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**WELCOME TO THE 3<sup>rd</sup> ANNUAL BALATONFURED STUDENT MEETING**  
**Tamas Peredy MD, President HMAA**

2010 Balatonfured HMAA Student and Alumni Conference

It gives me great pleasure to welcome you to the 3<sup>rd</sup> Annual HMAA Conference sponsored by the Hungarian Medical Association of America with generous support by the Hungary Chapter of the HMAA and the Student and Alumni Club of the HMAA.

The Hungarian Medical Association of America (HMAA) established in 1968 exists to preserve and promote the rich traditions and contributions by Hungarians to the practice of Medicine. The HMAA provides support for a medical student and fellow exchange between Hungary and the United States. The HMAA also encourages transatlantic collaboration through its annual October scientific meeting in Sarasota and through awards given to promising young researchers.

The Balatonfured conference is an opportunity for Hungarian students from all the Hungarian Medical Universities to showcase their research in a relaxed lakeside environment. Presentations in English are encouraged and the opportunity is available for the winner to travel to Sarasota to present their work. Social activities are planned so that participants may meet one another as well as HMAA leadership who are physicians in clinical practice in the United States.

The conference could not go on without the generous contributions of a number of individuals and institutions. I would like to thank Dr Gabor Veress, the Chief Physician and Director of the State Heart Hospital in Balatonfured for providing the venue. I would also like to thank Drs David and Adam Tarnoki for their vision and skills in making this conference not only a reality but a success. Dr. Istvan Somkuti, the incoming President of the HMAA, has worked tirelessly to review, edit and format the abstracts for publication. A word of appreciation also goes out to Dr Laszlo Csathy and others for their even-handed and fair judging of the presentations.

I wish all participants a productive and pleasurable experience. Like past conferences, I expect this year's gathering to be a great success.

Sincerely,

Tamas R. Peredy, FACEP  
President, HMAA

**ABSTRACTS**  
**3<sup>rd</sup> Annual Student Meeting of the Hungarian Medical Association of America**  
**Balatonfured, Hungary, August 20 – August 21, 2010**



## PEDIATRICS SESSION

### N2 AMBULATORY ARTERIAL STIFFNESS INDEX (AASI) IN RENAL TRANSPLANT CHILDREN

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**Keywords: stiffness, transplantation, children**

**Introduction:** Cardiovascular disease is the leading cause of death among renal transplant patients (Tx). AASI has been suggested as a marker of arterial stiffness and a predictor of cardiovascular morbidity and mortality.

**Aims:** Our aim was to evaluate the factors influencing AASI after transplantation.

**Methods:** 62 Tx patients were investigated and 29 Tx children were followed up for a year. The regression slope of diastolic on systolic blood pressure based on 24-h recordings was computed for each participant. AASI was defined as: 1-regression slope.

**Results:** AASI was independent of age and gender. There was a positive correlation between AASI and body mass index (BMI) Z-score ( $r=0.29$ ;  $p=0.018$ ). There was a connection between the stiffness index and the pulse pressure (active period of ABPM:  $r=0.387$ ;  $p=0.001$  passive period:  $r=0.312$ ;  $p=0.015$ ). There was a negative correlation between AASI and nocturnal diastolic blood pressure fall ( $r=-0.30$ ;  $p=0.019$ ). AASI did not differ significantly in the first year of follow up.

**Conclusion:** AASI representing arterial stiffness shows correlation with the nocturnal blood pressure fall, which is a well-known cardiovascular risk factor, and with pulse pressure—which also refers to the Windkessel-effect of the vascular system. The relationship between AASI and body mass index (BMI) calls attention to the harmful effect of obesity among renal transplant children.

### N3 INCREASED ARTERIAL STIFFNESS IN CHILDHOOD OBESITY

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**Keywords: Obesity; arterial stiffness; pulse wave velocity**

Childhood obesity increases the risk of cardiovascular morbidity due to accelerated atherosclerosis. The evaluation of the pulse wave velocity (PWV) has been established as a useful measure to characterize arterial stiffness.

**Aim:** a) to assess the connection between PWV, impaired glucose tolerance (IGT) and insulin resistance; b) to establish the metabolic parameters associated with the altered cardiovascular status.

**Methods:** PWV was measured by applanation tonometry (PulsePen device) ( $n=35$ ;  $13.85\pm 2.66$  years) and was expressed as standard deviation score (PWV-SDS). Glucose and insulin levels were measured, HOMA-index (Homeostasis Model Assessment) was calculated.

We used two patient classifications: one based on 120' glucose values: IGT or manifest diabetes (IGT-DM,  $n=7$ ) vs. normal glucose metabolisers (NG,  $n=28$ ); the second was based on HOMA-index: insulin resistant (IR,  $\text{HOMA}\geq 2.5$ ;  $n=10$ ) vs. insulin sensitive (IS;  $n=24$ ).

**Results:** Patients with pathological glucose metabolism had increased arterial stiffness: PWV-SDS of the IGT-DM group was increased compared to controls ( $1.45$  vs.  $-0.11$ ,  $p=0.001$ ). Further, patients in the IR group had elevated PWV-SDS too ( $0.95$  vs.  $-0.09$ ;  $p=0.02$ ). There was a significant difference in the insulin 120' value ( $p=0.04$ ), the BMI-SDS ( $p=0.03$ ), systolic blood pressure-SDS ( $p=0.02$ ), the triglyceride ( $p=0.01$ ) and HDL ( $p=0.02$ ) concentrations and the LDL/HDL atherogen index ( $p=0.03$ ) compared with IS.

**Conclusion:** The altered metabolic parameters in the morbid obese children are related to the increased arterial stiffness. Increased PWV is an early sign of altered arterial elasticity. Longitudinal interventional studies are needed to prove the reversibility of the pathological arterial processes.

### N4 MOLECULAR ANALYSIS OF PATIENT WITH CONGENITAL ADRENAL HYPERPLASIA, 21-HYDROXYLASE DEFICIENCY (CAH 21OHD) IN HUNGARY

**Judit Feher**

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**Keywords: congenital adrenal hyperplasia, 21-hydroxylase deficiency, mutation analysis, chimera, bidirectional sequencing**

CAH 21OHD is an autosomal recessively inherited disorder, which has three clinical forms: the simple virilizing (causing intermediate external genitalia in female newborns); the classic salt-wasting, (with virilization, hyponatremia and hyperkalemia) and the non-classic form, (asymptomatic in the neonatal period). CAH 21OHD is caused by mutation of CYP21A2 gene, located in the 6p21.3 region. It is 3.3 kb long, contains 10 exons, and has a 96% homologous pseudogene variation, CYP21A1, located in the same region. In more than 95% mutations are caused by intergenic recombination between the pseudogene and the "normal" gene. In 20% of these cases a ~30 kb long fragment is deleted due to unequal crossing over, producing a so called "chimeric" gene with a 5'end characteristic of the CYP21A1 gene, and 3'end characteristic of the CYP21A2 gene.

Setting the detection of the ~30 kb long deletion is important in the prenatal diagnostics. We applied bidirectional sequencing on the complete CYP21A2 gene, and used allele specific PCR to detect the chimeric gene and locate the breakpoints. Thus the detection of rare mutations was also possible: we could detect the p.R426H mutation in one patient, and the p.N493S mutation in another one, both in heterozygous form. Out of 171 suspected carriers, we could detect the ~30 kb long deletions on both alleles in 17, and on one allele in 81 patients.

The breakpoints of the chimeric genes in the studied patients were in intron 2, 3 and 6, which suggests that crossing over hot-spot regions can be found at these points.

#### **N6 THE PROGNOSTIC VALUE OF AMPLITUDE-INTEGRATED EEG ON OUTCOME AFTER HYPOXIC-ISCHEMIC ENCEPHALOPATHY IN FULL TERM INFANTS UNDER HYPOTHERMIA**

**Linda Pusztai, Anna Judit Csekő**

**1st Department of Pediatrics, Semmelweis University, Budapest, Hungary**

**Keywords: Hypoxic-ischemic encephalopathy, amplitude-integrated EEG, hypothermia**

**Introduction:** The cot-side amplitude-integrated electroencephalograph (aEEG) is essential in the early diagnostics and assessment of prognosis of hypoxic-ischemic encephalopathy (HIE) in newborn. The hypothermia treatment introduced in the past few years has reduced mortality and morbidity of HIE. We assume that the previously assessed prognostic value of aEEG decreases due to hypothermia treatment.

**Population and methods:** We detected continuously from the first days of life, biparietal aEEG's of n=51 (mean [SD]) gestational age: 38.6 ( $\pm$ 1.9) weeks, gestational weight: 3107 ( $\pm$ 538) g asphyxiated newborns treated with hypothermia. For the evaluation of the aEEG's we applied a score describing the severity of HIE from 0 to 4 set down by Hellström-Westas (2006) at every 6 hours. To compare the aEEG findings with the long-term outcome we used the Bayley neurodevelopmental test taken at 18-24 months of life.

**Results:** In predicting negative outcome the positive likelihood ratio (LR+) of the 0-2 aEEG score between 0-6, 6-12, 12-24, 24-48, and 48-72 hours of life was 1.56, 2.02, 3.75, 6.42 and 8.5 respectively. The LR+ of the 0-1 aEEG score was higher than the LR+ of the 0-2 aEEG score at every interval.

**Discussion:** We were the first to analyze the prognostic ability of aEEG on long-term outcome in asphyxiated newborns under hypothermia. We found that it is notably lower than the previously published results assessed on normothermic conditions. However the default of early (between 12-24. hours of life) progress in the background activity accurately predicts poor long-term outcome.

#### **N7 SPECTRAL ANALYSIS OF ENCEPHALOGRAPHIC ARTIFACTS INDUCED BY SHIVERING UNDER HYPOTHERMIA TREATMENT IN NEWBORN**

**Anna Judit Cseko, Linda Pusztai**

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**Keywords: shivering, NDMR, hypothermia, EEG**

**Objective:** To identify and characterize EEG artifacts presumably induced by tremor in skeletal muscles due to hypothermia treatment.

**Methods:** We analyzed changes in biparietal EEGs after administration of short acting non-depolarizing muscle

relaxant (NDMR) in ventilated asphyxiated newborns under hypothermia. From the detected 21 NDMR expositions 5 were chosen, where no other central nervous system effectors were given within 30 minutes and a definitive change was detected on the amplitude-integrated EEG after the NDMR exposition. Power spectral density (PSD) in the range of 0-30 Hz was composed after discrete Fourier transform of n=20 3 seconds long EEG samples chosen from 3 minutes before (BR) and after (AR) the NDMR exposition. We compared the frequency patterns of the BR and AR samples.

**Results:** In every studied newborn the PSD in the range over 9 Hz was significantly ( $p < 0.05$ ) lower in the AR than in the BR samples. The dominant frequency component of the EEG decreased by NDMR exposition was 16.18 ( $\pm$ 0.78) Hz. The changes found in the PSD in the range under 10 Hz show inter-individual diversity.

**Conclusion:** Based on NDMR effect the skeletal muscle shivering is represented by 15-18 Hz waves on the EEG. The detected EEG changes in for the newborns physiologically characteristic frequency range ( $< 10$  Hz) suggest that either the lower muscle-tone and afferentational excitation caused by NDMR modifies cerebral background activity, or the NDMR has a central effect getting through the blood-brain barrier damaged by asphyxia.

#### **N9 ORAL ANTICOAGULANT THERAPY IN CHILDREN WITH CONGENITAL HEART DISEASE**

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**Keywords: vitium, pediatric, anticoagulation, warfarin, acenocoumarol**

Survival rates of children with congenital heart disease significantly increased in the last decades as a result of improved diagnostic, surgical and interventional techniques. A number of children underwent complex corrective cardiac surgery or heart valves implantation have to be anticoagulated through their whole life, which is generally managed with oral vitamin K antagonists.

Many aspects of hemostasis are age dependent and drug metabolism is also altered in children. Therefore the aim of this study was to examine the applicability of the adult protocol in the children.

We compared retrospectively the INR values during acenocoumarol and warfarin management between 1996 and 2009. The INR was measured in 12 children, who are cared by the Pediatric Clinic at University of Debrecen.

We determined that the deviation of the INR values from the therapeutic range significantly decreased with warfarin therapy compared to acenocoumarol ( $0.28 \pm 0.02$  vs.  $0.35 \pm 0.03$ ,  $p < 0.05$ ). Bleeding complication manifested in 2 patients, the incidence was 0.8/year and the INR-average was  $4.74 \pm 0.55$ . Osteoporosis was identified in 2 children treated with acenocoumarol. We observed that the INR values - measured during an infection - were often (70.27%) deviate from the therapeutic range (by  $0.71 \pm 0.19$  in average,  $p < 0.001$ ). Among

the effect modifying factors of the coumarins: protein C deficiency, FV Leiden mutation and protein losing enteropathy occurred in 1 case each.

Our examination suggests that warfarin is more appropriate for the children's permanent oral anticoagulation after the corrective heart surgery, because it decreases the INR dispersion, so it could provide a balanced effect.

#### **N10 POLYCYSTIC OVARY SYNDROME IN CHILDHOOD**

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**Keywords: PCOS, hirsutism, obesity**

Polycystic ovary syndrome (PCOS) is one of the most common endocrine-metabolic disorders among women. The clinical features -caused by hyperandrogenism- are menstrual irregularities, hirsutism and acne. These symptoms are usually combined with obesity and insulin resistance.

In this study, data of 30 girls with PCOS -who were nursed by our department, between 2000 and 2009- will be presented.

Their ages were  $15.42 \pm 1.69$  years and their BMI was  $32.57 \pm 4.79$ . We created 2 groups on the basis of BMI: "obese" and "non obese". The aim of our study was to compare clinical and biochemical measurements in the 2 groups. We investigated physical status (hirsutism, acanthosis nigricans, obesity), sex-steroid levels, insulin resistance, dyslipidemia, and ultrasonography of the ovaries.

All of the patients had hirsutism. Prevalence of menstrual disorders in girls with PCOS was 73.3%, and 40% of them had acanthosis nigricans, which can be a physical marker of insulin resistance. Only 23.3% of the patients had obviously positive ultrasonography findings.

The most common findings of sex-hormones were: elevated LH/FSH ratio (1.8) and reduced SHBG levels.

