutations or polymorphisms were detected in 60 cases. We found five classical mutations. 59 patients had SNPs from which 50 were S1613G (heterozygote:41/homozygote:9). In 20 patients we found a cluster of 4 SNPs (S1613G-K1183R-E1038G-P871L). 14 other SNPs occurred. We identified benign breast lesions (BEN) in 29 patients, 28 of these have SNPs, in 27 cases S1613G. We detected significant correlations between the presence of BEN and SNPs ($p=0.036$), and S1613G ($p=0.01$). 34 patients [44,8 $\pm$ 9.5 year] had BC: 31 invasive ductal, 2 lobular, and 3 other carcinoma were detected (grade 2=10, grade 3=24). Biological subtypes: Luminal A=8; B1=8, B2=4; HER2+=1; triple negative=13 patients. Three of these patients had classical

mutations, 31 had SNPs. 23 was S1613G (19/4), the four-SNP-cluster was confirmed in 11. We did not find significant correlations between SNP profiles and hormone receptor/HER2 status nor the biological subtypes; however, triple negative tumors prevailed in all cases of polymorphisms or mutations. Conclusions: In our screened population the incidence of SNPs was considerably higher. In the aspect of BC patients, young age and high grade invasive ductal carcinoma were typical. In case of non-classical BRCA mutations none of the biological subtypes prevailed, however, with an increased number of enrolled patients our results could be refined. Additionally, the role of correlations between SNPs and benign breast lesions need to be clarified.

O/2. EXAMINATION OF PITUITARY ADENYLATE CYCLASE-ACTIVATING POLYPEPTIDE IN DIFFERENT PATHOLOGICAL CLINICAL SAMPLES

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Keywords: PACAP, tumor, blood,
radioimmunoassay, biomarker

Introduction Recent trends in pituitary adenylate cyclase-activating polypeptide (PACAP) research point to the clinical introduction of PACAP or its analogs/fragments possibly in the near future. Therefore, we aim to examine the relation between PACAP level of different human samples and different disorders. Earlier we showed that PACAP plays an important role

in different neurodegenerative diseases, the regulation of tumor cell proliferation, and in inflammations in animal models. We suppose, that it has a function in human pathological conditions. Previously we found significantly lower level of PACAP38 and PACA27 in tumor samples in both lung and colon cancers, and significantly higher in cardiac samples from ischemic heart diseases compared to normal healthy tissue. **Methods** In the present study we investigated the level of PACAP from human blood and tissue samples of patients with radioimmunoassay examination. We collected tissue samples from different urological disorders (kidney tumor, urinary bladder tumor and prostatic hypertrophy) and breast cancer and we collected blood samples from patients with diabetes, hypothyroidism, hyperthyroidism, acromegaly, hyperprolactinemia. **Results** Similarly to our earlier results in kidney tumor samples we found significantly lower amount of PACAP38 level compared with healthy tissue samples. We did not find significant alterations in the PACAP38 and PACAP27-level between healthy and tumoral urinary bladder and prostate samples. In blood samples we detected higher PACAP38-level in patients with hypothyroidism, hyperthyroidism and acromegaly as well as patient with long-time type II diabetes mellitus, who also had chronic heart and kidney complications. **Conclusion** Our results showed significant correlations with PACAP level in the human samples and severity of disorders, but further investigations are necessary to describe the exact function of PACAP in different pathological conditions, in order to be a biomarker in the future.

O/3. MORPHOLOGICAL ANALYSIS ON EXPERIMENTAL LIVER CIRRHOSIS MODELS

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Keywords: Fibrosis, cirrhosis, liver regeneration, progenitor cell, hepatocyte

Introduction: Liver fibrosis/cirrhosis is among the most common diseases in western societies. Yet, the exact mechanism how the liver structure is completely reconstructed is largely unknown. Recent theories emphasize the potential role of hepatic progenitor cell compartment in the process. In case of chronic parenchymal damage the progenitor cells would be responsible for the liver regeneration. The by-product of this activity would be the activation of hepatic myofibroblasts resulting in deposition of collagenous matrix and eventually the development of cirrhosis. **Methods:** This mechanism has been addressed in our experiment. Hepatic fibrosis has been induced by the continuous administration of thioacetamide (TAA) or carbon tetrachloride (CCl₄)/phenobarbital to male C57Bl mice. The fibrotic process has been modulated by enforced hepatic TGF-beta expression from a transgene or by the administration of the EGFR inhibitor drug, erlotinib. The animals have been sacrificed following 6, 9, 12, 15, 18 weeks of treatment. The extent of fibrosis was monitored by Picro Sirius red histological staining, the expansion of progenitor cell compartment by CK19 immunostaining. The proliferative activity of hepatocytes and progenitor cells was detected by the immunohistochemical detection of incorporated bromodeoxyuridine, which was administered to the mice before sacrifice.

Results: Both TAA and CCl₄ treatment resulted in progressive hepatic fibrosis in the experimental animals. TGF-beta enhanced the fibrosis, erlotinib decreased the extent of progenitor cell reaction. However, no correlation could be observed between the extent of fibrosis and progenitor cell reaction in the investigated models. Similarly, no decreasing BrdU incorporation into hepatocytes or increasing proliferation of progenitor cells has been observed with temporal progression of the process. **Conclusions:** Our data do not support the recently widely spread hypothesis about development of liver cirrhosis.

O/4. EFFICIENCY AND DIFFERENT STRUCTURAL DESIGNS IN EMERGENCY DEPARTMENTS

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Keywords: Emergency, triage, CTAS, RATS, waiting time

BACKGROUND: We studied the effect of the logistics on the Emergency Department's daily routine. In particular the influence of different structural designs, work division methods on the nurses' workload and the length of patients' waiting and medical care period. **AIMS:** The aim of this study was optimising of the most common procedures in nurses work. Our plan is to create a recommendation for work division which can increase efficiency in the ED, and improve patients' safety. Emergency units with different patient profile (internal medicine, trauma or mixed) were investigated. The logistics of different tasks (independently performed and cooperative tasks) were

examined as well. Our aim is to cooperate with the Hungarian initiation of the Canadian Triage Acuity Scale(CTAS). **METHODS:** Data from 7 Hungarian Emergency Department were analysed. Emergency Departments with different level of progressivity were included. Personal observation and questionnaire were used to estimate the time consumption of different tasks. The work division of different teams were analysed. MS Excel 2007 and SPSS 20 programmes were used. The analysis was carried out by t - tests (one-sample location test and two-sample location test) with the consideration of standard deviation. The relationships among these results were investigated by χ^2 distribution. **RESULTS:** According to the first results of our study shows we can save resources and time by uniting the advantages of different systems. Supposing a more effective system we will be able to increase the patients' safety and comfort by reduce the time of diagnostics and care. **CONCLUSION:** These results are worth to share with Hungarian Association of Emergency Medicine, a "Sürgősségi Ápolási Egyesület és a MESZK Sürgősségi Betegellátási tagozat" to influence further decisions. We expect those who read these results will consider our recommendations.