Although, all of the measured parameters showed higher level, among the obese patients, we found only one statistically significant difference. During OGTT, the obese group had significantly higher plasma glucose level at 120 min. Furthermore, the prevalence of IFG was 3.33% and the IGT was 13.3%.

In conclusion, PCOS is not only a problem of adulthood. Hirsutism and menstrual irregularity combined with metabolic disorders put serious pressure on girls and their family and they may require extensive treatment.

#### **RADIOLOGY-BIOPHYSICS SESSION**

#### **N12 THE INFLUENCE OF FECAL TAGGING ON DIAGNOSTIC EFFICIENCY OF VIRTUAL COLONOSCOPY**

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**Keywords: virtual colonoscopy, CT colonography, fecal tagging**

**Purpose:** The purpose of this study is to evaluate the diagnostic efficiency of virtual colonoscopy in detecting polyps and colorectal cancer with and without fecal tagging compared with optical colonoscopy as gold standard.

**Materials and methods:** Multicentric retrospective study, reviewing the CT colonography and colonoscopy findings of 142 symptomatic patients between September 2005 and April 2010 (58 male, 84 female, mean age  $62.5 \pm 11.1$  years SD). The examinations were executed in 2 CT and 3 endoscopic laboratories with an average difference of 54.9 days. 64 patients (45.0%) received oral contrast agent for fecal tagging during the bowel preparation, the other 78 patients (55.0%) did not receive any. The CTC findings were compared to the same segment's findings examined with colonoscopy. The findings were separated by type: tumours and polyps. The polyps were sorted by size (<5 mm; 5-10 mm; >10 mm). Statistical analysis was made by using MedCalc software.

**Results:** The difference between detection rate of CTC and colonoscopy among polyps and tumours was not significant ( $p > 0.05$  each). Both sensitivity and specificity for cancer were 100%, irrespective of the preparation. The per-polyp sensitivity/specificity for polyps 10 mm or larger was 100%/98.3% in the tagged group, 100%/100% in the untagged group. These results of polyps 5-10 mm were 100%/98.3% and 73.3%/80.7%. In case of polyps 5 mm or smaller the results were 72.7%/98.2% by tagged feces and 73.3%/80.7% in the untagged group. Only 3 of the 26 false positive findings were related to examinations with fecal tagging. The difference between positive predictive values of tagged and untagged group proved significant differences (both  $p < 0.01$ ) among the polyps <5mm and 5-10 mm.

**Conclusion:** With use of oral contrast agent during the preparation of CT colonography the diagnostic efficiency increases significantly by the diminutive size lesions.

#### **N13 THE ENDOLUMINAL TREATMENT OF THE RENOVASCULAR HYPERTENSION**

**Judit Niklai**

**Department of Radiology, University of Pecs, Pecs**

**Keywords: renovascular hypertonia, PTRAs, stent**

In the last few years more and more people suffer from hypertension. The cause of this is unknown, perhaps it develops due to environmental factors. But there are some cases, when you know the cause, for example renovascular hypertension. This disease can be treated with radiological interventions. The diagnostic study may also be curative. In our study we examined how we could successfully diagnose renal artery stenosis, which intervention method should we use to treat it and how the blood pressure changes, if we choose PTRAs or stent-implantation. In my presentation I will talk about the treatment options, about our outcomes and I will discuss two case studies.

#### **N14 CONTRAST AGENT-ENHANCED MAGNETIC RESONANCE RESEARCH OF THE LOWER EXTREMITIES**

**Szilvia Urai, Z. Morvay**

**Department of Radiology, University of Szeged, Albert Szent-Györgyi Medical and Pharmaceutical Center, Szeged**

**Keywords: MR angiography, Vasovist**

Up until now the MR investigation of the venous system of the body was only possible within limitations. Vasovist® is a contrast agent which is able to stay in the blood vessels for 1-2 hours, thereby making it possible to examine the condition of the venous system with the help of MR angiography. The veins of the 80 lower extremities of 40 patients have been examined. The superficial veins were analyzed in detail. We determined which anatomical structures could be seen and also searched for varicose veins, aneurysms and other abnormalities.

The great saphenous vein could be detected 77, while the small saphenous vein 67 times. Among the more significant main branches, the circumflex iliac vein could be seen in 60, the epigastric vein in 22, the pudendal vein in 48, the anterolateral vein of the thigh in 34, the posterolateral vein of the thigh in 40, the posterolateral vein of the calf in 62 cases. The Giacomini vein, which connects the great and the small saphenous veins, could be detected in 34 cases. Among the perforating veins, we have identified 23 Dodd, 31 Hunter, 48 Boyd, 61 Sherman, 146 Cokkett 1, 2 or 3, 35 Hach, 56 popliteal, 13 May and 73 lateral perforator veins. Based on our experiences so far, the Vasovist®-enhanced MR angiography makes it possible to analyze the venous system of the extremities in detail, helping to plan vascular surgical interventions.

#### **N15 MODERN EQUIPMENTS, METHODS AND OPPORTUNITIES IN THE EDUCATION OF IMAGING**

**Levente Istvan Láncozi, Andras Jakab, Ervin Berenyi**

**Department of BioMedical Laboratory and Imaging Science, University of Debrecen Medical and Health Science Center, Debrecen**

**Keywords: imaging, education, eMRI, internet**

Imaging is one of the most developing fields of medicine, thanks to the application of new methods and equipments and to the digital diagnostic image archives. The main points of the advances are the IT revolution and its application into the healthcare system.

The Department of BioMedical Laboratory and Imaging Science at University of Debrecen teaches imaging diagnostic analytic to BSc students and general medicine students. It is essential to apply all the available modern methods in the education. Many and permanently increasing radiologic archives are accessible for education and research. We can use our own clinical archives. The internet has databases as well. The websites [www.eurorad.org](http://www.eurorad.org) and [www.radiopaedia.org](http://www.radiopaedia.org) are going to be presented.

On-line internet education software packages are available as well. IMAIOS ([www.imaios.com](http://www.imaios.com)) is an on-line macroscopic and cross-sectional CT and MR anatomy teaching software. It is an excellent tool for teaching the recognition of the main anatomical parts on imaging scans.

Our department has a unique eMRI (Magritek Terranova MRI) equipment that works on the magnetic field of Earth. Students can examine physical and biological samples, study the basics of MR imaging. This easy to use, relatively cheap machine is an important educational tool.

The last topic of the presentation is about web2 and other offline tools and the connection of education of imaging. Facebook groups, medical blogs, iPhone and other applications will be shown.

The aim of our department is to integrate modern methods and tools into the education of imaging.

#### **N16 INTEGRATING STRUCTURAL, FUNCTIONAL AND CONNECTIVITY INFORMATION FOR NEUROSURGICAL TREATMENT PLANNING**

**Andras Jakab<sup>1</sup>, Peter Katona<sup>2</sup>, Ervin Berenyi<sup>1</sup>**

**Departments of (1) Biomedical Laboratory and Imaging Science, (2) Institute of Nuclear Medicine - University of Debrecen Medical and Health Science Center**

**Keywords: Neurosurgery, multimodal imaging, diffusion tensor imaging, functional MRI**

**Introduction:** Neurosurgery is dependent on image guidance: maximizing tumor removal while preserving neurological function is crucial in the therapy of brain malignancies. Magnetic resonance imaging is the first-line tool in the diagnostics of the central nervous system. The anatomical information of MRI can be extended by means of functional MRI and diffusion tensor imaging (DTI). Co-registration methods allow image fusions that exploit the abovementioned multimodal diagnostic spectrum. This study was designated to introduce our multimodal neurosurgical planning environment and to show its feasibility in preoperative visualizations.

**Material and methods:** Patient population comprised 12 cases with heterogeneous etiologies; malignancies of various histopathological subtypes and one focal cortical dysplasia were included. Preoperative workup consisted of "anatomical" MRI with sequences as follows: 3DT1, T2, FLAIR. Image data were transformed to the coordinate system of the T1 MRI. During fMRI, speech lateralization and motor paradigms were employed. Segmentation was used to visualize the cortex, tumors, skin markers and vessels. Near-eloquent white matter areas such as the optic radiations, corticospinal tract and long-range association fibers were depicted by tractography.

**Results:** Image fusions were carried out with feasible geometric accuracy. Illustrative images were used in the treatment planning by neurosurgeons; it was possible to avoid major postoperative neurological deficits or forecast such events.

**Conclusions:** Treatment of brain tumor patients remains a major challenge of oncology despite major revolutions of

diagnostics and surgical therapies. Integrating patient-specific information from various diagnostic modalities allows accurate evaluation of the surgical area and can enhance the power of modern imaging.

#### HEALTH BEHAVIOR-PSYCHOLOGY SESSION

##### **K1,3,5 HUMANIA PEER-LED PROFESSIONAL TRAINING PROGRAM – VOLUNTARY PEER TRAINING FOR FUTURE DOCTORS**

**Szilvia Fesus, Dora Anita Horvath MD, Zsuzsanna Almasi, Istvan Karacsony, Katalin Hegedus**

**Department of Behavioral Science, Semmelweis University, Budapest, Hungary**

**Keywords: peer education, health-care profession, professional training, human skills, burnout prevention**

The aim of this lecture is to review the methods of peer training groups operating in Hungarian and foreign universities, and to present HuMania Peer-Led Professional Training Program, a peer training group at our university. Peer training is a globally prevailing educational method that is based on the behavior-influencing role of peers close in age to students. Apart from preventive activities aimed at primary and high school students, peer training has also gained ground as complementary to conventional education in higher education. It is particularly suitable for institutions training health-care professions by helping them not only in developing practical skills, but also maintaining the health of the trainees in these professions. HuMania Peer-Led Professional Training Program is a voluntary organization funded in 2002, and it is run by undergraduates of Semmelweis University at the Department of Behavioral Science. The aim of the organization is to develop social skills of undergraduates, to form a supportive community, to popularize Bálint Mihály's group method, and in the long run, to prevent burnout of future doctors, and to develop educational and leadership skills and self-awareness of peer trainers. Since 2005, HuMania has been a two-semester course of four credits instructed by Ferenc Túry. A further group at the University of Debrecen was established in 2008. The course is available in the third year of medical university and it consists of 10 each 3.5 hours long session led by two tutors. The semester began with a large scale Induction Day. We also organize 3 day long Winter Camps and facultative activities. Our methods include: team-building and trust-improving activities, interactive lectures, group sessions, role-plays, situational practice, relaxation activities, outdoor exercises, Junior Balint groups. Our topics include: positive suggestions, reframing, patient education, assertivity, empathy, prejudices, and limitations to our competences and boundaries of our profession. Professional background: team leader-training, supervisions, individual trainings. So far 344 students have completed the course, 44 of whom became tutors. In 2009 we have started a long-term questionnaire-based research to survey the efficiency of the program. The results will be presented in the next lecture.

##### **K2,4,6 MOTIVATIONS FOR CHOOSING THE “HUMANIA PEER-LED PROFESSIONAL TRAINING PROGRAM”**

**Zsuzsanna Almasi, Istvan Karacsony, Szilvia Fesus, Andrea Udvarhelyi, Thege Barna Konkoly, Katalin Hegedus**

**Department of Behavioral Science, Semmelweis University, Budapest, Hungary**

**Keywords: peer education, health-care profession, professional training, human skills, burnout prevention, efficiency survey**

**Introduction:** The presentation will outline the preliminary results of a survey conducted to determine the efficiency of HuMania Peer-Led Professional Training Program. It is a two credit peer training course funded in 2002 that aims at developing communication and coping skills of undergraduate medical students, to make medical students familiar with Bálint Mihály's group method and to decrease the risk of burning out of future doctors. The survey was conducted at the beginning and at the end of the 2009/2010 school year; this lecture covers the results of the first survey.

##### **Methods:**

Questionnaire survey

WHO Well-being Index

Bergen Social Relationship Scale

Brief version of Lazarus' Ways of Coping questionnaire

Maslach Burnout Inventory for undergraduate students

And questions of our own

165 students participated in the survey, 40 of them were HuMania members and 125 students were control.

**Results:** Attendance to psychological development groups was significantly higher among HuMania members ( $p=0.001$ ). HuMania members had lower psychological well-being ( $p=0.01$ ), while their social anxiety was higher ( $p=0.01$ ), they also scored better in questions measuring emotion-based coping ( $p=0.05$ ). HuMania members had a tendency for burnout scores. The other questions did not show any significant difference between the two groups.

**Conclusion:** As Kutacher (1984) showed, 75% of American undergraduates would like to have psychological or other form of assistance if it would not bear a negative stigma. On the other hand, HuMania is a supportive community without any negative stigma that responsive students choose eagerly. The end-term questionnaire may answer the following questions: Is there any improvement in psychological well-being and social anxiety? Is there any change in coping strategies of HuMania members? Can the burnout tendency be reversed?

##### **K8 PSYCHOSOMATICS**

**Marietta Kékes Szabo**

**SZTE BTK PI, KGRE BTK PI, University of Szeged, Szeged**

**Keywords: Asthma, panic disease, interview, Tennessee scale, JEPQ questionnaire**

I have done research on the background causes of and the predisposing factors to the psychosomatic disease of adolescents suffering from asthmatic and panic disorders in an analytical approach. My hypothesis was that similar family and upbringing circumstances and personality traits were lying in the background as factors determining the young people's life, their interactions manifested in their social relations and basic behavior pattern. A control group was also investigated in order to allow comparison with a healthy peer group and to evaluate the weight of the results obtained in this way. A personal questionnaire interview, the Tennessee – self concept scale and the JEPQ personality questionnaire helped me to explore the indicators of life history, self concept as well as extraversion – introversion, neuroticism, psychoticism and lying. The results obtained with the tested samples show that the proportion of adolescents with earlier asthmatic problems was high, and even significant compared to the controlled group, among adolescents with current panic disorder. Low self-esteem, shyness and anxiety were common in the patients. The more intense experiencing of physical symptoms – similarly to low self-esteem – also enhances anxiety. In the course of interviews exploring life history, young people in puberty recalled a dominant mother who regularly saw to their physical needs but showed only few emotional manifestations towards them, and the persons in the study still have stronger ties with their mothers, which is a striking phenomenon in the period of separation from the parents. From among the components of the Tennessee – self concept scale, body image, individual and overall self-image typically had low or extremely low values, the value of SC, self-criticism, was extremely high in all cases, while TF, true or false, the orientation of answers, generally revealed high values. The results of the control group – although with greater standard deviation – showed more balanced results. While the former findings are suggestive of the excessive rigor of a significant other person, low confidence and emotional support, the latter ones indicate difficulties of self-acceptance and lack of self-knowledge. The complaints – in the absence of an organic background – can be cured with cognitive behavioral therapy.

#### **K9 VULNERABLE ADOLESCENT SUBPOPULATIONS FROM THE VIEWPOINT OF SMOKING: THE ROLE OF THE RESIDENCE**

Mate Adam Balazs<sup>1,2</sup>, Bettina F. Piko<sup>2</sup>, Randy M. Page<sup>3</sup>

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**Keywords: adolescents, smoking, rural-urban differences, risk factors**

**Summary:** Smoking is one of the most important public health problems facing countries throughout the world. Smoking raises the risk of lung cancer and different other chronic diseases, for instance, atherosclerosis and ischemic heart disease. The adolescent population is especially vulnerable in

terms of initiation of smoking; it is triggered by different social and cultural effect, e.g., smoking symbolizes adulthood. Different type of residence may also provide altering cultural environment for them to experience smoking. The primary goal of our study was to analyze the relationship between smoking behavior, specific attitudes, type of residence, and whether one commuted to school or not. The sample consisted of 546 adolescents from elementary, grammar, and secondary schools of Mako, Hungary. It represented the given population of age in this town. The pupils were questioned anonymously about their substance use habits, lifetime and monthly prevalence of smoking and drinking, beliefs and attitudes related to substance use and sociodemographic factors. Cross-tabulations and chi-square tests were used to test these relationships. We did not find any relationship between smoking behavior and gender, or according to the type of residence. However, whether one commuted to school or not was significantly associated with lifetime prevalence of smoking and smoking-related attitudes. Therefore, to take effective steps to reduce the high level of adolescents' smoking the professionals should pay attention to these vulnerable subpopulations during the prevention and health promotion programs.

#### **PULMONOLOGY-RHEUMATOLOGY-BIOCHEMISTRY-MICROBIOLOGY SESSION**

##### **K10 LUNG FUNCTION INFLUENCES ATHEROSCLEROSIS – RESULTS OF INTERNATIONAL TWIN STUDY 2009**

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**Keywords: lung function, twin research, atherosclerosis**

**Background:** An association between reduced lung function and an increased risk of vascular events has been reported but the underlying mechanisms are unknown. So far no twin studies have examined the association between atherosclerosis and lung function.

**Objectives:** To estimate association of arterial stiffness and lung function and to assess heritability and environmental effects on these parameters.

**Subjects and Methods:** 264 (179 monozygotic /MZ/ and 85 dizygotic /DZ/) (age yrs 50.5±15.4; mean±SD) twin pairs were included in this classical twin study as part of



International Twin Study 2009. Augmentation index on brachial artery (Aixbra) and Pulse Wave Velocity on aorta were measured to reflect arterial stiffness (TensioMed Arteriograph) and FVC with FEV<sub>1</sub> (MIR Minispir) for lung function. Heritability and the correlation coefficient (CC) between variables were determined.

**Results:** Age and gender-corrected heritability of FVC and FEV<sub>1</sub> were 0.74 and 0.75 ( $p < 0.01$ ). Shared and unshared environmental effects were found to be 0, 0.26 ( $p < 0.01$ ) and 0, 0.25 ( $p < 0.01$ ) for FVC and FEV<sub>1</sub>, respectively. CCs between FVC and (PWVao) were -0.42 ( $p < 0.001$ ) and -0.29 ( $p < 0.001$ ), respectively. CCs between FEV<sub>1</sub> and Aixbra and PWVao were found to be -0.47 ( $p < 0.001$ ) and -0.38 ( $p < 0.001$ ), respectively.

**Conclusions:** Lung function is strongly heritable and is associated with arterial stiffness. The observed relationship can aid to understand the background of vascular changes in different airway diseases.

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#### **K11 THE EFFECTS OF MARIJUANA SMOKE ON THE AIRWAY IN A PREDICTIVE MOUSE MODEL**

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**Keywords: marijuana smoke, peripheral effects, airways**

The changes caused by marijuana smoke in the CNS are well known but we have less and inconsistent data about the peripheral effects primarily on the airways. Our purpose was the complex examination of the effects of marijuana smoke in a chronic mouse-model. During one, two, three and four months CD1 male mice inhaled marijuana smoke by whole-body exposure. We used tobacco-smoking groups for comparison. Awake respiratory function tests were done weekly by whole-body plethysmography. After the homogenization of the lungs, the cell compound was analyzed from bronchoalveolar lavage (BAL) and cytokine concentrations were measured by flow-cytometry. Determining the number of granulocytes/macrophages, myeloperoxidase (MPO) activity was measured by spectrophotometry and histological examinations were done. Marijuana smoke caused significant hyper-reactivity of the airways, which invariably held up during the four months. In the tobacco-smoking group we experienced similar hyper-reactivity only after the 2nd month. In the 4th week of marijuana smoking significant perivascular/peribronchial edema, atelectasis, apical emphysema, neutrophil/macrophage infiltration was detected. From the 8th to the 12th week perivascular granulocyte infiltration, macrophage-like giant-cells, irregular bronchiolus surface and increased number of mucus producing cells were typical. By the 16th week chronic lobal reaction, serious atelectasis and emphysema, obstructed and destruated bronchiols and endothel proliferation was identified. We found milder inflammation, lower MPO activity and inflammatory-cytokine concentration in the tobacco-smoking group

than in the marijuana-smoking group. The highest increase in the number of BAL inflammatory cells was shown at the end of the 2nd month, which is in line with the histological results. The results show that marijuana smoke causes more serious and earlier airway hyper-reactivity, inflammation and emphysema than tobacco smoke. During four months of smoking the histological changes from acute/subacute pneumonitis led to total tissue destruction.

#### **K12 EXHALED BREATH SMELLPRINT IS ALTERED IN PREGNANCY**

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**Keywords: electronic nose, pregnancy, exhaled biomarkers**

Changes during pregnancy (accelerated metabolism, increased oxidative stress, hormones and probably pheromones) influence the level of different biomarkers in blood and urine and presumably these changes also appear in exhaled breath.

Electronic nose is able to separate the biomarker pattern of different volatile substances. It can distinguish the smellprint of lung cancer and COPD one from the other and also from healthy controls.

We examined if exhaled breath biomarker pattern of pregnant and non-pregnant women differs. Our subjects were non-smoker, non-allergic, healthy women (19 pregnant in the 3<sup>rd</sup> trimester and 13 non-pregnant).

After inhaling until FVC then exhaling through a flow-control we collected the air samples in a special teflon-coated bag and we examined them with the help of electronic nose Cyranose 320 (Smith Detections, Pasadena, USA). For statistical compare of data we used Mahalanobis-distance (MD) and principal component analysis. The counted factors of the 2 groups were compared by t-probe.

We found significant difference between pregnant and non-pregnant biomarker pattern. MD was 2.975 and factor analysis also showed significant difference.

In our measurement e-nose could recognize pregnant and non-pregnant with 78% sensitivity, 80% specificity, 87% positive predictive value and 67% negative predictive value.

Our results may predict that during pregnancy there are some typical changes in volatile compounds. But the origin of it and its role in monitoring pregnancy needs further research.

#### **K13 THE BIOLOGICAL HAZARD OF 166-HOLMIUM-PHYTATE COMPARED TO 90-YTTRIUM IN RADIOSYNOVIORTHESIS (RSO)**

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**Keywords: Radiosynoviorthesis, Holmium, Yttrium**

**Background:** Chronic synovitis is characterized by the inflammation and proliferation of synovial tissues and often

leads to the destruction and deformity of the involved joints. The synovial lining of the arthritic joint becomes hyperplastic. RSO is the ablation of inflamed synovium by intraarticular injection of a beta-emitting radionuclide in colloidal or particulate form. The first trial of radiation synovectomy was in 1952.

**Aim:** The biological hazard of 166-Holmium-phytat compared to 90-Yttrium RSO

**Materials and Methods:** We analyzed liver, lymph nodes and blood radioactivity of the injected isotopes by a gamma camera scan. We examined data of 307 patients.

**Results:** We found 0.22% radioactivity in liver, 0.32% radioactivity in lymph nodes in case of the Holmium- phytate. The average radioactivity of this isotope is 0.54 %. In case of the 90-Yttrium the average radioactivity is 6%.

**Conclusion:** Holmium-166 phytate isotope is an effective radiopharmacy treating synovitis. Due its advantageous features it produces less radioactive damage on the organism than the traditionally used 90-Yttrium isotope.

#### **K14 DESCRIPTION AND APPLICATION OF THE THRITTENE RADIOIMMUNOASSAY**

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**Keywords: Thrittene, radioimmunoassay, somatostatin**

The peptide hormone – called Thrittene – has the same amino acid structure as Somatostatin-28 N-terminal (1-13) amino acid sequence. It was detected in mammalian gut; furthermore, that it's is secreted into the circulation during food intake. Our workgroup considered that it is important to develop a special Thrittene RIA method that is specific and sensitive enough for Thrittene.

During the development of RIA method, the sensitivity of the C-terminal antiserum (TH3) was produced by the immunization of rabbits by administering Thrittene-BSA antigen subcutan. To show the antibody attachment we used iodogen method, <sup>125</sup>I isotope-labeled, mono-iodinated Tyr-Thrittene. Tyr-Thrittene was used for the determination the attachment in 0-1000 fm/ml range.

After ten measurements the D<sub>50</sub> value of the calibration curve was 8.61±1.22 fmol/ml. The detection limit of our method was 0.2 fmol/ml Thrittene. The cross-studies showed that the antiserum used in our RIA method has a limited cross-reactivity with other peptides with similar structure. By determining the Thrittene content of the rat GIT tissue the highest concentration was measured in duodenum and jejunum; however, all the examined tissues contained enough Thrittene for the measurement. Eventually, the receptor of the Trittene in rat brain tissue was identified using receptor binding assay (Bmax: 0.23/+0.05 fmól/mg fehérje, Kd=9.5+/-1.8 nM, n=5).

The Thrittene RIA method developed by our team has high sensitivity and peptide specificity. It is suitable for determining tissue and plasma concentrations and it helps to

get further information about the biological role of the peptide hormone.

#### **K15 RESISTANCE MECHANISMS IN GRAM-NEGATIVE NONFERMENTATIVE BACTERIA**

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**Keywords: P. aeruginosa, S. maltophilia, colistin, cotrimoxazole, interpretation**

Due to worldwide use of antibiotics newer and newer resistance mechanisms are being developed in bacteria, especially among nosocomial pathogens. Gram-negative nonfermentative bacteria such as *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia* represent one of the most emerging therapeutic challenges. Highly increasing number of clinical isolates turn out to be resistant even to polymyxin group of antibiotics resulting in infections that cannot be specifically treated due to the lack of efficient antimicrobial agents. The incidence of *S. maltophilia* strains being resistant to sulfamethoxazole/trimethoprim combination and colistin is highly increasing (over 10% and 50% of our isolates, respectively). We have investigated the antibiotic susceptibility of four colistin-resistant *P. aeruginosa* and seventy-two *S. maltophilia* clinical isolates with different methods as well as molecular mechanisms resulting in colistin-resistance in clinical *P. aeruginosa* isolates: we have investigated the effects of inhibition of efflux pumps with different agents. Western-blot and mass spectrometry analysis for other putative resistance mechanisms are under process.

#### **K16 DIRECT ROLE OF GENES IN PHAGOCYTOSIS THAT ARE UPREGULATED IN MACROPHAGES DURING THE PHAGOCYTOSIS OF APOPTOTIC NEUTROPHIL GRANULOCYTES**

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**Keywords: Phagocytosis, siRNA, ICAM3, blocking antibody**

**Introduction:** The daily clearance of 500 billion physiologically dying cells is performed safely mainly by the Mononuclear Phagocyte System. The engulfing cells can recognize dying cells by several cooperative mechanisms using bridging molecules and receptors that show high redundancy.

**Objectives:** Our TaqMan Low Density Array measurements predicted the important role of several genes in phagocytosis process, since their expression level was highly elevated during the early stage of phagocytosis. The goal of our investigations was to knock-down the four genes with the most enhanced expression (ADORA2A, FPRL1, ICAM3, THBS1) in human macrophages by RNA-interference and analyzing their phagocytic capacity.

**Materials and Methods:** Monocytes were isolated from human blood and after their differentiation siRNA was transfected into the cells by electroporation. The knock-down effect was controlled by RT-QPCR and Western-blot. Apoptotic neutrophil granulocytes were isolated from human blood before the phagocytosis assay was performed using fluorescent labeled cells and the incorporated cell-rate was measured by flow cytometry.

**Results:** Powerful knock-down effect was experienced at each of the four investigated genes, but decrease in phagocytic capacity was observed only after knocking-down ICAM3. Reduction of phagocytosis was also noticed after macrophages were pre-incubated with ICAM3 blocking antibody.

**Conclusion:** ICAM3 is an immunoglobulin-like molecule that participates in the recognition of apoptotic neutrophils by macrophages not only as an adhesion molecule but also as an initiator of signaling pathways mediated by tyrosine kinases. We proved that it has a role not only as a surface protein of neutrophils but also as recognition receptor of macrophages.

#### ANESTHESIOLOGY-INTENSIVE CARE SESSION

##### **N17 IMPORTANT DIFFERENCES IN THE PRACTICE OF EMERGENCY MEDICINE IN THE UNITED STATES COMPARED WITH ANESTHESIA AND CRITICAL CARE MEDICINE.**

**Tamas Peredy**

**President of HMAA**

**Medical Director, Northern New England Poison Center**

**Assistant Medical Director York Count Center for Wound Healing and Hyperbaric Medicine**

**Assistant Professor of Emergency Medicine, Maine Medical Center, a Tufts University School of Medicine Affiliate**

**Introduction:** In the 1960s, the practice of Emergency Medicine was developed in the United States in response to a specific need for dedicated physicians to manage a variety of acute and oftentimes critically ill patients. Prior to the establishing of a standard of care though the development of training programs, the after-hours care was provided by the most junior physicians or specialists moon-lighting in the Emergency Ward.

**Methods:** A literature search was performed for articles regarding resuscitation, airway management, trauma and pediatric emergency care as it related to cross-specialty differences. The curricula for training programs in EM, Anesthesia and Critical Care were reviewed. Expert opinion was also sought regarding the differences in work habits, resource management and specialty development. **Results:** Significant differences exist between Emergency Medicine and other overlapping medical specialties even within the approach to a common clinical problem. Challenges exist to find mutual understanding to deliver coordinated care.