O/5. DEXMEDETOMIDINE IN AWAKE CRANIOTOMY

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Keywords: Dexmedetomidine, craniotomy, sedation, cooperation, airway control,

Introduction: Awake craniotomy is rare and challenging intervention for either the neurosurgeons and the anesthesiologists. The

intense affinity of the Dexmedetomidine to the alpha-2 adrenergic receptors makes optimal conditions for the awake craniotomies. However, its usage is not spread in Hungary. In our study we would like to show our experiences about using the combination of Dexmedetomidine and local anesthetics in certain neurosurgical procedures. (We have a short demonstrating VIDEO.) Methods: At the Neurosurgical Department of the University of Szeged, we collected data since 2009 until 2014. Among ASA-1 and ASA-2 patients, the resections of space occupying lesions were carried out with i.v. administered Dexmedetomidine 6 times (Group DEX), and without Dexmedetomidine 16 times (Group NODEX). During the operations the analgetic-sedation was completed with Midazolam, Propofol or Morphine. The duration of anesthesia was between 125-195 minutes, the duration of the operation usually was 75-135 minutes long. In our study we compared the complications' incidence, the demand for analgetic- and antihypertensive drugs between the two groups. Results: In the Group DEX, the demand of analgetic drugs was significantly lower, and the patients of this group needed less antihypertensive drugs. The risk of respiratory depression is low. To maintain the sedation and the patient's ability of cooperation, we need to modify the speed of the drug intravenous application. By applying the Dexmedetomidine 45 minutes prior to the incision we can provide analgesia and sedation with stable cardiovascular state and there is no risk of loss of airway control. Conclusions: The Dexmedetomidine in Awake Craniotomy provides complication - safe method for patients, based on the latest data of our Department.

O/6. LONG-TERM FUNCTIONAL OUTCOME OF TRAUMATIC BRAIN INJURED PATIENTS WITH REFRACTORY INTRACRANIAL HYPERTENSION TREATED WITH LUMBAR CEREBROSPINAL FLUID DRAINAGE.

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Keywords: Lumbar liquor drainage, Traumatic brain injury, Intracranial pressure, Prognosis, Outcome

Introduction: Traumatic brain injury (TBI) is one of the leading causes of death in the young population. Intracranial pressure (ICP) remains refractory to standard treatment in several cases of moderate and severe TBI. Lumbar liquor drainage (LD) used to be considered contraindicated in elevated ICP, however recent studies reported promising evidence supporting the efficacy and safety of its application. We are still lack of evidence regarding long-term outcome. Methods (and Patients): In Baleseti Központ, LD is used as a second-tier therapy for salvageable, moderate and severe TBI patients' with refractory ICP, associated with discernible basal cisterns. Functional outcomes were assessed by phone interviews with Glasgow Outcome Scale. Then we calculated prognosis by the TBI-IMPACT, and the CRASH prognostic calculators based on admission data, like GCS, reactivity of the pupils, etc. After that, we compared our data with the calculated prognosis, with data gained from similar recent publications, and from national registers. Results: Finally, 16 patients were taken into our study (between 2008 and 2012). This relatively small number doesn't allow us to show significant statistics, but in this topic articles have been reported with similar sized populations. Mortality rate

at 6 month follow-up was as predicted (25% to 26.9%). Unfavorable outcome was lower than predicted (38% to 61% and 40%), and lower than what other studies showed (38-51%). Meningitis was observed in the same frequency as the control group (17% to 13%) Conclusion: Other second-tier measures in the current guidelines are getting controversial. Decompressive Craniectomy, for instance, turned out to be worsening long-term outcome, Barbiturates are not lowering mortality, literature suggest, and therapeutic hypothermia is waiting for being approved. All these suggest LD could be an effective and safe second-tier measurement in the TBI patients if certain criteria are met. However, further investigations, like a controlled trial are needed.

MULTIDISCIPLINARY SESSION XI.

P. Dentistry-Pharmacy

P/1. INVESTIGATION OF THE PUTATIVE ANTITUMOR EFFECTS OF CANNABIDIOL ON HUMAN ORAL SQUAMOUS CELL CARCINOMA

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Keywords: cannabidiol, antitumor, reduced proliferation, tribbles homolog-3, apoptosis-dominated cell death

Introduction: Beneficial effects of plant-derived cannabinoids have already been described in various tumors, but we still lack data about their effects against oral squamous cell carcinoma (OSCC), which shows regrettably high prevalence in Hungary. Therefore, in the current study, we aimed at exploring the putative “anti-OSCC” effects of a non-psychotropic, plant-derived cannabinoid (cannabidiol, [CBD]).
Methods: Experiments were performed by

using the CAL 27 human OSCC-derived cell line. Viability and cell death were investigated by MTT- and DilC1(5)-SYTOX Green assays, whereas proliferation was monitored by CyQUANT-assay. Gene expression was followed by RT-qPCR and Western blot. $[Ca^{2+}]_{IC}$ was investigated by Fluo-4 AM-based Ca^{2+} -imaging. Results: First, we showed that CBD (applied in 10-50 μM) reduced proliferation of CAL 27 cells in a dose-dependent manner (24-48-72-hr treatments). Moreover, we also showed that it induced apoptosis-dominated cell death (30-50 μM ; 24-hr treatments). Next, we aimed at assessing the mechanism of the above beneficial in vitro antitumor effects. We found that 24-hr CBD-treatment was able to up-regulate the expression of tribbles homolog-3 (TRIB3, a pseudokinase possessing remarkable antitumor activity), and down-regulated the expression of Ras guanyl releasing peptide 3 (RasGRP3, a well-known proto-oncogene), suggesting that opposing regulation of the above molecules might be an important factor in the development of the observed antitumor effects of CBD. Finally, to further dissect the mechanism of the above antitumor actions, we investigated the effects of CBD on the Ca^{2+} -homeostasis of the cells. Of great importance, we found that CBD-treatment increased the $[Ca^{2+}]_{IC}$ of CAL 27 cells in a dose-dependent manner. Conclusion: Our data suggest that CBD could be exploited as a promising, novel tool in the adjuvant treatment of OSCC. This research was supported by the European Union and the State of Hungary, co-financed by the European Social Fund in the framework of TÁMOP-4.2.4.A/ 2-11/1-2012-0001 ‘National Excellence Program’.

P/2. CHANGES OF THE SEROTONINERG INNERVATION PATTERN AND MAST CELL DEGRANULATION IN RAT SALIVARY GLANDS AFTER CHRONIC FLUOROQUINOLONE TREATMENT

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Keywords: pefloxacin, serotonin, nerve growth factor, parotid gland, neuropathic pain

Introduction: Fluoroquinolone antibiotics (FQAs) are broad-spectrum antibiotics used in dental practice. Apart from their advantageous therapeutic characteristics, they also have some adverse side effects. Following FQA medication, the patients sometimes suffer from dry mouth, and peripheral neuropathic pain. In the background of these adverse effects, the reported neurotoxicity of FQAs might be presumable. To reveal this we examined the serotoninergic innervations pattern in rat salivary glands after FQA treatment. Methods: Female rats (n=8) were treated with an intraperitoneal injection of pefloxacin, an FQA, while the control animals (n=8) were treated intraperitoneally with physiological saline. Results: After three- or seven-day treatment, the serotoninergic fibers were visualized with fluorescent immunohistochemical methods and mast cells with toluidine blue staining. We calculated the number of fibers that expressed serotonin compared with control values at 3 and 7-days after treatment. After 3-days of

treatment, the number of serotoninergic fibers was significantly increased. After 7-days of treatment, the number of serotonin positive nerve fibers was decreased to levels near those of the control group. In addition, we observed alteration in the number of mast cells, which paralleled the changes in serotonin expressing fibers during the treatment periods. Conclusions: These findings suggest that pefloxacin can modify the finely controlled communication between the immune and nervous systems. As a consequence of altered serotoninergic innervation pattern the activated mast cells can release different mediators which might be responsible for the decreased saliva flow and the neuropathic pain.

P/3. ORAL HISTOMORPHOLOGICAL INVESTIGATIONS BY TRANSPARENT, TRUE 3D MICROSCOPY

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Keywords: clearing, homogenize, stereoconverter, depth of field (DOF), paradigmatic change

Our methodical innovation consists of 3 separate developments: 1) The optical clearing solutions, which are able to homogenize the refractive indexes of tissue components, thus increasing their transparency. 2) The assembling of a true 3D investigating system, including the so called

„stereoconverter”, that is able to increase the magnification of our traditional stereomicroscope by 5-20 fold without decreasing its depth of field (DOF). 3) The development of a true 3D measuring and modeling computer software for the analysis of spatial structures and functions. The function of our clearing solutions and this true 3D system were tested on the gingiva and submandibular gland of rats in vivo. Beside soft tissues, we also commenced the development of hard tissue (tooth, bone) specific clearing solutions in vitro. We immersed the unprepared or decalcinated jaws of rats and the extracted healthy or decayed human teeth for a couple of days into our clearing solutions and investigated them by our system. With the aid of our clearing materials, we were able to make the structures of deeper gingival layers examinable in vivo, e.g. to study the microcirculatory system. Due to the increase of magnification and the relative enlargement of DOF, quite thick tissue sections or blocks can be imaged. Even a whole tooth can be made transparent in vitro. Additionally, we can also study the surface structures of root cement in vitro. The true 3D way of thinking instead of planar approach can result in paradigmatic change also in the field of microscopy and may lead to the development of a new scientific branch i.e. the “transparent, true three-dimensional qualitative and quantitative microscopy”. The identification and modeling of the delicate spatial structures of soft and hard tissues might not only provide substantial, new, qualitative and quantitative knowledge, but also might influence their therapy.

P/4. THE EXPRESSION AND ROLE OF THE HSP 60 DURING THE DEVELOPMENT OF THE TOOTH GERM

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Keywords: Hsp 60, tooth development, NF- κ B, IKK, morphology

The heat shock protein 60 (Hsp60) is an ubiquitous protein of eukaryotic cells, however previous studies did not investigate the pattern and the role of this protein during the tooth development. According to the literature, the Hsp60 is able to bind to the IKK, which causes the modulation of it and results in the influence of the NF- κ B pathway. The NF- κ B is the effector molecule of the Ectodysplasin/TNF signal transduction cascade during the tooth development. Our goal is to describe the localization of the Hsp60 and determine the role during the development of the tooth germ. To reach our goal, we detected the Hsp60 in different structures of the tooth germ using immunohistochemistry and in situ hybridization. The evaluation of our results is that the stratum intermedium, enamel knot and ameloblasts consist much Hsp60 protein. During the culturing we used exogen Hsp60 protein in the case of the treated tooth germs, the medium of the control group did not contain Hsp60. In case of the treated tooth germs the enamel knot was enlarged and the distal parts were blunt. The control tooth germs had normal morphology. We performed Apoptag TUNEL-Assay and BrdU incorporation test to gain information about the effect of Hsp60 on the life-cycle of the cells. The BrdU incorporation test did not find any difference between the groups. The TUNEL Assay detected several apoptotic cells around the enamel knot. We

detected and described the localization of the Hsp60 during the development of tooth germ. During the in vitro experiments we simulated the effect of the Hsp60, the treated tooth germs had abnormal morphology, the control tooth germs had normal morphology. According to our results the Hsp60 influences not only the morphology but also the life-cycle of the tooth germs' cells.

P/5. SYNTHESIS OF ANTICOAGULANT PENTASACCHARIDE SULFONIC ACIDS

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Keywords: heparin, anticoagulation, pentasaccharide, sulfonic acid, glycosylation

INTRODUCTION: Heparin is a linear, highly sulfated polysaccharide that has been used clinically as an antithrombotic agent since 1940s. Heparin interacts with antithrombin, a serine protease inhibitor that blocks thrombin and factor Xa in the coagulation cascade. We have been dealing with the synthesis of sulfonic acid analogues of the anticoagulant pentasaccharide domain of heparin. Longer duration of action and increased activity of the molecules are expected by exchanging the primary sulfate esters to bioisosteric sodium-sulfonatomethyl moieties. **METHODS:** We have been preparing a series of pentasaccharide sulfonic acid analogues via [2+3] block synthesis by using different trisaccharide acceptors and disaccharide donors containing sulfonatomethyl moieties at different positions. After the assembly of the fully protected pentasaccharides, further eight more synthetic steps including deprotection

and O-sulfation are required for each derivatives. During the organic preparative work, the reactions were monitored by thin layer chromatography. Column chromatography was used for separation and purification. NMR spectroscopy, mass spectrometry and elemental analysis were used for structural determination. **RESULTS:** Two sulfonic acid analogues were successfully synthesized in good yields, a disulfonate and a trisulfonate analogues. In vitro evaluation of the anticoagulant activity of these new sulfonic-acid derivatives revealed that the disulfonate analogue has an outstanding anti-Xa activity, however the trisulfonate analogue inhibited the factor Xa with significantly lower efficacy. As a continuation of this research, synthesis of other sulfonic acid derivatives has been decided. **CONCLUSIONS:** In the frame of this work, we have found that the pentasaccharide sulfonic acids inhibited efficiently the blood coagulation factor Xa, however, in a substantially different rate depending on the number and position of the sulfonatomethyl groups. We plan to finish the deprotection reactions of all derivatives, and then our series of pentasaccharide sulfonic acids will be useful as probes for structure-activity studies and potential leads for new anticoagulant drugs.

MULTIDISCIPLINARY SESSION XII.

Q. Prevention-Pulmonology

Q/1. SMOKING AND FAMILY INTERACTIONS AMONG ADOLESCENTS

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Keywords: smoking, adolescence problem, behaviour, risk factors, family interactions

Adolescence is a critical life period from the viewpoint of different substance uses, for instance smoking and alcohol consumption. The family has an essential role in case of adolescents' problem and health behaviour. Family relationships and different family interactions have a significant influence on the adolescents' behavioural patterns. In this life period the social network is usually reorganised and the relationship between the adolescents and parents also changes. The study was performed in all of the elementary and high schools of Mako and the villages in its area in Hungary. The pupils of grade from 7 to 13 were questioned anonymously in 2013 the study consisted of 2011 pupils. Self-administered questionnaires were applied. The survey included sociodemographic variables, lifetime and monthly prevalence of problem behaviours (smoking and alcohol drinking), different influencing factors, beliefs, attitudes related to substance use and family interactions. Descriptive statistics, cross-tabulations and chi-square tests were used to test these interrelationships with SPSS MS 19.0 statistical program. Significant relationship was detected between negative family interactions and substance use. The parents' critical behaviour could be increase the risk of substance use. The family is an important microenvironment for the adolescents therefore the relationships and interactions among family members could be protective and risk factors too. The appropriate management of family conflicts could contribute to decrease the risk of different problem behaviours or risky substance use. This research was supported by the European Union and the State of

Hungary, co-financed by the European Social Fund in the framework of TÁMOP-4.2.4.A/2-11/1-2012-0001 'National Excellence Program'.