**Conclusion:** Emergency Medicine in the United States has evolved into a well-established specialty with homogenous training and standards of care. Differences exist between

Emergency Medicine and other specialties even in the approach to overlapping clinical problems.

##### **N21 DEVICE-ASSOCIATED INFECTIONS AT A MEDICAL INTENSIVE CARE UNIT – A PROSPECTIVE EPIDEMIOLOGICAL STUDY**

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**Keywords: Nosocomial, infection, device-associated, ICU**

**Introduction:** It is essential to use invasive devices to monitor and treat seriously ill patients at an intensive care unit. These devices often give rise to different infections. Our goal was to get a clear picture of the incidence and prevalence of device-associated infections at a medical intensive care unit in Szeged.

**Patients and Methods:** Patients treated for more than 48 hours at the tertiary Intensive Care Unit of the Department of Anesthesiology and Intensive Therapy, Faculty of Medicine, University of Szeged between November, 2009 and the end of April, 2010 were included in the study. Data were collected prospectively on the use of invasive devices and the signs indicating infection.

**Results:** 122 patients were treated for more than 48 hours at the unit. The number of patient days was 1454. The most often used device was the urinary catheter, the device utilization ratio was 0.946. The highest infection rate was associated with ventilation. Figures were compared with the results of the National Nosocomial Infections Surveillance System data issued in 2004 and that of the Hungarian National Nosocomial Surveillance System of 2005.

**Discussion:** At the highest level of healthcare, treatment exposes patients to a higher risk of acquiring nosocomial infections. This study gives an overview of infection rates at this ICU and it enables us to effectively plan infection control measures.

##### **N22 STATUS DYSTONIA: LIFE-THREATENING FORM OF A RARE DISEASE**

**Laura Szabo<sup>1</sup>, I. Balas<sup>2</sup>, R. Herold<sup>3</sup>, J. Janszky<sup>4</sup>, N. Kovacs<sup>4</sup>, E. Eze<sup>1</sup>**

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**Keywords: status dystonia, muscle**

**Introduction:** Status dystonia (SD) is an extreme rare disease, which is characterized by generalized, permanent muscle-contractions. The definition of SD was as a continuously seriously generalized form of the dystonia by Jankovic and Penn in 1982 written, which requires hospital care

immediately. It can develop in two ways: primary or secondary. Provocated factors are infection, operation, the use of a new medication (s.a. zinc, D-penicillinamin and clonazepam) or a sudden stoppage of an earlier medication.

Case history: SD is a disease, which requires therapy in the intensive care unit, but in spite of adequate therapy the mortality is 10-15%. The muscle-contractions in SD can lead to damage of muscles, increased cardiopulmonary load and ultimately death. Therapies and the etiology of SD will be discussed.

### **N23 THE AWARENESS AND ACCEPTANCE OF A LIVING WILL AMONG THE FUTURE GENERATION OF HEALTH PROFESSIONALS**

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**Keyword: living will**

The living will is an official document in which persons of age in possession of their faculties make a statement on what end-of-life procedures they accept or refuse if they become incapacitated.

The aim of my research was to evaluate the awareness and acceptance of the living will at the University of Pecs Medical School and Faculty of Health Sciences. Bringing attention to this important issue granted an opportunity to future health professionals to consider the possibilities and problems regarding the living will.

### **N24 THROMBOCYTE AGGREGATION IN SEPTIC PATIENTS**

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**Department of Anaesthesia and Intensive Therapy, University of Pecs**

**Keywords: Platelet aggregation, ICU, sepsis**

**Introduction:** Severe sepsis and multiple organ dysfunction syndrome are still a challenge in intensive care. Platelet activating factor assemble a link between inflammation and clot formation. We investigated inducible platelet aggregation in severe sepsis and focused on the presence of spontaneous aggregation.

**Methods:** Blood samples were taken from 45 patients (average age:  $60.7 \pm 13$ ) daily for 5 days consecutive. We measured inducible platelet aggregation (adrenalin (ADR), adenosine diphosphate (ADP) and collagen (COL)) and aggregation with normal saline (SAL). Multiple Organ Dysfunction Score (MODS) and Sequential Organ Failure Assessment (SOFA) score systems were used to follow the clinical status. We compared our patients with 30 healthy controls.

**Results:** Inducible aggregations were reduced in septic patients in all 5 days (ADR, ADP and COL), while SAL aggregation increased during our study period. Patients with low platelet count showed deteriorated aggregation with ADP on all 5 days, with ADR on the 2nd, 3rd, 4th, and 5th days and

with COL on the 1st, 2nd and 3rd days ( $p < 0.05$ ) while SAL aggregation represented no significance. We found non-significant difference between the platelet aggregation of surviving and non-surviving patients. Spontaneous aggregation group had tendentiously higher platelet count, while procalcitonine levels were lower on the 1st, 3rd, and 4th days.

**Conclusion:** We demonstrated the presence of spontaneous platelet activity, while overall inducible platelet aggregation was significantly impaired in our patients. There were no significant differences found between the normal and the low platelet count group and inducible platelet function was not predictive of mortality.

### **N25 COAGULOPATHY AND SEVERE HEAD INJURY** **Barbara Benkovics<sup>1</sup>, Endre Czeiter<sup>2,3</sup>, Andras Buki<sup>3</sup>, Janos Sandor<sup>4</sup>, Livia Dan<sup>5</sup>, Erzsébet Ezer<sup>5</sup>**

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**Keywords: coagulopathy, ICU**

**Objective:** We analysed the “Pécs Severe Head Injury Database” to assign the proportion of primary and secondary coagulopathies among our patients, their effect on mortality especially in correlation with age. We would identify the diagnostic subgroup which is the most sensitive for changes in coagulation. We also try to determine the threshold INR value for coagulopathy.

**Methods:** Between July 2002, and December 2008, 305 consecutive severe TBI cases were treated, 71 (23.3%) female and 234 (76.7%) male. Inclusion criteria were head injury and  $GCS \leq 8$  during the hospitalization. The criteria of primary coagulopathy was  $INR > 1.4$  on admission, secondary coagulopathy was defined as  $INR < 1.4$  on admission but  $INR > 1.4$  at least once during the hospitalization period in our department. For statistical analysis we utilize one and multiparametric logistic regression applying SPSS 11.5 software.

**Results:** From the 305 severe head injured 135 died, the overall in-hospital-mortality was 44.3%. According to our criteria 144 patents was found with coagulopathy from them 80 person had primary (55.6%) and 64 secondary coagulopathy (44.4%). It means that from the 305 patients 26.23% had primary and 20.98% secondary coagulopathy. The mortality of patients with primary coagulopathy was 57.5% and in case of secondary coagulopathy the mortality was 81.25%. According to our “Receiver Operating Curve” we found that the INR value 1,245 has the best specificity and sensitivity to determine primary coagulopathy.

**Conclusions:** Our results underline the necessity of the rigorous compliance with the international guidelines for anticoagulation therapies and need for strict follow up of patients who live under the influence of altered coagulation.

According to our results we also state that in cases of severe head injury the prevention of secondary coagulopathy is of utmost importance.

## **N26 MICROPARTICLES IN CRITICAL SEPTIC ICU PATIENTS**

**Gabor Woth<sup>1</sup>, Margit Tokes-Fuzesi<sup>2</sup>, Tamas Magyarlaki<sup>2</sup>, Diana Muhl<sup>1</sup>**

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**Keywords:** ICU, sepsis, microparticles, flow cytometry, platelets

**Introduction:** We investigated the alterations of platelet, endothelial and leukocyte derived microparticles (MP) in severely septic patients. Our aims were: 1. the examination of MP amount changes 2. to assess value of MP measurements in the identification of the microbial background of sepsis. 3. to analyze the mortality predictive value of MPs in severe sepsis.

**Methods:** 24 severe septic patients ( $\geq 2$  organ failure,  $\geq 5$  ng/ml procalcitonine) were studied in a 5 day period. In addition to regular laboratory test we performed flow cytometry on the 1st, 3rd, and 5th day. Total MP count and the expression of CD13, CD14, CD31, CD41, CD42, CD45, CD61, and CD62e were measured. We also performed electron microscopy imaging in certain cases. An age and sexuality matched group was applied as control (n=10).

**Results:** We have found elevated total MP count during our study period ( $p < 0.01$ ). Platelet derived MPs carrying CD41 and CD61 were significantly elevated in severe sepsis ( $p < 0.05$ ). Separating patients by mortality and survival during our study period showed no significant difference in MPs. Patients with identified Gram-positive, Gram-negative or fungal infection presented no significant alterations in MP profile. Electron microscopy revealed blebbing platelets and vesicular fragments with platelet morphology.

**Conclusion:** The role of MPs in the clotting system is yet unclear. According to published results we have found elevated MP amount in septic patients. The elevated amount of platelet MPs and the tissue factor and phospholipids carried by the particles may contribute to the microvascular abnormalities of severe sepsis.

## **N27 POSTOPERATIVE PAIN AUDIT AT THE UNIVERSITY OF SZEGED**

**Szonja Szabo<sup>1</sup>, Lorand Matusek<sup>1</sup>, Zsolt Molnar<sup>2</sup>, Judit Meray<sup>2</sup>**

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**Keywords:** Postoperative pain reducing, VAS, patients

**Introduction:** Postoperative pain management has developed a lot over the last years, but there are still many problems to be solved.

**Terms of reference:** To audit the quality of pain control, and patient satisfaction in the first 24 postoperative hours.

**Methods:** Within a one week observation we audited the severity of the operation (rate 1-4), the difference between the ordered and the received analgesics in all surgical departments in our university. Pain was assessed by the "visual analog scale" (VAS:1-10), together with the satisfaction of the patients (1-5). Data are presented as median and interquartile range.

**Result:** Over the observation period 68 patients (38 male and 30 female) patients were recruited. The median age of children was 5 (3-6.5), the adult group 53 (34.5-62). The analgesics as prescribed by the anesthetists were received by 72% of patients. After the operation the VAS was 5(3-8), the next morning it was 2 (1-4). The patient's satisfaction rate was 4 (3-5).

**Conclusion:** The observation that one third of the patients didn't get the ordered painkilling regimen and the median level of postoperative VAS was above the acceptable 4 precipitates the correction of the actual practice (initiation of protocols and regular measure of pain rate). **Reference:** JL Apfelbaum Anesth Analg 2003;97:534-40

## **OBGYN SESSION**

### **N28 UPDATE IN PREIMPLANTATION GENETIC DIAGNOSIS**

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**Keywords:** PGD, IVF, blastocyst, genetic disorders, embryo biopsy

We will review the latest developments in preventing the transmission of diseases via the use of embryo biopsy utilizing assisted reproductive technologies specifically with in vitro fertilization and molecular biological techniques.

### **N29 HEPCIDIN LEVELS AND CHARACTERISTICS OF IRON HOMEOSTASIS IN PREECLAMPSIA**

**Gergely Toldi, B Stenczer, A Molvarec, Z Takats, G Beko, J Rigo Jr, B.Vasarhelyi**

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**Keywords:** hepcidin, IL-6, iron homeostasis, preeclampsia

**Introduction:** Preeclampsia is an inflammatory complication of pregnancy characterized by hypertension and proteinuria. Plasma iron levels were found to be elevated in preeclampsia, contradicting the ongoing inflammation. The link between iron homeostasis and inflammation is a recently described acute phase protein, hepcidin.

**Aims:** We aimed to characterize hepcidin levels and their association with iron homeostasis in preeclampsia.

**Methods:** We took peripheral blood samples from 30 preeclamptic and 37 healthy pregnant women. Plasma hepcidin levels were measured with a modified method of mass spectrophotometry developed at our laboratory. We

further determined IL-6 levels, complete blood cell count and parameters describing iron homeostasis. Mann-Whitney test was used for statistical analysis.

**Results:** Plasma hepcidin, IL-6, iron and ferritin levels were elevated, whereas plasma transferrin levels, total iron binding capacity and mean corpuscular hemoglobin concentrations were lower in preeclampsia compared to healthy pregnancy. No difference was revealed in other parameters investigated. Plasma iron levels are elevated in spite of high hepcidin levels in preeclampsia, thus our finding might indicate a resistance to the iron-decreasing action of hepcidin. This mechanism may be an important contributing factor to the pathogenesis of preeclampsia due to the elevated generation of reactive oxygen species and the exacerbation of the ongoing inflammation.

**Conclusion:** Our results raise the notion that the need for iron supplementation is to be reconsidered in preeclamptic pregnancies, and the appropriate level of iron intake should be set individually for preeclamptic pregnant women based on their actual iron homeostasis.

### **N30 DIAGNOSTICAL DIFFICULTIES OF HYPERTENSIVE DISEASES IN PREGNANCY**

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**Keywords: chronic hypertension in pregnancy, preeclampsia, gestational hypertension**

**Introduction:** The classification of hypertensive disorders in pregnancy differs notably according to the various recommendation systems. It makes the diagnosis more difficult and influences the therapy.

**Aims:** The aim of our survey was to study in the clinical practice how the first diagnosis of hypertension in pregnancy altered during the progress of pregnancy and 90 days after delivery.

**Methods:** We have investigated 400 gravidas suffering from hypertensive diseases during pregnancy who were treated at the 1<sup>st</sup> Department of Obstetrics and Gynecology in Budapest, in the frame of an observational cohort study. In the course of the study we considered the recommendation of NHBPEP (2000).

**Results:** Of 400 patients, 155 had chronic hypertension (CHT), 140 gestational hypertension (GHT) and 105 had preeclampsia (PE) at the time of entering the survey. 36.8% of the CHT gravidas were normotonic 90 days after delivery. In the GHT group the hypertension persisted in 10.7% of the cases. Among the GHT patients PE evolved in 37.1% and in this subgroup the high blood pressure existed postpartum in 13.5%. Persistent hypertension was observed in 9.5% of the PE gravidas. On the whole, during the pregnancy in 21.8%, 90 days postpartum in 31.8% of the cases required a change in the initial diagnosis.

**Conclusion:** The results show that in one third of the initial diagnoses of hypertension, it was necessary to change the diagnosis during the pregnancy or postpartum.

### **N31 CHILD BEARING AMONG WOMEN WITH MULTIPLE SCLEROSIS**

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**Keywords: Multiple sclerosis, immunomodulate therapy during pregnancy, shubrate**

**Introduction:** Multiple sclerosis (MS) typically appears in women of reproductive age.

Epidemiological studies of well-known that during pregnancy the clinical worsening of the number decreases, however, in the postpartum period, the symptoms of MS recur.

**Objectives:** Our aim was to examine the outcome of pregnancies in women with multiple sclerosis, the development parameters of their offspring, to identify the age of conception, and risk exposure during pregnancy of immunomodulatory therapy, as well as the evolution of the disease after giving birth.

**Patients and methods:** Between 1998 and 2009, the Department of Obstetrics Clinic, treated and cared for, 57 patients from the Department of Neurology. A retrospective analysis of pregnancy data, compared to international research was carried out.

**Results:** In 57 female patients, the average number of pregnancies was 2.2 (SD±1.3), the average fetal weight: 3076.3±622 g. In our study both the annual analysis of trends and the overall spontaneous abortion rate was significantly higher in MS patients, as the reference population (p = 0.0006). Vaginal delivery incidence was 56.1%, cesarean section 33.3%, premature births was 14% and 33.3% incidence of interruption. Metrorrhagia was seen in 26.3% and myomas were seen in 15.8%. There were no significant trends observed between the groups. 90% of the patients did not experience any change in their MS symptoms after giving birth. Department of Obstetrics Clinic annals was used as a reference standard.

**Summary:** This 11-year period of clinical experience and literature suggest that MS does not adversely affect pregnancy.

### **N32 TREATMENT OF UTERINE FIBROIDS**

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**Keywords:** fibroid, myomectomy, hysteroscopy, laparoscopy, hormonal treatment

**Introduction:** Uterine fibroids are the most common benign tumors of the female genital tract. Their occurrence increases with age, and they are found in 20–50% of all women of reproductive age. The variation on number, size, and location of myomas results in a spectrum of clinical symptoms and signs. Approximately 20–50% of myomas produce symptoms, such as menstrual abnormalities, infertility, spontaneous abortion, pelvic pressure and pain, but many patients are asymptomatic. The last few decades have seen rapid advancements in the diagnosis and treatment of uterine leiomyomas. The introductions of operative endoscopic techniques emphasize the usage of the organ saving procedures. A new situation developed in the treatment of fibroids – keeping in mind the frequent occurrence of fibroids in elderly age – since maternal age at the first pregnancy has increased, and the assisted reproductive techniques are used more frequently.

**Study objective:** In our study we compare the advantages and disadvantages of the laparoscopic myomectomy with laparotomy. We analyze the postoperative recovery of patients undergoing myomectomy and the reproductive outcome before and after myomectomy in patients with myomas.

**Conclusions:** Laparoscopic myomectomy is still the best treatment option for symptomatic women with uterine fibroids who wish to maintain their fertility. Hysteroscopic myomectomy is an established surgical procedure for women with excessive uterine bleeding, infertility or repeated miscarriages. The administration of special hormonal treatments also requires consideration in the therapy of fibroids.

## INTERNAL MEDICINE-FAMILY MEDICINE SESSION

### N34 PATHOPHYSIOLOGICAL CHARACTERISTICS OF ADULT PATIENTS SUFFERING FROM CONGENITAL ADRENAL HYPERPLASIA TAKING GLUCOCORTICOIDS

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**Keywords:** adrenogenital syndrome, treatment

**Introduction:** Congenital Adrenal Hyperplasia (CAH) is a rare genetic disease that is an autosomal recessive inheritance with a frequency of 1:14,000. In our open, cross-sectional examination continuously carried out, we chose adult patients that had been diagnosed with 21-Hydroxylase enzyme deficiency in their childhood, and therefore are subject to chronic glucocorticoid replacement. Our examination started in September 2008 and is still in progress.

**Problem Statement:** Whether there is a connection between the average daily dose of glucocorticoid replacement, the frequency of metabolic differences, the morphology of adrenal glands and the hormonal features showing the efficiency of the

treatment in the case of adult CAH patients subject to chronic glucocorticoid replacement.

**Methods:** We placed 27 CAH patients into our study that are being treated in the Second Department of Internal Medicine, Budapest. We measured the anthropometric features of the patients (weight, height, waist-hip ratio, BMI) and blood lipid levels, analyzed the daily portion of glucocorticoid treatment, the hormonal features showing the efficiency of the treatment (plasma 17 hydroxyprogesterone, testosterone, androstenedione and ACTH), and finally we evaluated the results of the adrenal gland-CT-examination. We used Student T and Mann Whitney tests during the data analysis, and we applied the Fisher exact test for the statistic examination of the differences between the frequencies.

**Results:** Among the 27 patients, there were 12 salt-wasting (SW) and 15 simply virilizing (SV) phenotypes. The average daily dose of glucocorticoid replacement was higher in the SW group. We found significant connections between the average daily dose of hormone replacement and body weight ( $p=0.041$ ), and the waist-hip ratio, cholesterol and LDL concentration. The adrenal gland-CT-examination showed pathological change in the case of 11 (8 females and 3 males) out of the 27 patients. Among male patients we observed significant connection between the size of the adrenal gland and the serum 17-Hydroxylase, androstenedione and plasma ACTH concentrations.

**Conclusions:** In the case of CAH patients subject to chronic glucocorticoid replacement since their childhood, significant anthropometric and lipid changes can be observed.

In spite of treatment with regard to the hormonal parameters reflecting the efficiency of the treatment and constant care, there occurs a pathological change in the adrenal gland in the case of about 40% of the patients. Despite higher than average glucocorticoid dose in the case of men, the hormonal features are more disadvantageous and show connections with the pathological change of the adrenal gland.

### N35 KNOWLEDGE AND ATTITUDE OF HUNGARIAN GENERAL PRACTITIONERS AND YOUNG PHYSICIANS TO OBESITY

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**Keywords:** obesity, family doctor, attitude

**Background:** Obesity is one of the most serious public health problems of the world. GPs have important role to recognize and treat it.

**Aim:** To estimate the knowledge and the attitude of Hungarian GPs and young doctors to obesity.

**Method:** 291 GPs and 62 young doctors (60% women; average age  $56 \pm 34$  years) completed the validated questionnaire which contains 90 questions. We fixed the demographical parameters of the doctors as well.

**Results:** 56% of the GPs think that obesity is an illness, 88% of them use weight loss programs in practice. 49% of them were unaware of the BMI-criteria for obesity. The GPs use

these programs on an average of 10 patients per month and they last an average of 15 minutes. Only 17% of the family doctors feel it is successful among their obese patients. Only 64% of them order a 5-15% reducing of weight. The age of the doctors correlates negatively, but their weight, the localization of their practice, and the number of their special examinations correlates positively with their attitude toward the treatment of obesity. Only 8% of GPs felt well prepared to treat their obese patients.

**Conclusion:** Family physicians often have deficient knowledge about the causes and the dangers of obesity, but at the same time they order very strict aims to their obese patients. Employing dietetics, interactive education about the treatment of the obesity, less administrative work and financed programs by the Hungarian National Health Insurance Fund may lead to changing the attitude of GPs toward obesity.

### **N36 DOUBLE-BALLOON ENDOSCOPY FOR THE DIAGNOSIS AND TREATMENT OF SMALL INTESTINAL DISEASE: A SINGLE-CENTER EXPERIENCE IN HUNGARY IN 150 EXAMINATIONS AND COMPARISON WITH RESULTS OF CAPSULE ENDOSCOPY,**

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**Keywords:** double-balloon endoscopy, capsule endoscopy, obscure GI bleeding, IBD, polyposis syndrome

**Background:** Until recently, only the proximal small bowel was accessible for diagnostic and therapeutic endoscopy. Recently, Yamamoto et al have developed a new method, double-balloon enteroscopy (DBE) that allows high-resolution visualization and therapeutic interventions in all segments of the GI tract. Our aim was to report our experience with the Fujinon EN-450 T5 therapeutic double-balloon endoscope and to compare our findings with the results of previous capsule endoscopy.

**Methods:** Between August 2005 and July 2009, 150 DBE procedures were conducted in 139 consecutive patients (M/F: 67/72, age: 51.1 SD 18.6 years) presenting at our tertiary referral hospital (112 and 16 patients from the oral and the anal route, respectively; 11 patients from both). Result of previous capsule endoscopy was available in 27 patients. The indication for DBE was suspected small-bowel GI bleeding in 83, suspected or known IBD in 25 and polyposis syndrome/suspected neoplasia in 29 patients and ERCP in one

patient. All procedures were performed using i.v. anesthesia, at our outpatient clinic. After the procedure, the patients were monitored in a recovery room for at least 4h before discharge.

**Results:** In obscure bleeding, an abnormal small-bowel finding was found in 50 patients (60.2%) including angiodysplasias, erosions, small ulcers. Malignancy was found in 6 patients (7.2%, 3 GIST, 1 NHL, 1 melanoma, 1 tumor in the duodenum) Intervention was done in 24 patients. In suspected IBD, IBD was diagnosed in 5 out of 13 cases. In known IBD, assessment of the extent, disease behavior and activity was the indication for DBE. In patients with polyposis syndromes or suspected malignancy, polyps were removed by snare polypectomy from the small bowel in 8 patients with Peutz-Jeghers syndrome, while primary adenocarcinoma was diagnosed in 4 patients. The concordance of capsule and DBE findings was only 51.8% (14/27), while in two cases DBE added significant new finding including one malignancy. The average insertion length was approx. 213 cm (range 70 - 480 cm, SD 111).

**Conclusions:** Based on our experience, DBE is a safe and useful method for evaluating and treating small bowel disease in selected patients with obscure bleeding, IBD or polyposis syndromes, including patients with suspected small-bowel strictures, in whom capsule endoscopy is contraindicated.

### **N37 POLYMORPHISMS OF THE GLUCOCORTICOID RECEPTOR GENE ASSOCIATED WITH HORMONALLY INACTIVE ADRENAL ADENOMA**

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**Keywords:** glucocorticoid receptor gene, polymorphisms, haplotypes, adrenal incidentaloma, cortisol producing tumor

**Introduction:** Altered sensitivity against glucocorticoids is influenced by polymorphisms (SNP) of the glucocorticoid receptor gene (GR). The aim of the present study was to explore whether SNPs or a specific haplotype of the GR could be associated with tumor formation or hormonal activity.

**Methods:** The study included 134 patients with adrenal adenoma (102 with hormonally inactive adrenal adenoma: HI; and 32 with cortisol producing: CP tumor) and 129 controls. Hormonal evaluation of the hypothalamo-pituitary-adrenal (HPA) axis, measurement of metabolic parameters was carried out in patients, and genetic analysis in all subjects. Polymorphisms of GR were detected by allele-specific PCR methods for N363S and BclI polymorphism, with RFLP for ER22/23EK and with Taqman allele discrimination assay for A3669G.

**Results:** The prevalence of N363S was higher and A3669G was lower in HI than in CP or controls, especially in patients with bilateral HI tumors: (N363S: 10.5% vs. 2.7% p<0.05;



A3669G: 10.5% vs. 22.1%  $p < 0.05$ ). The prevalence of haplotypes containing N363S variant was significantly higher and haplotypes containing A3669G was lower in patients with HI than in controls or patients with CP. The ER22/23EK was identified both in patients and controls together with A3669G. In CP group no associations between GR SNPs were observed  
**Conclusions:** The pathogenesis of HI adrenal tumors is different than of hormonally active adenomas. The increased prevalence of N363S and the decreased prevalence of A3669G variants of the GR by increased sensitivity against endogenous glucocorticoids can play a role in the pathogenesis of hormonally inactive adrenal incidentalomas especial in bilateral cases.

## PHYSIOLOGY-PATHOPHYSIOLOGY SESSION

### K17 COMPARISON OF ANTIOXIDANT EFFECTS OF SUPEROXIDE DISMUTASE (SOD) AND HYDROGEN SULPHIDE (H<sub>2</sub>S) IN ISOLATED SMALL VEINS

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**Keywords:** oxidative stress, antioxidants, isolated vessels, small veins, vasomotor tone

Recent studies suggest that H<sub>2</sub>S is a potent antioxidant that improves cardiovascular function. Our aim was to compare the antioxidant properties of hydrogen sulphide (H<sub>2</sub>S) to that of superoxide dismutase (SOD) on superoxide-induced vasomotor activity.

Small gracilis veins of Wistar rats were mounted in a myograph (Experimetria-WPI) filled with Krebs solution (37°C) and gassed with 95% O<sub>2</sub>. A basal tone was established, then 60 mM KCl was used to induce pre-contraction. Then the vasomotor effects of the superoxide generator pyrogallol (10<sup>-5</sup> mM) were measured. The chamber was washed out and the vessels were pre-contracted and incubated with SOD (120 U/ml). The contractions to pyrogallol were obtained again. Subsequently, the effect of the H<sub>2</sub>S donor NaHS (10<sup>-5</sup> M) was measured.

In small veins KCl elicited a substantial vasomotor tone (0.63 ± 0.1 mN), which increased after pyrogallol administration (1.3 ± 0.2 mN,  $p < 0.05$ ). In the presence of SOD the pyrogallol elicited contraction was significantly reduced (0.9 ± 0.2 mN,  $p < 0.05$ ). In the presence of H<sub>2</sub>S, the pyrogallol elicited contraction was similar to the control (1.3 ± 0.2 mN). Also, SOD significantly decreased the KCl induced vasomotor tone (0.5 ± 0.1 mN,  $p < 0.05$ ), whereas H<sub>2</sub>S did not affect it (0.6 ± 0.1 mN).

In the present study H<sub>2</sub>S did not prevent the pyrogallol-induced contraction, whereas SOD significantly decreased it. These results suggest that the previously described antioxidant effects of H<sub>2</sub>S are unlikely to be mediated by its direct

interaction with superoxide. (Supported by OTKA K71591 and K67984.)

### K18 CHRONIC PARTIAL OBSTRUCTION OF THE SAPHENOUS VEIN AS A PROBABLE MODEL OF VARICOSITY

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**Keywords:** saphenous vein, varicosity model, partial obstruction of veins

Venous diseases affect up to 50% of adults. This underscores the importance of understanding the pathophysiology of venous diseases especially varicosity. This is the newest method creating varicosity artificially in rats.