Q/2. THE AWARENESS AND ATTITUDE OF THE HPV VACCINE

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Keywords: HPV, vaccine, prevention, cross-sectional survey, STD

Introduction: HPV is an STD and a common tumour virus which causes mainly cervix cancer in women and oropharyngeal cancer in women and men. Vaccine is available against HPV, until nowadays in Hungary people needed to buy this vaccine, but from next years it will be free for girls at the age of 12-13. We investigated the awareness and attitude about the HPV vaccine among university students. **Methods:** We prepared a cross-sectional online survey. 167 people filled in our questionnaire. 21 responders were excluded because of being out of the target group. The statistical analyses based on descriptive statistics and Chi2-probe to test the differences between the women and men, medical students and non-medical students and vaccinated and not vaccinated groups. **Results:** We found that 73% of our responders are not vaccinated, and women were in majority ($p < 0.0001$). Women are mainly not vaccinated, because of the expenses, men, because they do not feel compromised themselves ($p = 0.0002$). The sources of information were the health

professionals among women ($p=0.0124$) and vaccinated population ($p=0.0164$) and the internet among men and not vaccinated population. 82% of our responders supported the vaccination of the men. 80% would not pay more than 10,000 HUF and 93% of the responders supported the free vaccination. Conclusion: It would be necessary to inform men about the importance of the HPV vaccine, the main channels would be the internet and health professionals. It would be important to inform the population about the safety of the vaccine and to take the advantage of the internet and mass media to inform people. It would be necessary to vaccinate men, most of our responders supported it and 75% of the men would be willing to get a vaccine. The free vaccination program probably would have a positive result on the vaccination coverage.

Q/3. COMPARISON OF THE ANGIOGENIC FEATURES OF HUMAN EMBRYONIC AND INDUCED PLURIPOTENT STEM CELL DERIVED ENDOTHELIAL CELLS

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Keywords: human embryonic stem cells, induced pluripotent stem cells, endothelial cells, angiogenesis, regenerative therapy

Introduction Cardiovascular derivatives of stem cells are promising candidates for regenerative therapies of ischemic tissues, however the most appropriate stem cell type for this purpose is still undetermined. The aim of this study was to compare the therapeutic competence of human embryonic and induced pluripotent stem cell derived endothelial cells (hESC-EC and iPSC-EC) based on their angiogenic features. **Materials&methods** Endothelial cells were differentiated from hESC and iPSC, the

CD31 positive cells were separated by FACS. As positive endothelial control human umbilical vein endothelial cells (HUVEC) were used. The stem cell-derived endothelial cells were characterized in vitro by immunocytochemistry staining and their gene expression profile was assessed by qPCR. In vivo experiments were performed in immunodeficient rats: endothelial cells were implanted subcutaneously, two weeks later cells were reisolated for further qPCR analysis and immunohistochemistry was performed. Slides treated with CellTracker antibody were analyzed with ImageJ. Results Both stem cell derived endothelial populations behaved alike HUVEC in vitro: formed capillary-like network and expressed numerous endothelial marker genes (CD31, Notch1, Notch 2). In vivo both hESC-EC and iPSC-EC remained viable and formed capillary networks. Immunohistochemistry proved the reserved endothelial phenotype after transplantation. The established vessel networks were quantified with ImageJ. No significant difference was found between hESC-EC and iPSC-EC regarding the proliferative activity and cell-cell connections. The stem cell derivatives showed similar functional features as HUVECs, proving their mature endothelial fate. During transplantation the expressions of proangiogenic genes (Angiopoietin, NOS3) were upregulated and no significant difference was shown between hESC-EC and iPSC-EC (hESC-EC: Angiopoietin2 mRNA levels: preimplantation 1 ± 0.11 , postimplantation 86.23 ± 26.34 ; iPSC-EC: NOS3 preimplantation 1 ± 0 , postimplantation 2503.94 ± 0.43 $n=3$ $p<0.05$). Conclusion Human pluripotent stem cell-derived endothelials have the features of mature endothelial cells. The angiogenic potential of iPSC-EC is similar to hESC-EC, promising this new cell type future therapeutic options in ischemic cardiovascular diseases.

Q/4. REVOLUTION OF CONNECTED HEALTHCARE

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Keywords: Non-adherence, Smart device, Innovative approach, Pill dispensing system, Telemedicine

Introduction Patient non-adherence is a very serious issue that has been researched and confirmed by many, but still hasn't had any big breakthroughs or game-changing ideas to solve it. **methods** Our goal was to analyze the findings of available publications on accessible adherence improvement methods. We validated and discussed our results from these studies with medical professionals from the concerned fields of hypertension and epilepsy. **results** Major problems were found in the adherence of patients. Patients tend to forget to take their medications and thus their health is being risked by possible complications of their illness. By misreporting to their doctors, the physicians might get misleading information about the treatment's going. **conclusions** Many problems could be addressed by making the management of medications and patient data more efficient and automatized. Concerning available methods still no complex solution to this problem has been developed, according to our findings. **conclusions** A device which stores all of the patient's medications, reminds the patient to take them and accurately dispenses the pills, could lead to better compliance. With the documentation of pill-taking habits medical professionals could get much solicited data about the treatment. Considering different segments of our research data, specific features of the projected idea are being analyzed and a first prototype of such a medical device is under development.

Q/5. THE EFFECT OF COMBINED HYPOXIA AND CIGARETTE SMOKE EXTRACT (CSE) TREATMENT ON THE PROLIFERATION AND SURVIVAL OF ALVEOLAR EPITHELIAL CELLS

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Keywords: lung, COPD, hypoxia, cigarette smoke, HIF-1 alpha

Introduction: Chronic obstructive pulmonary disease (COPD) is a global health problem. Smoking - as a chronic stress effect - is a main risk factor in developing COPD. However, the pathomechanism of the disease is not yet clear. In COPD alveolar hypoventilation caused by obstruction leads to alveolar hypoxia. The hypoxia-inducible factor 1 α (HIF-1 α) has a remarkable role in protecting the cells against hypoxic damage. The effect of combined hypoxia and CSE on developing COPD is not yet known. **Methods:** We measured the change in cell number in immortalized alveolar epithelial cells (A549). The following groups were analyzed: FiO₂ 20,9% (control); 13%; 6%; 1%, treatment with cigarette smoke extract (CSE) and a combined group (FiO₂ 13% + CSE; 6% + CSE; 1% + CSE). We examined the protein expression of HIF-1 α with flow cytometry. We took photos of each treated groups with optical microscope. **Results:** The number of epithelial cells decreased in each CSE treated group compared to groups

without CSE treatment (FiO₂ 20,9%: 169375±13113 vs. 413125±28646; 13%: 71667±16832 vs. 345000±25729; 6%: 173333±26932 vs. 353333± 30287; 1%: 176667±15405 vs. 320000±22627; p<0.01). The apoptosis increased significantly at each oxygen tension when treated with CSE, while the expression of HIF-1 α decreased significantly in the same circumstances compared to the control (FiO₂ 20,9%: 14983±2386 vs. 47317± 8860; 13%: 9683±3912 vs. 27227±5559 ; 6%: 13137±3072 vs. 28332±8450; 1%: 21510±5128 vs. 38183±7117; p<0.01). Morphological changes on photos return. Conclusions: The number of alveolar epithelial cells falls significantly in each CSE treated group. The apoptosis of the cells rises significantly when treated with CSE. The HIF-1 α protein expression decreases significantly when the cells are treated with CSE. Hypoxia causes peculiar morphologic changes in alveolar epithelial cells.

Q/6. THE EFFECT OF PLATINUM-BASED CHEMOTHERAPY ON THE ACTIVITY OF THE MTOR KINASE PATHWAY IN LUNG CANCER

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Keywords: non-small cell lung cancer (NSCLC), mTOR pathway, immunohistochemistry, neoadjuvant chemotherapy, changes in mTOR activity

Introduction: Lung cancer is the leading cause of cancer death worldwide with a poor survival rate, close to 70% of lung cancers are inoperable at the time it's diagnosed. The

neoadjuvant chemotherapy may allow surgical removal of the tumor. Dysregulation of the mTOR signaling pathway promotes tumor cell survival and proliferation. This pathway is also involved in the pathogenesis of lung cancer; therefore, we investigated the effect of neoadjuvant platinum-based chemotherapy on the activity of mTOR kinase pathway in lung cancer. **Methods:** Ten patients with non-small cell lung cancer (NSCLC) – 5 adenocarcinomas (ADCs), 5 squamous cell cancers (SCCs) – were included in current study. After the tissue microarray construction from the surgically resected specimens we used immunohistochemistry to evaluate the expression of p-S6, p-mTOR, Rictor and p-PTEN in the prechemotherapeutic bronchoscopic biopsies and the postchemotherapeutic surgically resected tumors of each patient. **Results:** The expression of p-S6 and p-mTOR correlated well in the bronchoscopic samples, both markers showed high mTOR activity. The p-PTEN expression corresponded to the mTOR activity. The activity of mTOR signaling pathway was significantly higher in SCCs than in ADCs. In most cases we observed a decrease in the expression of p-S6 and p-mTOR in SCCs due to the neoadjuvant chemotherapy (p-S6: 5/5 cases, p-mTOR: 4/5 cases). In ADCs we found mainly minor changes, however, in many cases, the chemotherapy caused increased expression of the markers. The potential activity of mTORC2 was also significant, this can be deduced from the expression of Rictor. In the postchemotherapeutic surgical samples we observed higher expression of all markers in ADCs than in SCCs. **Conclusion:** Our results show, that the platinum-based chemotherapy reduces the activity of mTOR signaling pathway in SCCs, while in ADCs the mTORC1 and/or mTORC2 activity was increased in most cases after chemotherapy.

POSTER SESSION III. - CLINICAL SCIENCES

R. Neurology - Ophthalmology - Dentistry - Behaviour Sciences - Immunology-Cell Biology

R/1. NEUROPROTECTIVE EFFECT OF EARLY POSTNATAL ENVIRONMENTAL ENRICHMENT IN A RAT MODEL OF PARKINSON'S DISEASE

**Gabor Horvath, Adel Jungling, Zsolia
Nozomi Karadi, Dorottya Csilla Farkas,
Gergely Novogradez, Anna Kovacs, Peter
Kiss, Balazs Gaszner, Dora Reglodi,
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Hungary**

Keywords: Neuroprotection, environmental
enrichment, Parkinson's disease, rat,
substantia nigra

Introduction: Environmental enrichment is a popular strategy of neuroprotection. The aim of our study was to investigate the effect of early postnatal environmental enrichment in a rat model of Parkinson's disease in adulthood. Methods: We used adult Wistar rats in the experiment. The animals of the standard group were placed under regular circumstances. For environmental enrichment, we placed rats in larger cages, supplemented with different toys during the first five postnatal weeks. Two months later the rats were treated with unilateral injections of 2 µl 6-OHDA (5 µg/ 1 µl) into the left substantia nigra, control animals received 2 µl physiological saline. Behavioral experiments were done preinjury, and 1 & 10 days after the operation. Tyrosine-hydroxylase immunohistochemistry was performed after the behavioral testing to label dopaminergic

cells of the substantia nigra. Results: We found that physiological saline did not make significant difference between the treated and non-treated side of the brain. The 6-OHDA treatment made significant cell loss in the standard group: more than 40% of dopaminergic cells died, while in rats which were kept in enriched environment the cell loss was significantly lower. Conclusions: Our experiments provided evidence for protective effect of early postnatal environmental enrichment in adulthood, because rats under regular circumstances showed more severe acute neurological signs and dopaminergic cell loss after 6-OHDA lesion of the substantia nigra compared to animals grew up in environmental enrichment. Support: PTE-MTA „Lendület” Program, Arimura Foundation, OTKA K104984, PD109644, TAMOP 4.2.2.A-11/1/KONV-2012-0024, TAMOP 4.2.4.A/2-11-1-2012-0001, „National Excellence Program”, Bolyai Scholarship.

R/2. DETECTION OF DIFFERENT GENE EXPRESSION IN HUMAN RESIDUAL EPITHELIAL CELLS OF ANTERIOR LENS CAPSULE AFTER MANUAL AND FEMTOSECOND LASER PERFORMED CAPSULORHEXIS

**Andrea Krisztina Sükösd MD¹, Judit
Rapp², Dia Feller², Prof. Dr. Judit E.
Pongrácz², Andrea Kerek³, Beáta Gáspár³,
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Keywords: apoptotic profile, recovery,
epithelial cell, inflammatory profile, anterior
lens capsule

Introduction: Cataracts occur commonly and incidencies increase with age. Nowadays, two surgical methods are available in Hungary, the conventional manually performed and femtosecond laser-assisted cataract surgery. We hypothesized that the laser-assisted method causes less stress to the epithelial cells; therefore the regeneration of epithelial layers is faster than in conventional manual surgery. To investigate the above theory cell culture and molecular studies were performed. **Methods:** Samples were obtained from patients who were diagnosed with cataract (n=12) and were operated on either using the traditional or the laser-assisted method. The removed anterior lens capsules were maintained up to 14 days in tissue culture to obtain information about the residual epithelial cells. Ultrastructural investigation was performed using transmission electronmicroscope. Changes of gene expression levels were analyzed with qRT-PCR targeting genes regulating apoptotic, proliferative and inflammatory processes (p53, Bcl2, CyclinD1 and Cytokeratin-7, TNFalpha, IL-6, IL-8). **Results:** Several ultrasturctural changes in both surgery samples were observed. To study the molecular background of the structural changes, we examined four genes related to apoptosis, the cell cycle and differentiation. Our results showed that the Bcl-2 expression levels in both samples were reduced which makes epithelial cells more sensitive towards apoptotic signals. In contrast to manual surgery samples the laser-assisted samples showed more elevated levels of Cyclin-D1, indicating more active proliferation. Investigation of prominent inflammatory cytokine expression TNFalpha, IL-6 and IL-8 revealed a marked increase in IL8 mRNA levels in the manual samples. **Conclusion:** In the present work we compared two surgical methods in terms of epithelial cell survival and inflammatory

cytokine profile. Based on the electronmicroscopic images and the molecular analysis, the manually performed samples showed a more active apoptotic and inflammatory profile, supported by decreased Bcl-2 and increased IL-8 expression levels. Additionally, the laser-assisted samples showed higher division rate and lower apoptotic levels indicating a faster recovery rate.

R/3. INVESTIGATING THE RETINOPROTECTIVE EFFECTS OF PACAP EYE-DROP IN ISCHEMIC RETINOPATHY

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Keywords: PACAP, BCCAO, retina ischemia, retinal layers

Pituitary adenylate cyclase activating polypeptide (PACAP) has neuroprotective effects in different neuronal and retinal injuries. Retinal ischemia can be effectively modelled by permanent bilateral common carotid artery occlusion (BCCAO), which causes chronic hypoperfusion-induced degeneration in the entire rat retina. The retinoprotective effects of PACAP 38 and vasoactive intestinal peptide (VIP) are well-established in ischemic retinopathy. Our research group previously investigated and proved the retinoprotective effect of intravitreal administered PACAP. However, little is known about the effects of PACAP eye-drop, which is an easier form to use in clinical practice. The aim of the present study

was to investigate the potential retinoprotective effects of PACAP 1-38 and 1-27 eye-drops in BCCAO-induced ischaemic retinopathy. Wistar rats (3-4 months old) were used in the experiment. After performing BCCAO, the right eyes of the animals were treated with PACAP 1-38 or 1-27 eye-drops (1 µg/drop). Each eye-drop contained different vehicles: saline, aqua destillate, thiomersalo, benzalkonium-chloride. The left eyes, serving as control eyes, were treated with the adequate vehicle. Sham-operated (without BCCAO) rats received the same treatment. Rats were treated by 2x1 drops a day for 5 days. Routine histology was performed 2 weeks after the surgery, cells were counted and the thickness of retinal layers were compared. According to our results the PACAP 1-27 solved in benzalkonium-chloride was the most retinoprotective eye-drop in ischemic retinopathy.