We fixed the outer diameter of the saphenous vein of rats at 500 µm causing partial obstruction of the vein by using a plastic clip on one side. We performed our experiments with the main branch and the network of the saphenous vein also in vitro after clipping at 4, 8 and 12 weeks using the opposite side as control. We studied the biomechanics of the main branch, conducted histological experiments and prepared corrosion plastic preparates.

We found that the outer diameter and the wall cross section of the main branch decreased. We also found brushlike small vessel network developed and strengthening collaterals to serve the proper venous circulation.

Our findings correlate with the development phases of human varicosity that were caused by a yet unknown mechanics.

### K19 ROLE OF HEMODYNAMIC FORCES IN THE REGULATION OF VASOMOTOR TONE OF SKELETAL MUSCLE VENULES

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**Keywords:** venules, hemodynamic forces, thromboxane A<sub>2</sub>, cyclooxygenase

**Background:** The vasomotor role of intraluminal pressure has been well characterized in arterioles. Much less is known regarding the importance of pressure-induced regulation of vascular resistance in small vein and venules. We hypothesized isolated small veins develop myogenic tone – albeit in less magnitude than that of arterioles - in response to elevation of intraluminal pressure.

**Methods:** Gracilis muscle venules were isolated from Wistar rats, then cannulated and incubated in PSS in the presence of 10 mmHg of intraluminal pressure (Pi) at T=37°C in a special vessel chamber. Changes in diameter were measured in response to step increases in intraluminal pressure, H<sub>2</sub>O<sub>2</sub> and vasoactive agents. To elucidate cellular mechanisms blockers of cyclooxygenases (indomethacin) and TXA<sub>2</sub> receptors (SQ 29,548) were used.

**Results:** We have found that increases in pressure elicited the development of myogenic tone. That is, the active diameters

of venules were significantly less than the passive diameters obtained in Ca-free solution at the corresponding pressures. Also, H<sub>2</sub>O<sub>2</sub> (10<sup>-7</sup> - 10<sup>-5</sup> M) elicited concentration dependent constrictions (max.: 137+/-8 to 61+/-18 µm, at 10<sup>-5</sup> M), which were inhibited by the presence of indomethacin (2.5×10<sup>-5</sup> M, 30 min.) max.: 135+/-13 µm. vs. 133+/-13 µm, at 10<sup>-5</sup> M. We have also found that H<sub>2</sub>O<sub>2</sub> elicited constrictions were inhibited by the presence of SQ 29,548.

**Conclusion:** Skeletal muscle venules exhibit myogenic response, which is - in part - mediated by H<sub>2</sub>O<sub>2</sub>, which elicits the release of constrictor TxA<sub>2</sub>. These responses and mediators are likely to have important roles in the regulation of resistance of skeletal muscle venules by changes in intraluminal pressure. (Supported: Hungarian Sci. Res. Funds/OTKA – T48376, K67984; AHA Founders Aff. 0855910D, AHA NE Aff. 0555897T; Health Sci. Council/ETT 364/2006)

## **K20 INVESTIGATION OF THE PTDINS(4,5)P2 DEPENDENCE OF AT1 RECEPTOR ENDOCYTOSIS IN LIVING CELLS**

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**Keywords: Internalization, lipid-dependence, confocal microscopy, BRET**

Since many of the molecules participating in the process of endocytosis can bind PtdIns(4,5)P<sub>2</sub>, a role of this lipid in the regulation of the internalization of receptors seemed possible. In this study we focused on the investigation of the lipid dependence of the internalization of Angiotensin II receptor type 1 (AT<sub>1</sub>). We wanted to study which steps of the endocytic process were blocked if we reduced the PtdIns(4,5)P<sub>2</sub> level in the cell. We used confocal microscopy and the highly sensitive method of bioluminescence resonance energy transfer (BRET), which allows the detection of molecular closeness between two proteins. By fusing AT<sub>1</sub> plasma membrane receptors to *Renilla* luciferase and applying YFP-tagged proteins as components of the endocytic machinery (β-arrestin, PM-targeted YFP, Rab proteins) we could follow the process with high temporo-spatial resolution in HEK cells. To decrease the plasma membrane PtdIns(4,5)P<sub>2</sub> level we used the previously developed rapamycin-induced heterodimerization system, in which PtdIns(4,5)P<sub>2</sub> depletion was achieved by the recruitment of 5-phosphatase enzymes to the plasma membrane. First we measured the BRET ratio between the receptors and plasma membrane-targeted YFP, which decreased upon stimulation with the appropriate agonist. When we watched the BRET ratio between the receptor and β-arrestin, we found that the PtdIns(4,5)P<sub>2</sub>-depletion didn't affect the interaction between these molecules, but we found that the BRET ratio decreased between the Rab5-YFP and the AT<sub>1</sub>R-Rluc in case of lipid depletion. After optimizing our system we were able to show that the internalization of AT<sub>1</sub> receptor was significantly reduced after depletion of the lipid.

## **K21 THE DOPAMINE RECEPTOR AGONIST ROPINIROLE ALTERS THE ELECTROPHYSIOLOGICAL PROPERTIES OF ISOLATED CANINE VENTRICULAR MYOCYTES**

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**Keywords: ropinirol, dog, heart muscle, QT-time**

Recent studies have shown that dopamine receptor agonists – widely used in the treatment of Parkinson's disease – may prolong the QT interval, and possibly lead to Torsades de Pointes ventricular tachycardia. Ropinirole blocked hERG potassium channels expressed in CHO-K1 cells, and prolonged the action potential (AP) of canine Purkinje fibers. Ropinirole shortened the PR-interval and lengthened the QTc interval in canine, but its effects in isolated cardiomyocytes are not known. Therefore, we studied the effects of ropinirole on AP morphology in isolated canine ventricular cells.

Single canine myocytes were obtained by enzymatic dispersion. The APs were recorded using sharp glass microelectrodes at 37°C. Concentration-dependent effects of ropinirole were determined in a cumulative manner between 0,1 and 300 µM.

Ropinirole displayed biphasic effect on AP duration. In 11 cells 10 µM ropinirole significantly increased the AP duration measured at 90% of repolarization (APD<sub>90</sub>), from 221.9±8,3 ms to 239.8±10.8 ms, but 300 µM ropinirole decreased the APD<sub>90</sub> to 214.5±1 ms. 100 µM ropinirole reduced the amplitude of early repolarization to 70.27±4.63%, and the maximum rate of depolarization to 83.9±2.5% of control. Ropinirole failed to induce significant changes in the resting membrane potential and the amplitude of the AP.

In conclusion, ropinirole lengthened the AP between 1 and 100 µM, but 300 µM ropinirole shortened APD. Since the lowest concentration of ropinirole causing statistically significant changes in our study was much higher than the usual peak plasma concentration, it's unlikely that normally dosed ropinirole can alter cardiac electrogenesis in healthy individuals.

## **K22 AGE-RELATED TENDENCY IN THE EFFECTS OF CENTRAL NEUROPEPTIDES ON ODY WEIGHT REGULATION IN RATS**

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**Keywords: alpha-MSH, NPY, neuropeptide, body weight, age**

**Introduction:** Both weight gain of middle-aged and excessive weight loss in the elderly population result in significant public health problems worldwide. Complex age-related

alterations in the effectiveness of central regulatory neuropeptides may be occurring. It is suggested that the responsiveness to orexigenic and anorexigenic neuropeptides in the hypothalamus changes with age, which may contribute to the development of the metabolic dysregulation.

**Aim:** Our aim was to study the central effects of catabolic alpha-melanocyte-stimulating hormone ( $\alpha$ -MSH), catabolic corticotropin releasing factor (CRF), and of anabolic neuropeptide Y (NPY) on food intake (FI) in rats of different age-groups.

**Methods:** Male Wistar rats aged 6-weeks, 3-4-, 6-, 12-, 18- or 24-months represented the human juvenile, young adult, 2 middle-aged and 2 old groups, respectively. Cumulative FI-values were measured in a Feedscale system (Columbus) following intracerebroventricular (ICV) injections of  $\alpha$ -MSH (5  $\mu$ g), CRF (0.3  $\mu$ g), NPY (5  $\mu$ g) or saline.

**Results:** Central administration of  $\alpha$ -MSH considerably attenuated both spontaneous FI and re-feeding following 24-h fasting. The FI suppression at the second hour of re-feeding varied between age groups: 22 % reduction was seen in juvenile, strong suppression (69 %) in young adult rats, which was attenuated by middle-age (56 % or 26 %), and was extreme (94 % or 74 %) in old animals. The catabolic effects of CRF were also less in middle-aged rats in comparison with young ones. Anabolic NPY, on the other hand, showed improved efficacy in the young, and decreased one in the old groups, but the most pronounced FI elevation was found in the middle-aged rats.

**Conclusions:** Characteristic age-related tendencies in the responsiveness to centrally applied neuropeptides suggest an orexigenic predominance in the middle-aged groups, while an anorexigenic dominance in the old population. Our results raise that age may have a direct effect in the long-term energy regulation, and might contribute to the explanation of both the development of middle-aged obesity and the sarcopenia of elderly.

### **K23 THE THERMOREGULATORY EFFECTS OF ALPHA-MELANOCYTE STIMULATING HORMONE**

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**Keywords: alpha-MSH, HS024, thermo regulation**

Neuropeptides play an important role in body weight- and body temperature regulation. Alpha-melanocyte stimulating hormone ( $\alpha$ -MSH) has coordinated catabolic actions: it suppresses food intake and increases metabolic rate (MR). In addition,  $\alpha$ -MSH is also regarded as an antipyretic substance. We investigated whether the thermoregulatory effects of  $\alpha$ -MSH are also coordinated and analyzed the antipyretic actions.

Adult male Wistar rats were injected 0.9 % saline,  $\alpha$ -MSH (5  $\mu$ g) or a selective melanocortin 4-receptor (MCR4) antagonist (HS024 0.5, 1, 2  $\mu$ g) via a chronic intracerebroventricular

(ICV) cannula at different ambient temperatures ( $T_a$ ). In other cases, 120-min prior to the ICV  $\alpha$ -MSH injection, 10  $\mu$ g/kg LPS was administered intravenously. Heat production (indirect calorimetry), heat loss (tail skin temperature) and colon temperature ( $T_c$ ) were continuously recorded. At a cool ambient temperature,  $\alpha$ -MSH induced marked elevation of MR, which was not antagonized by skin vasodilation, leading to a pronounced  $T_c$ -rise. Slightly below thermoneutrality, the rise in MR and  $T_c$  was accompanied by a delayed skin vasodilation preventing any further  $T_c$ -elevation. At a slightly higher ambient temperature, skin vasodilation occurred more promptly and prevented any rise in  $T_c$ . In febrile rats  $\alpha$ -MSH showed antipyretic effect by inducing skin vasodilation. In contrast, acute injections of HS024 resulted in a coordinated response, the decrease in  $T_c$  and MR was accompanied by vasodilation. Thermoregulatory effects of  $\alpha$ -MSH depend on initial  $T_c$  and  $T_a$  and do not show a coordinated pattern, while a MCR4 antagonist elicited a coordinated thermoregulatory response. These findings suggest a role of MCR4 in thermoregulatory processes.

### **K24 AGE-RELATED ALTERATIONS IN THE REGULATION OF ENERGY-BALANCE: EFFECTS OF A 7-DAY LONG CENTRAL ALPHA-MSH INFUSION**

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**Keywords: Aging, melanocortin, alpha-MSH, energy homeostasis**

Hypothalamic melanocortins, e.g. alpha-melanocyte stimulating hormone ( $\alpha$ -MSH) play an important role in the regulation of energy balance: they suppress food intake (FI), enhance metabolic rate (MR) and decrease body weight (BW). Trends in long-term BW regulation are characterized by obesity in the middle-aged and later anorexia of aging. The dominant catabolic system, the melanocortins may participate in these alterations.

Male Wistar rats aged 2-, 4-, 12- and 24-months represented human juvenile, young, middle-aged and old age-groups, respectively. Body temperature ( $T_c$ ), spontaneous activity, heart rate (HR, indicator of MR) were recorded in a biotelemetric system. An osmotic minipump was implanted providing a 7-day-long intracerebroventricular infusion of 1 microg/microl/h alpha-MSH.

Decline of FI and BW during the infusion was weakest in the 12- and most pronounced in the 24-month-old rats. Body temperature showed a different pattern. No effects developed in juvenile, modest daytime changes were seen in the young and old groups. Both day- and nighttime values increased significantly in middle-aged animals. Tachycardia developed only in the two older groups. In the oldest rats, the rise in nighttime HR lasted for 4 days, whereas middle-aged animals maintained high night- and daytime HR throughout the infusion.

Middle-aged rats appear to be insensitive to the anorexigenic but not to the metabolic effects of alpha-MSH. Their slight

weight loss may be attributed to an MR-rise. FI and BW are particularly sensitive to melanocortins in aged rats. The effects of alpha-MSH on different parameters of energy balance do not change parallel to one another during aging.

#### **K25 EFFECTS OF CENTRAL ALPHA-MSH INFUSION IN DIFFERENT NUTRITIONAL STATES**

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The alpha-melanocyte stimulating hormone (alpha-MSH) is an endogenous agonist of the hypothalamic melanocortin (MC) system. It acts mainly on the hypothalamic MC4-receptors, has coordinated catabolic effects by decreasing food-intake (FI), increasing metabolic rate and thus leading to a decrease in body weight (BW). The adipocyte-derived leptin is an important peripheral catabolic hormone, which stimulates the central melanocortin system. Despite obesity-induced leptin-resistance, alpha-MSH activity might still be maintained. The aims of the present study were to investigate the responsiveness of the MC system in rats of different nutritional states – the present data were compared to our previous results of effects of the centrally applied leptin infusion in different nutritional states.

A biotelemetric system was used to record core temperature (Tc), heart rate (HR, as an indicator of metabolic rate) and activity of three groups [calorie-restricted (CR6), *ad libitum* fed (NF6) and a high-fat-diet-induced obese (HF6) group] of 6-month old male Wistar rats. After the implanting an Alzet osmotic minipump, the effects of a 7-day long, 1 ug/ul/h intracerebroventricular infusion of alpha-MSH was studied. The FI and BW were measured manually every day.

Central alpha-MSH infusion reduced BW in all the groups. The most pronounced BW loss was seen in NF6 animals but – in contrast to the leptin infusion – alpha-MSH was able to cause a significant drop in BW also in CR6 animals. A minimal decrease in FI occurred in CR6, a significant one in NF6 and HF6 animals. The rise in the Tc minima and HR minima were strongest in the CR6 and weakest in the HF6 group.