This research was supported by the European Union and the State of Hungary, co-financed by the European Social Fund in the framework of TÁMOP-4.2.4.A/2-11/1-2012-0001 'National Excellence Programs' OTKAK104984, PD109099, GVOP-3.2.1-2004-04-0172/3.0, TÁMOP-4.2.2.A-11/1/KONV-2012-0053, TÁMOP-4.2.2.A-11/1/ KONV-2012-0024, NAP, PTE-MTA Lendület Program, and Arimura Foundation

R/4. TOOTH DEVELOPMENTAL DIFFERENCES BETWEEN WILD TYPE AND PACAP-DEFICIENT MICE

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Keywords: PACAP, PACAP deficient mice, tooth development, Raman spectra, MicroCT

Teeth are derived from the ectoderm of the first branchial arch and the ectomesenchyme of the neural crest, therefore, their development shows similarities with the development of the nervous system. Pituitary adenylate cyclase activating polypeptide has protective effects in the nervous system and it plays a role in its development. PACAP-immunoreactive fibers have been found in the tooth pulp, but there is no data about the effect of endogenous PACAP on tooth development. Morphometric and structural comparison of the developing teeth was performed on native histological sagittal sections from the skull of 7-day-old wild type and PACAP-deficient mice. The structural analysis was carried out with Thermo Scientific DXR Raman microscope. In adult mice (1-year-old) morphometric, and hard tissue density measurements were done on prepared mandibles with Micro CT. During the morphometric comparison of the 7-day-old samples we found that the dentin was significantly thinner in the molars of PACAP-deficient mice. The Raman spectra of the enamel in the wild-type mice demonstrated a broader range of 1240/1270 ratio, indicating a higher diversity in secondary structure of enamel proteins. In the dentin of PACAP-deficient mice higher intracrystalline disordering in the hydroxyapatite molecular structure was found. With Micro CT the tooth volume, the pulp chamber and the density of the dentin was significantly smaller in the incisors of the adult PACAP-deficient mice. These observations suggest that PACAP plays a role in tooth development. PACAP-deficient mice show alterations in the tooth development compared to wild-type animals. Support: TAMOP 4.2.4.A/2-11-1-2012-0001 „National Excellence Program”, PTE-MTA „Lendület” Program, Arimura Foundation, OTKA K104984, TAMOP 4.2.2.A-

11/1/KONV-2012-0024, OTKA PD 109644, Bolyai Scholarship, PTE ÁOK Research Grant KA 34039 04/2013.

R/5. COMPLEMENT FACTOR H AUTOANTIBODIES B CELL EPITOPE ANALYSIS IN AUTOIMMUNE HAEMOLYTIC UREMIC SYNDROME

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Keywords: hemolytic uremic syndrome, autoantibodies, complement factor H

Introduction: One of the most common factors evoking acute renal failure in children is hemolytic uremic syndrome (HUS), the rare form of which is mediated by autoantibodies against complement factor H (FH). In patients with anti-FH autoantibodies mutation of FH related proteins (CFHR), most often CFHR1-3 is observed. FH domains 19-20 and the homologous ones of CFHR1 differ in two amino acids. This slight difference could result in a binding site for the antibodies on both FH and CFHR1. **Purpose:** B-cell epitope mapping of anti-FH autoantibodies, and investigation of the inhibitory effect of CFHR1 domains 4-5 on antibody binding to FH. **Methods:** We analysed 5, anti-FH IgG positive patients' sera taken in the first episode of the disease. As control sera of healthy children and patients' sera from remission served. The amount of reacting antibodies with certain peptides of FH and CFHR1 was measured by altered ELISA method. We used competitive

ELISA technique to investigate antibody binding to FH in presence of FH domains 19-20 and CFHR1 domains 4-5. **Results:** In controls enhanced reactivity was measured in three regions (AA1142-1156, AA1182-1196, AA1192-1216). In these regions appreciable antibody binding was observed in patients' sample, and in two more, in controls undetected positions (AA1157-1171, AA1177-1191). Antibody binding was detected in patients' sera to CFHR1, too. Although in competitive assays FH showed significantly stronger inhibition than CFHR1, both were capable to maximally inhibit antibody binding to FH. **Conclusion:** We identified specific epitopes localised on FH domains 19-20 in autoimmune HUS patients, further analysis of which might lead to the exploration of the autoantibody productions' mechanism. Besides we found that several surface epitopes of FH and CFHR1 determine the inhibition of antibody binding to FH, according to which the effect of CFHR1 is to be considered when applying plasmatherapy in acute phases of autoimmune HUS.

POSTER SESSION IV.

S. Pediatrics-Obstetrics & Gynecology -Surgery -Internal Medicine-Family Medicine-Orthopedics

S/1. COMPARATIVE ASSESSMENT OF QUALITY OF LIFE (QOL) AMONG THE 6-17 YEARS OLD PATIENTS SUFFERING FROM ISOLATED ALLERGIC RHINITIS (AR), ALLERGIC RHINITIS AND ASTHMA (AR+A), ISOLATED ASTHMA (A)

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Keywords: allergic rhinitis, asthma, quality of life, comparative assessment, AdolRQLQ, PRQLQ, PAQLQ

Introduction Depending on the severity of the examined symptoms of A and AR, it can significantly worsen the QOL. Processing of the data collected from the patients through questionnaires serves to demonstrate the QOL. **Method** Symptoms affecting the nose, eyes and other symptoms, practical problems, partial incapacity and the impact of the diseases, alteration of emotional life on QOL, have been surveyed with PRQLQs, AdolRQLQs, PAQLQs in groups of AR, AR+A, and A in 87 children with the mean age of 13.6years $\pm$ 2.9SD. The studied sample consists of outpatient and school surveys from capital and countryside. In each cases we used Mann-Whitney test. **Results** The results of the 67 PAQLQs show, that comparing with A, AR+A caused somewhat more setback in QOL, and of all the domains, the symptoms were the most affected, then the activity, followed by emotions. Considering the results of the 17 PRQLQs we can declare that eventhough the number of cases is low, QOL is mostly disturbed by the symptoms affecting the nose, followed by practical problems, partial incapacity, other symptoms and least by eye connected symptoms. Of the AR and AR+A groups the second shows slightly more severity in the domains of nasal symptoms, partial incapacity, and practical problems. The results of the 44 AdolRQLQs indicate that there is no remarkable difference between the AR and AR+A groups regarding the quality of life. The common problems, nasal symptoms, activities, then general symptoms, emotions and symptoms affecting the eyes are all involved. **Conclusion** The levels of QOL mostly disturbed by symptoms. The

rhinitis QOL doesn't differ statistically significantly in the groups of those suffering from isolated upper respiratory symptoms or comorbid asthma. Asthma QOL of the isolated A and the AR+A patients doesn't differ significantly. Surveying of QOL of comorbid respiratory allergies would need special questionnaires.

S/2. POSTPARTUM CONTRACEPTION IN SOUTH-EASTERN HUNGARY - PRELIMINARY RESULTS OF THE QUESTIONNAIRE BASED STUDY

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Keywords: postpartum contraception, lactational amenorrhoea, breastfeeding, sexual activity, menstruation after pregnancy

Introduction Predictors and influencing factors of the choice of contraceptives in the postpartum period have scarcely been investigated. **Objective** The objective of our study is to determine the exclusive breast-feeding practices, return of menstruation, sexual activity and contraceptive practices among breast-feeding mothers in the 6 weeks, 6 months and 12 months after the delivery. **Patients and methods** All women who delivered between 1st September 2013 and 24 th March 2014 in the Department of Obstetrics and Gynaecology, University of Szeged were invited to answer the questionnaire A structured questionnaire was

sent by post or partakers will receive a code to a secured webpage by email. Results Data of 200 6th week questionnaire were analysed. 12.6 % of women used oral contraceptives, at 6 week after delivery. 3.7 % of women reported that used intrauterin device. 4 % of participants was levonorgestrel containing IUD user and 2.7 % of the study group was underwent sterilisation. 53.2 % of the 200 couple was used not reliable contraceptive methods as (40.7%) condom, (10.7%) withdrawal, (0.9 %) vaginal douche and (0.9%) spermicide. 18.4 % of women not used any contraceptive methods at 6 weeks after delivery during the study period. Conclusion According to our best knowledge this is first study in Hungary regarding the postpartum contraceptive practice, sexual activity and breastfeeding pattern. Acknowledgement: The project was supported by the European Society of Contraception and Reproductive Health.

S/3. EFFECT OF DECREASING PATHOGEN MICROBES ON THE WOUND SURFACE FOR THE HEALING OF CHRONIC WOUNDS

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Keywords: chronic wound, lower limb, modern techniques, ulcer, decrease bacteria CFU

Introduction In Hungary at least 80% of lower limb amputations caused by diabetes mellitus or vascular diseases. These kinds of circulation defects could manifest as leg ulcers. Usually these ulcers turn into chronic wounds and infected by several kinds of microbes -mainly bacterias-, so their managemant is really hard. The fact is that lower amount of bacterias in the wound means better chance to heal. Our group wanted to prove the effectiveness of modern

devices and methods used by us during the wound managemant. Methods Our gruop use Versajet II hydrosurgery system combined with octenidine-dihydrochloride desinfectant and nano crystal coating. We chose the Envirocheck Contact TVC to make examinations, which give semi-quantitative result. We took samples from 17 patients in total 20 times from the wound surface before and after the hydrosurgery treatment to count the number of bacteria colony forming unit (CFU). Our new project is still in progress in which we expanded our trial to take samples not just after the hydrosurgery treatment but after a one minute contact time of octenidine-dihydrochloride. Results The samples we took were evaluated by me with help of a microbiologist and a density chart. We found before the treatment the CFU was 350 or more pro cm2 while after the treatment except for two cases the CFU was 58 or less pro cm2 . After the use of octenidine -dihydrochloride the maximum CFU was 17 or less pro cm2 until that time, but this trial has not finished yet. Conclusion All in all we can say the right usage of these kinds of modern devices and methods can dramatically decrease the CFU of pathogen microbes on the wound surface, which means there is a bigger chance for total wound healing in compare with other conservative therapies used for chronic wound management.

S/4. RISK-BENEFIT DECISION MAKING FOR TREATMENT OF INFECTED AORTIC GRAFT COMPLICATION

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Keywords: atherosclerosis, aortobifemoral bypass surgery, silver graft prosthesis,

infected aortic graft, autologus transplantation

Atherosclerosis, aortobifemoral bypass surgery, silver graft prosthesis, infected aortic graft, autologus transplantation, Introduction: Atherosclerosis, a disease of the large arteries, is the primary cause of heart disease, stroke and occlusion of the peripheral arteries. In westernized societies, it is the underlying cause of about 50% of all deaths. Different medications are available to protect against atherosclerosis, but in case of the inefficiency of the conservative therapy, reconstructive vascular surgeries are reasonable. These surgeries have already well known and treated consequences, such as bleeding, neurological and metabolic disorders, but the most threatening and still unsolved complication is septic graft infection which can aggravate the healing or the accidental operations. We would like to describe a solution of the infected grafts in the following case. Methods: 58-year-old female patient with iliofemoral occlusion and trophic disorder was scheduled to undergo aortobifemoral bypass surgery with Y-shaped prosthesis implantation three years ago. Despite of the medications septic complications and graft occlusion occurred and these disorders led to Y-shaped prosthesis change to a silver graft. As an early complication, graft failure evolved again and deep vein reconstructive surgery with much higher operational risk was required to be performed to solve the septic graft infection. Results: Deep vein autologus transplantation despite of its much higher operational risk is likely to reduce the septic graft infections and the tolerance of the patient is better than after a silver graft surgery. Conclusions: We can make conclusions that the most trustworthy but also most straining method is the reconstruction using an autologus graft, but at the same time

the importance of the technical/infrastructural possibilities, the loadability and physical status of the patient should be also highlighted to set up the right surgical strategy.

S/5. RARE ANTIBODIES IN SYSTEMIC SCLEROSIS AND THEIR CLINICAL ASSOCIATIONS

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Keywords: systemic sclerosis, autoantibodies, RNA Pol III, Th/to, Topoisomerase

Introduction: Systemic Sclerosis (SSc) is a rare autoimmune disease characterized by vascular abnormalities and extent fibrosis. The main types of the disease are the limited cutaneous systemic sclerosis (lcSSc) and the diffuse cutaneous systemic sclerosis (dcSSc). Almost 100% of the patients carry antibodies. Objective: To investigate the presence of rare antibodies and their clinical associations in a large series of patients and compare our results with previously published data on the correlation of presence of these antibodies and the clinical manifestation. Patients and methods: Patients carrying the different antibodies were chosen from our register. Fisher exact test was used to compare the different subgroups. Results: Among the 82 anti-centromere antibody positive patients (23.5%) lcSSc and female gender were significantly frequent ($p < 0.05$). Anti-topoisomerase antibody showed 39% of prevalence. The presence of the antibody was associated with the diffuse subset, digital ulcers and pulmonary involvement. Among patients with anti-RNA polymerase III positivity dcSSc and male gender appeared significantly often ($p < 0.05$). The coexistence of anti-RNA Polymerase III and interstitial lung disease was more frequent in our

patients compared to patients from other centers. Antibody to Th/To complex was present in the 8.8% of the examined patients. The presence of pulmonary arterial hypertension and lcSSc did not show significant difference among patients carrying anti-Th/To antibody, but a tendency of higher prevalence was present. Out of the examined patients 8 showed anti-U1RNP positivity, 9 anti-U3 positivity, 15 anti-Ku positivity, 1 anti-PmScl positivity and 12 anti-Ro52 positivity. Conclusions: Based on the presence of the antibodies we can draw conclusions on the clinical manifestation. The presence of rare antibodies, especially the presence of anti-RNA Pol III, shows large prevalence.