Our data showed that the catabolic effects of a central alpha-MSH infusion are dissimilar in rats of different nutritional states. In addition, the data suggest that the catabolic effects of alpha-MSH and leptin show independent characteristics. Alpha-MSH can reduce BW in CR6 rats and, despite obesity-induced leptin resistance, alpha-MSH responsiveness is still maintained for some parameters (Tc, HR).

#### **K26 EXOGENOUS METHANE REDUCES MESENTERIC BARRIER DAMAGE CAUSED BY ISCHEMIA-REPERFUSION INJURY**

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**Keywords: methane, ischaemia-reperfusion, microcirculation**

**Introduction:** Circulatory shock conditions lead to severe splanchnic microvascular dysfunction and damage in the short run. The mesenteric perfusion disorder leads to mucosal injury, increased permeability of the intestinal wall, and results in bacterial translocation and septic complications. Our previous *in vitro* studies have revealed a methane-generating response to hypoxia and earlier experiments with mitochondria and endothelial cells demonstrated the effectiveness of methane to decrease oxygen free radical generation (*Ghyczy M et al. Cell Physiol Biochem 2008*). To understand the significance of non-microbial methane formation, our aim was to investigate the effects of exogenous methane administration on ischemia-reperfusion (I/R)-induced mesenteric inflammation, where the pathophysiology critically involves the generation of oxygen radicals.

**Methods:** We have monitored mean arterial pressure and superior mesenteric artery blood flow changes for 4 hrs in anesthetized rats. Control, I/R, I/R with methane treatment (I/R+Met) groups were used (n=6 each); I/R+Met animals were treated with artificial air containing 2.5% methane in the last 5th min of ischemia and for 10 min during reperfusion. Blood-gas parameters and small intestinal superoxide (SOX) levels were measured 3 times during the experiments. Myeloperoxidase enzyme activity (MPO), tissue-type superoxide production, nitrite/nitrate and nitrotyrosine (NTyr) levels were determined from biopsy samples, fluorescent dextran (intraluminal or iv) was used to measure epithelial (EP) and vascular permeability (VP) changes.

**Results:** Significant elevation was detected in small intestinal SOX, NTyr levels, MPO activity and EP after I/R, while vascular permeability did not change. The pathological changes were significantly reduced in I/R+Met animals. Tissue nitrite/nitrate level was decreased during reperfusion and methane inhalation corrected this change also back to control level.

**Conclusion:** Methane is bioactive and anti-inflammatory. Exogenous methane administration contributes to the neutralization of oxygen- and nitrogen-centered radicals after I/R, which improves mucosal microcirculation.

#### **K27 FLOW-INDUCED VASOMOTOR RESPONSES CEREBRAL MICROVESSELS ARE LOCATION SPECIFIC**

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**Keywords: Pressure/flow myograph, vasomotor response, Monroe-Kelly**

**Background:** Mechanical forces, such as blood pressure and wall shear stress (WSS) known to affect the smooth muscle tone of blood vessels. It is well established that increasing

pressure elicits myogenic constriction, which plays substantial role in the regulation of cerebral blood flow. However, changes in intraluminal pressure are accompanied with changes in intraluminal flow, thus WSS. Interestingly, less is known regarding the responses of cerebral vessels to increase in flow/WSS and the underlying cellular mechanisms. We hypothesized that - because of the limitation of intracranial space - small cerebral arteries constrict to increase in flow/WSS, as well.

**Methods:** Changes in diameter of isolated middle cerebral arteries (MCA, n=20) of rats and intracerebral arterioles of human brain samples (n=2) were measured in response to stepwise increases in pressure and flow/WSS. Experiments were conducted in control conditions and in the presence of cyclooxygenase inhibitor indomethacin, TXA<sub>2</sub> receptor antagonist SQ 29,548, or scavengers of reactive oxygen, superoxide dismutase (SOD) and catalase (CAT). Finally, the passive diameter (PD) of vessels was measured in passive/Ca<sup>2+</sup>-free solution.

**Results:** MCA maintained a constant diameter in the face of increasing pressure in a pressure range of 40-150 mmHg (~58% of passive diameter), and significantly constricted to increases in flow/WSS (from 61±1.2 to 50±1.3% of passive diameter, p<0.05). Flow/WSS-induced constrictions significantly augmented pressure-induced constrictions. Importantly, we have found that human arteries also constricted to increase in flow/wss (for example, at max. flow: from 332 to 267 µm, at 80 mmHg, PD: 409 µm). Flow/wss-induced constrictions of MCA were abolished by indomethacin or SQ 29,548 and significantly attenuated by SOD/CAT.

**Conclusion:** Increases in flow/WSS elicited constrictions - instead of dilation - of cerebral vessels of rats and humans and augmented myogenic vasomotor tone. The potential mechanisms involve constrictor prostanoids and reactive oxygen species. We suggest that changes in mechanical forces - pressure and flow/WSS - contribute to the regulation of cerebral blood flow.

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## SURGERY SESSION

### K28 LAPAROSCOPIC TREATMENT OF FOCAL HEPATIC DISEASES

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**Keywords: Laparoscope, focal, hepatic, surgery**

Laparoscopic hepatectomy is used particularly for healing benign disorders, less commonly treating malignant focal diseases.

**Methods:** There was 42 laparoscopic hepatectomies between 2001 and 2008 in the Surgical Institute of the Medical and Health Science Center in Debrecen. 31 of the patients were women and 11 men. In 39 cases, the indication was benign

tumor 11 FNH, 8 hemangioma, 4 simple cyst, 3 echinococcus cyst, 1 adenoma, 2 biliary dysplasia, 10 other benign disorders, and in 3 cases colorectal metastases were removed. In 31 cases it was atypical, and in 8 cases anatomical resection, and there was 3 pericystectomy as well. The average size of the tumors were 1.18 inch. In 3 cases the synchronous cholecystectomy was indicated. The average duration of the surgeries was 55 minutes.

**Results:** the conversation to laparotomy was needed on 3 occasions. There was 1 reoperation; the reason was bile leakage. As early postoperative complication fever, temporary increase of hepatic enzymes, bile leakage came forward. 3 patients needed transfusion. The average hospitalization was 5 days long. The institute did not lose any patient in the early postoperative period.

**Conclusion:** laparoscopic hepatic resection can be suggested for the therapy of small sized, mainly benign and peripheral localized hepatic tumors. By choosing the correct operative technique, the number of bleeding and other complications can be reduced, and all advantages of the minimally invasive operative method become apparent.

### K29 THERAPY WITH ANTIBIOTIC FILLED PMMA-SORBITOL CAPSULE FOR EXPERIMENTAL OSTEOMYELITIS DUE TO STAPHYLOCOCCUS AUREUS IN RABBITS

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**Keywords: PMMA capsule, chronic osteomyelitis, surgical debridement**

**Introduction:** The Department of Surgical Research and Techniques at the University Medical School of Pecs, launched a new research program, for testing a new capsule form of the widely-known polymethyl-metacrylate (PMMA), as a drug delivery system. The research aimed at developing a new medical tool.

**Methods:** To induce the tibial osteomyelitis, the tibia of 110 mixed sex New Zealand rabbits were infected with *S. Aureus*. The procedure was performed under ketamine narcosis and included the following steps: first a window (4×2mm) was prepared on the anteromedial surface of the tibia, then the eliminated bone was devitalized in boiling water. This was followed by the implantation of the bone into the marrow cavity and the *S. Aureus* (2×10<sup>9</sup> CFU) was introduced into the marrow cavity, using a syringe. The methods used, are in accordance with the Hungarian legal regulation on animal experiments. The follow up of the sepsis, included the monitoring of the animals' physical state, blood test, checking body temperature and the state of the wounds. Infected areas were detected using radiological, microbiological, and histological methods. The implantation of the antibiotics filled PMMA capsules was carried out six weeks after the preparation phase. The procedure included treating all the

animals with surgical debridement, then the randomly grouped animals underwent the following procedures: tygacillin, gentamycin, tobramycin, vancomycin and clindamycin was administered on one and only surgical debridement was applied on their other legs. In the second phase of the experiment, the tibias were removed under sterile conditions, and sent for radiological, microbiological, histological, and hematological analyses to gain an insight into the process of healing and information on the degree of systemic antibiotic concentration.

**Results:** During the preparation phase the typical macroscopic signs of osteomyelitis occurred. The radiological and the microbiological analyses proved the presence of chronic osteomyelitis. A regression of the chronic inflammation was noticeable at the end of the therapy, which was confirmed with histological and radiological methods. No remarkable systemic antibiotic concentration was detected

**Conclusion:** Our findings suggest that the method might be effectively used for modeling osteomyelitis. Each of the treatment modalities resulted in a significant therapeutic effect. Due to its ability to quickly release large amounts of several antibiotics, the PMMA drug delivery system maybe a promising tool in the surgical management of osteomyelitis.

### **K30 OUTCOME PREDICTION IN CASE OF SEVERE TRAUMATIC BRAIN INJURY: APPLICATION OF THE IMPACT OUTCOME CALCULATOR FOR A HUNGARIAN COHORT**

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**Keywords:** severe skull injury, IMPACT database

Traumatic brain injury (TBI) represents the leading cause of mortality in the first four decades. Several recent surveys in Hungary have proven that in-hospital mortality of severe TBI is unacceptably high reaching up to 43-54%.

Among these studies, in 2002 prospective multicenter data collection was performed in Hungary involving 66 hospitals to provide a better insight into the epidemiology of severe TBI in Hungary, enrolling 267 patients (Csepregi et al.). In 2007 after detailed analysis the data of 8509 patients from the IMPACT (International Mission for Prognosis and Analysis of Clinical Trials) database Steyerberg et al. have developed a web-based prognostic calculator based on those admission parameters which were found highly predictive.

Our study was aimed to assess the predictive power of the IMPACT calculator retrospectively for those patients enrolled into the Hungarian database. We also intended to analyze the

correlation of expert opinion provided by three neurosurgeons experienced in the field of neurotrauma care blinded for the outcome of our patients and the predictive power of the IMPACT calculator.

Of the 267 case report forms there were only 193 where the patients were over 14 at the time of the injury and contained all admission data to fulfill the criteria of the "Core" model of the prognostic calculator as well as reliable outcome data. When we compared the mortality predicted by the outcome calculator with actual GOS values at discharge we found a significant correlation: 0.42, similarly, all four experts were able to predict outcome at a similar level: 0.40; 0.43; 0.46 Pearson coefficients, respectively. We may state that 0.42 is about 18% of mortality could be interpreted on the basis of the "Core" parameters of the outcome calculator.

In conclusion we have proven that the IMPACT outcome calculator is applicable on Hungarian TBI patients however further investigations are justified to clarify the reasons of the extremely high mortality of severe TBI patients in our country.

### **K31 INVESTIGATION OF FOCAL VIRUS PERSISTENCE IN IDIOPATHIC CARDIOMYOPATHY**

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**Keywords:** idiopathic cardiomyopathy, focal virus, DCM

Previous research has already shown connection between viral infections and dilated cardiomyopathy (DCM). To proof the viral etiology we use endomyocardial biopsy from the right ventricle. Our theory is that after some kind of virus infections, the virus particles can persist focally in the myocardium. If our assumption is true, then the results of the EMB-s can be falsely negative. In the research we took samples explanted hearts from recipients during cardiac transplantation. We processed 18 ischemic, 17 idiopathic and 20 control patients' hearts. The muscle samples were taken from five regions: right ventricular antero-septal and postero-septal region, left ventricular anterior region, posterior region and left ventricular apex. At the same time, we took blood samples for viral assessment as well to rule out systemic viral infection. The samples after storage were investigated by polymerase chain reaction technique for enterovirus, adeno, and herpesvirus. The resulting data were analyzed by Fisher's exact test. A total of 175 samples were tested, eleven samples showed positive results for infection. 10 virus samples and 1 sample showed the presence adenovirus and herpesvirus. The patient blood sample excluded the possibility of acute inflammation. The statistical analysis showed a significant difference between the DCM's and the control group in the case of adenovirus. The patterns of the positive regions were different at all patients, and we could not find any patient who had all regions positive. The results support the theory that adenoviruses can persist focally in the myocardium. Based on the results we think we should take multiple samples to clarify the infective etiology in the case of DCM.

### **K32 IS THE PELVIC INCIDENCE TRULY CONSTANT?**

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**Keywords: Pelvic incidency, Duval-Beaupere, EOS 2D/3D, scoliosis, reconstruction**

**Introduction:** Among the saggital pelvic parameters -introduced by Duval-Beaupere in 1997- the pelvic incidence is a data that is independent from the position and typical for the concrete person. Based on publications and informations about our operated pations with scoliosis it's supposable that PI is not constant in some cases.

**Aims:** To compare the saggital pelvic parameters of standing to sitting positions. And find any clinically significant difference.

**Methods:** Identify saggital pelvic parameters on 22 patients (age: 17.93  $\pm$ 9.42 year) using standing and sitting X-ray photos. These results took as a basis 3-3 independent measurement made by 4 experimented examiners. We worked with the EOS 2D/3D (Biospace, France) totalbody X-ray machine, it uses ultralow dosis. We got surfacial, solid spine-reconstructions and automatically calibrated clinical parameters. The sources of our results are the calculations of sterEOS 3D. This computer program works with two oriented 2D EOS X-ray photos. The differences between standing and sitting PI datas were analyzed by 2 patterned t-test and SPSS 16.0 statistical program.

**Results:** Among standing and sitting PI datas 5 from 22 were found to be more than 6, other 3 occasions more than 3 degrees. These are statistically significant ( $p < 0.05$ ). 4 other occasions the differences were 1-3 degrees, these are not clinically significant.

**Conclusion:** The PI datas change while the bodyposition switch from standing to sitting. It may means that in some people the PI are not an anatomical constans. This supposition could play a main role in compensatorical deformations in saggital curves of the spine.

### **K33 HISTOLOGICAL AND FUNCTIONAL CHANGES FOLLOWING ND YAG LASER PHOTOCOAGULATION OF RAT GASTRIC MUCOSA**

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**Keywords: pediatric surgery, urology, bladder augmentation.**

**Aim of the study:** Surgical enlargement of the urinary bladder is frequently performed using segments from the gastrointestinal tract (stomach, small- or large bowel). When full thickness of the stomach-wall is used, complications (hematuria-dysuria, etc.) have been reported. This animal study investigates histological and functional changes following NdYAG laser photocoagulation of rat gastric mucosa used as a graft for bladder enlargement.