S/6. GAIT ANALYSIS IN FLEXIBLE FLATFOOT

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Keywords: Flexible flatfoot, gait analysis, kinematics, kinetics, dynamic

Purpose: Flexible flatfoot is one of the most frequent disorders in childhood. General ligament laxity, obesity, valgus knee deformity are the most commonly mentioned factors for etiology. Several clinical tests can be assessed for evaluating calcaneal valgus position, the height of the longitudinal arch, the abduction and pronation of the forefoot usually by static, weight bearing position. However less is known about these parameters under dynamic conditions. The aim of this study was to describe foot kinematics during gait in flexible flatfoot. **Methods:** 23 patient with flexible flatfeet were included in the study compared to 66 healthy volunteers. Diagnosis of flatfoot based on the clinical finding of severe

calcaneal valgus position. 3D gait analysis was performed with Oxford Foot Model marker protocol. 3D kinematics of the hindfoot and forefoot such as the dorsal/plantar flexion- and the valgus/varus position of the hindfoot and the abduction/adduction- and the pronation/supination of the forefoot were measured. The frontal plane kinetics of the hip-, the knee- and the ankle were also evaluated. Results are presented as means $\pm$ SD. Results: In terminal stance -16,18 $\pm$ 9,00° vs. 3,5 $\pm$ 2,5° of calcaneal valgus position and decreased plantarflexion was observed in the flatfooted patient group (-9,75 $\pm$ 4,9° vs. -20,00 $\pm$ 7,0°). In midstance forefoot abduction (-14,78 $\pm$ 9,82° vs. 3,00 $\pm$ 6,61°) and forefoot supination was measured (24,23 $\pm$ 17,25° vs. 3,50 $\pm$ 4°) in the flatfooted group. Assessing frontal plane kinetics, external varus momentum was decreased in the knee (0,14 $\pm$ 0,04 Nm/kg vs. 0,60 $\pm$ 0,14 Nm/kg) and also in the ankle (-0,0026 $\pm$ 0,0049 Nm/kg vs. 0,17 $\pm$ 0,13 Nm/kg). Non-significant kinetic changes were observed in the hip joint. Conclusions: In this study authors showed the biomechanical changes in pediatric flexible flatfoot under dynamic conditions. Observations are presented on how flatfoot interfere with physiologic gait. Oxford Foot Model is a suitable tool for quantification in foot kinetics and kinematics under dynamic conditions in flexible flatfoot.

SPECIAL TEACHING SESSION

T. 2014, the year of COPD

Session of Hungarian Society of Pulmonologists

T/2. CURRENT ISSUES OF ASTHMA BRONCHIALE

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Keywords: asthma bronchiale, control, inhaled corticosteroid, therapy, phenotyping

Studies show that more than 35-40% of asthma patients are inadequately controlled despite treatment recommendations of professional guidelines. There can be many reasons. The well controlled asthma treatment aims to maintain the level of control that can be achieved with current and future asthma ensuing risk reduction. The most important determinants of increased future risk: acute exacerbation, the current inadequate level of control, smoking, drug-induced side effects, unstable disease and the rapid decline in lung function. We can improve the first four of these with proper maintenance therapy and patient's cooperation. There is a consensus regarding that asthma therapy has developed greatly over the past 20 years. This development didn't stop yet. Important pillars have formed during the development of asthma therapy over the past decades. Pillar 1.: the therapy is based on the reduction of inflammation. The appearance of inhaled corticosteroids was a milestone in the treatment of asthma. It is well known that only ICS reduces mortality. Pillar 2.: ICS+ LABA combination further improved the quality of life. Pillar 3.: the increase of deposition in the lungs has further improved the efficacy of the treatment. Pillar 4. flexibly adapted treatment on symptoms resulted in significant reduction in exacerbations. Pillar 5.: customizing the therapy, which is about giving the right therapy to the right patient in time to achieve the most effective treatment for asthma therapy. This is based on phenotyping the patients, with the refinement taking place today. Phenotyping is important to classify patients into subgroups which provide prognostic information and allow us to better determine individualized therapies that can further improve the clinical results. Powerful

phenotyping of patients can increase the safety and clinical benefits beyond conventional therapy and reduce the development of undesirable social and insurance expenses.

T/4. STATE-OF-THE-ART LUNG CANCER THERAPY

1 Zoltan Lohinai, 1 Gyula Ostoros, 2 Erzsebet Raso, 2 Jozsef Timar, 3 Katalin Fabian, 4 Ilona Kovalszky, 3 Judit Moldvay, 5 Balazs Hegedus, 1 Balazs Dome

1 National Koranyi Institute of Pulmonology, Budapest, Hungary;

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Keywords: Lung cancer, EGFR mutations, KRAS mutations, Epidemiology, Targeted therapy

Lung cancer is the most frequently diagnosed malignancy worldwide and Hungarians have the world's highest death rates. The term lung cancer represents a rather heterogeneous group of diseases including conditions of varying etiology and molecular background. Previously, it was sufficient to differentiate - based on the histopathological subtype - between small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) for the therapeutic strategy. However, the new molecular diagnostic and therapeutic

possibilities have altered dramatically the classification and management of NSCLC. Nevertheless, the determination of "driver" oncogenic mutations (e.g. KRAS, EGFR, ALK) that play a decisive role in tumor development can help to identify targets for therapy. Additionally, the development of rapid and accurate molecular biological methods (such as Next Generation Sequencing (NGS) and Mutant-Enriched sequencing) revolutionized the identification of biomarkers. The complex treatment of advanced NSCLC includes chemotherapy, irradiation and targeted therapies such as anti-angiogenesis drugs, EGFR tyrosine kinase inhibitors and ALK inhibitors. Immunotherapy also seems to be a promising future direction. Recently, our Tumor Biology Research Group at the National Koranyi Institute of TB and Pulmonology has demonstrated that subtype-specific molecular analysis can identify clinically relevant subgroups of patients (rare EGFR mutants) that ultimately may influence treatment decisions. On the other hand, we pointed out - in the so far largest cohort of Caucasian patients - that clinical responses to classical therapeutic regimens within a molecular subgroup (KRAS mutation subtypes) may also vary. We also have shown that there are basic differences in genetic alterations between smokers and non-smokers. Identification of the so called 'driver' oncogenic mutations with the most advanced molecular techniques plays a decisive role in the identification of different tumor types and therapy targets. This opens the way to precision medicine in this challenging and also dynamically emerging field of oncology.

X. HOW-TO-SESSION

X/2. REWARDS OF BEAUTY: THE OPIOID SYSTEM MEDIATES SOCIAL MOTIVATION IN HUMANS

Olga Chelnokova, Bruno Laeng, Marie Eikemo, Jeppe Riegels, Guro Løseth, Hedda Maurud, Frode Willoch, and Siri Leknes

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Keywords: human brain opioid system, social motivation, social reward, facial attractiveness

Affiliation is crucial for healthy human development. Many psychiatric conditions are associated with disturbances in affiliation and attachment. Facial attractiveness is an important cue which guides affiliative responses. The human brain finds reward in looking at beautiful faces, and the limbic reward system has a high density of μ -opioid receptors. In non-human animals, opioid signaling is essential for food reward and affiliative behavior. In a double-blind, placebo-controlled study, we used a novel psychopharmacological combination in healthy humans to show that opioid agonism increased and opioid antagonism decreased, both aesthetic evaluation of and motivation for viewing opposite-sex faces. The opioid manipulations most strongly affected the most valuable stimuli in evolutionary terms, i.e. the most beautiful women. The causal role of the opioid system in mediating human social motivation demonstrated here corroborates the importance of the opioid system for attachment, as demonstrated by rodent and primate research.

X/3. AND STILL ABOUT MEDICAL SPELLING

Éva Kovács, András Bíró

Semmelweis University Centre of Language Communication

Keywords: orthography/orthographia, diagnostics/diagnostic CT, MR(I), Latin-Greek-English

How to write or how to pronounce the technical terms used in oral or written information contained in medical texts, text books or at conferences is still an ever green issue for both the medical professionals and patients alike. Should the terms be written in Hungarian, Latin or ancient Greek? Which

words belong to the strictly taken technical terminology, which have gone into common usage, the everyday language? One thing is sure: the usage has been chaotic since the beginning, far from being uniform and putting terminology in order is beyond hope. In other word we have the diagnosis but we do not have the right therapy of the disease. What can we language teachers do? Can we contribute anything to the solution of the matter at all?

EDITOR'S NOTE:

All abstracts available to the Editorial Office as of July 21, 2014 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,
Istvan Somkuti MD PhD**

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