**Material and methods:** In twenty -three rats gastrotomy on the acid producing part of the rat stomach was performed. Applying different energy levels (10, 20 and 50 J/cm<sup>2</sup>) of NdYAG laser we examined the acute and chronic reactions. The animals were divided in two groups based on histological changes and functional evaluation (basic and histamine stimulated acid production).

**Results:** The 10 and 20 J/cm<sup>2</sup> energy levels caused similar histological changes. Ulceration was observed macroscopically and microscopically at 50J/cm<sup>2</sup> level and a moderate degree of regeneration in one week. In the functional group we observed decreased acid production at all laser energy levels. Similar results were observed 7 days following surgery.

**Conclusion:** In this in vivo model, the exposure of 50 J/cm<sup>2</sup> of NdYAG laser caused ulcer, destruction in rat gastric mucosa. At 10 and 20 J/cm<sup>2</sup> much less severe changes were observed. The gastric mucosa showed decreased acid production following all three kinds of laser treatment used both in acute and chronic setups. Further studies are warranted for the evaluation of the value of laser photocoagulation to decrease the complications of gastric mucosa in urinary bladder augmentation surgery.

### **K35 ANTI-INFLAMMATORY EFFECTS OF NMDA-TYPE GLUTAMATE RECEPTOR INHIBITION IN EXPERIMENTAL COLITIS**

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**Keywords: IBD, N-methyl-D-aspartate receptors, kynurenic acid, motility, microcirculation**

Inflammatory bowel diseases are often accompanied by severe gastrointestinal functional damages and recent data suggest that glutamatergic neurotransmission elements are involved in the signal transduction during these conditions. Our aim was to investigate the consequences of peripheral N-methyl-D-aspartate (NMDA)-sensitive glutamate receptor (NMDA-R) blockade on motility changes and accompanying inflammatory responses in a rodent model of ulcerative colitis. Macrohemodynamics, serosal microcirculation (intravital videomicroscopy), inflammatory enzyme activities (xanthine oxidoreductase (XOR), myeloperoxidase (MPO), nitric oxide synthase (NOS), tissue TNF- $\alpha$  levels and colonic motility (strain-gauge technique) were studied at two stages of 2,4,6-trinitrobenzenesulfonic acid (TNBS)-induced colitis in anesthetized rats. In both series two groups received NMDA-R antagonist treatments (the endogenous antagonist kynurenic acid (KynA) or SZR-72, a blood-brain barrier-permeable synthetic KynA analogue). The first series involved acute studies with 17 h observation after colitis induction, while a 6-days period was chosen for the subchronic time frame.

TNBS enema induced hyperdynamic circulatory reaction, increased serosal capillary blood flow, elevated mucosal XOR,

MPO, NOS activities and TNF- $\alpha$  levels, and significantly increased colonic motility as compared to controls by the end of day 1. After 6 days identical alterations were noted except for motility, which was strongly depressed in this phase of colitis. Treatments with KynA and SZR-72 significantly decreased XOR, NOS and MPO activities, permanently decreased motility index and increased colonic tone when administered at the 1st day. The NMDA antagonists had similar effects on inflammatory markers at the 6th day, and decreased TNF- $\alpha$  levels also.

These data demonstrate a potential modulatory effect of NMDA-Rs in the colitis-induced functional changes. Inhibition of the enteric NMDA-Rs may provide a therapeutic option to influence intestinal hypermotility and inflammatory activation simultaneously.

## OPHTHALMOLOGY SESSION

### N38 CORNEAL CROSS-LINKING: TREATMENT RESULTS IN KERATOCONUS PATIENTS

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**Keywords: Keratoconus, Cross-linking, Riboflavin, Pentacam**

**Background:** Keratoconus is a non-inflammatory disorder, characterized by corneal thinning and anterior protrusion. These changes in corneal shape induce irregular astigmatism and myopic shift, causing gradual impairment of vision. Recently corneal cross-linking with riboflavin/UVA has been developed for the treatment of keratoconus, as it markedly stiffens the cornea.

**Purpose:** The aim of the present study is to evaluate the effect of the treatment on keratoconic eyes.

**Patients and methods:** Cross-linking was performed in seven keratoconus cases. The mean age of the patients was 32.57 years  $\pm$  10.06 (SD). The corneas were examined before and 6 months after treatment. UCVA and BSCVA were evaluated, examination of the corneas was performed with Pentacam Scheimpflug camera.

**Results:** We compared the mean values of corneal parameters before and 6 months after the treatment. Statistical analysis was performed by the Wilcoxon test. The steepest keratometry reading (K2), the mean keratometry reading (Kmean) and posterior elevation decreased significantly. Preoperative K2 was 52.4  $\pm$  5.4 D, postoperatively 51.6  $\pm$  5.28 D (p=0.016). Kmean changed significantly from 49.47  $\pm$  5.16 D to 48.79  $\pm$  5.09 D (p=0.028). Posterior elevation showed a significant decrease from 86.29  $\pm$  27.93  $\mu$ m to 74.14  $\pm$  22.07  $\mu$ m postoperatively (p=0.028). BSCVA, astigmatism, anterior elevation and descriptive parameters for the progression didn't changed significantly.

**Conclusion:** The procedure is the newest non-surgical method for the treatment of keratoconus. Stable corneal parameters suggest that cross-linking is an effective method to stop the progression of keratoconus.

### N39 RETINOPROTECTIVE EFFECT OF PITUITARY ADENYLATE CYCLASE ACTIVATING POLYPEPTIDE I STREPTOZOTOCIN-INDUCED DIABETIC RETINOPATHY IN RATS

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**Keywords: PACAP, diabetes, retinoprotective**

Pituitary adenylate cyclase activating polypeptide (PACAP) has been shown to exert protective effects in different neuronal injuries in vivo. Diabetic retinopathy is a leading cause of blindness in adults. Effects of neurotrophic factors (such as PACAP) have not yet been characterized in diabetic retinopathy.

Diabetes was induced by streptozotocin in male Wistar rats. We administered PACAP-injection 3 times into the vitreous body of the right eye by Hamilton-syringe. For evaluation of the treatments we used different kinds of immunohistochemical and molecular biological methods in histological preparations, and also functional tests (electroretinography, ERG).

Diabetic retinopathy resulted in significant reduction of dopaminergic amacrine cells in the inner nuclear layer. Surviving cells showed severe degeneration, demonstrated by the shape of their soma and their processes. PACAP-treatment led to a nearly intact appearance of the soma, processes and also led to an increased cell number.

According to molecular biological analyses, pro-, antiapoptotic signaling molecules and TH immunostaining was altered by PACAP treatment compared to control diabetic retinas indicating the possible mechanisms of effect of PACAP treatment. We have also evaluated ERG changes in diabetic control, and diabetic PACAP-treated rats 4 weeks after the streptozotocin injection.

In summary, intravitreal PACAP administration protected retinal cells, demonstrating its therapeutic potential in streptozotocin-induced diabetic retinopathy.

### N40 ASSESSING THE IMPACT OF DEVIATIONS OF THE EYE USING MULTIFOCAL ELECTRORETINOGRAM

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**Keywords: strabism, electrophysiology, emmetropy, myopia**

**Objective:** This study was designed to investigate the cooperation of both eyes or strabismus artificial established deviation event.



**Patients and methods:** In our study 10 patients participated in cross-eyed, whom orthoptical therapy resulted in visual acuity was 1.0 in both eyes, but the remaining strabismus. Control 10 well-sighted, without strabismus person, occasioned by the prism deviation of eyes. It emmetropic 5 persons (unadjusted 1.0), and 5 persons myopic (correction 1.0) was. The subjective methods orthoptical addition, electrophysiological studies also tried to objectively determine the degree of strabismus. The Multifocal ERG binocular and monocular stimulation test was also performed.

**Results:** In normal vision, squint binocular stimulation of the patients received the best response to the same location of the strabismus angle. Binocular the case of each eye fixation of "best" response to stimulation was below the monocular response amplitude values. The resulting prism deviation is not significantly altered by the mfERG parameters.

**Summary:** The Senso-motor anomalies in strabismus, which not only deviant, but the dominant response of the eye is affected. The mfERG in central retinal area of 30 stimulation procedure used. Artificial deviation event was no significant difference in the two eyes retinal function of the pins.

#### N42 THE POSSIBLE ROLE OF THE GLUCOCORTICOID RECEPTOR GEN POLYMORPHISMS IN THE DEVELOPMENT OF CENTRAL SEROSAL CHORIORETINOPATHY

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**Keywords: Chorioretinopathia Centralis Serosa (CSC), glucocorticoid receptor (GR)**

**Introduction:** CSC of the retina and the choroid is one of the less frequent idiopathic diseases that presents with limited detachment of the serous neuroretina in the macula. Stress factors said to have an important role in the development of this disease.

**Goals:** Research the morphology (optical coherency tomography, OCT) and the function of CSC patients (multi focal electroretinography, mfERG). Explore the possible connections between the polymorphism of the glucocorticoid receptors and CSC

**Methods:** 66 CSC patients (59 male, 7 female; age 40.6±6) were analyzed in a planned case-controlled study by OCT (active phase 50, finished CSC 16 eyes follow up 23 months ± 9.7 months). mfERG in the active phase n= 33; non-active phase n=16 eyes. DNA examination of the peripheral blood sample, and the lymphocytes by PCR technique to recognize the: Bcl1, N363S, A3669G polymorphisms (n= 66). Compare the allele frequency with the healthy control group (n=160). Statistics: Spearman correlation, Fisher test, MannWhitney U test.

**Results:** OCT: In 8 patients without complaints, the pigment layer of the other eye was detached. After CSC there were no difference in the thickness of the retina between the hit and the intact eye. During mfERG examination in those eyes that were in acute phase the response density was reduced in the

central ring (average response density 41.4 nV/deg<sup>2</sup>; p=0.04), after the acute phase of CSC no difference was measured between the hit eye and the intact one. No significant differences could be found compared to healthy group in the allele frequency of Bcl1 and N363S polymorphism. The allele frequency of A3669G polymorphism was significantly lower compared to control group. (p=0.035).

**Conclusion:** In the patients with CSC, decreased allele frequency of A3669G polymorphism might cause an increased glucocorticoid sensitivity.

#### PATHOLOGY-ONCOLOGY SESSION

##### N44 CELL CYCLE REGULATION PARALLELS WITH THE PROGRESSION OF GIANT CELL TUMOR OF BONE (GCTB) I.

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**Keywords: cell cycle, GCTB, prognostic factors**

Giant cell tumor of bone (GCTB) is a benign but potentially malignant and locally aggressive, osteolytic lesion (WHO). The tumor consists of neoplastic stromal cells, monocytic cells and their progeny osteoclast type giant cells. GCTB is responsible for 2-9% of primary, and ~20% of benign bone tumors. Histopathological features cannot predict clinical progression of GCTB. A comprehensive study of cell cycle regulation was performed in 280 primary (P), primary recurrent (PR) and secondary (R) GCTB samples of 187 patients focusing on the expression of proteins of replication licensing (mcm2), cell cycle progression (Ki67, cyclinD1, -D3, -E and -A; cdk2, cdk4) and cell cycle control (p16ink4, p21waf1, geminin) by using immunohistochemistry in tissue microarrays and digital microscopy. The cell proliferation marker Ki67 (B56), G1-phase promoter cyclinD1, -D3 and cdk4, G1-phase inhibitor p21waf1 and the S-phase promoter cyclinA and cdk2 positive mononuclear cell fractions showed significant positive correlation with clinical progression. The proportion of mcm2 (replication licensing) and geminin (late control of refiring) positive cells was the same in all groups indicating completed replication in most licensed cells without major defect in the cell cycle regulation. Hierarchical cluster analysis revealed a cluster of 41 cases dominated by the progressive recurrent cases. Initiated replication in giant cells might be abortive due to the nuclear expression of G1-phase inhibitors p21waf1 and p16ink4 and the lack of mcm2. Our results suggest a biomarker panel of cell cycle regulators (cyclinA, -D, cdk2, p21waf1 and Ki67) which may help predict the clinical behavior of GCTB.

##### N45 CELL CYCLE REGULATION PARALLELS WITH THE PROGRESSION OF GIANT CELL TUMOR OF BONE (GCTB) II.

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**Keywords: cell cycle, GCTB, prognostic factors**

Giant cell tumor of bone (GCTB) is a benign but potentially malignant and locally aggressive, osteolytic lesion (WHO). The tumor consists of neoplastic stromal cells, monocytic cells and their progeny osteoclast type giant cells. GCTB is responsible for 2-9% of primary, and ~20% of benign bone tumors. Histopathological features cannot predict clinical progression of GCTB. A comprehensive study of cell cycle regulation was performed in 280 primary (P), primary recurrent (PR) and secondary (R) GCTB samples of 187 patients focusing on the expression of proteins of replication licensing (mcm2), cell cycle progression (Ki67, cyclinD1, -D3, -E and -A; cdk2, cdk4) and cell cycle control (p16ink4, p21waf1, geminin) by using immunohistochemistry in tissue microarrays and digital microscopy. The cell proliferation marker Ki67 (B56), G1-phase promoter cyclinD1, -D3 and cdk4, G1-phase inhibitor p21waf1 and the S-phase promoter cyclinA and cdk2 positive mononuclear cell fractions showed significant positive correlation with clinical progression. The proportion of mcm2 (replication licensing) and geminin (late control of refiring) positive cells was the same in all groups indicating completed replication in most licensed cells without major defect in the cell cycle regulation. Hierarchical cluster analysis revealed a cluster of 41 cases dominated by the progressive recurrent cases. Initiated replication in giant cells might be abortive due to the nuclear expression of G1-phase inhibitors p21waf1 and p16ink4 and the lack of mcm2. Our results suggest a biomarker panel of cell cycle regulators (cyclinA, -D, cdk2, p21waf1 and Ki67) which may help predict the clinical behavior of GCTB.

**N46 PSMB7 GENE A NEW PROGNOSTIC BIOMARKER IN BREAST CANCER**

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**Keywords: PSMB7, breast cancer, biomarker, doxorubicin, gene expression**

To date individual markers failed to correctly predict resistance against anticancer agents in breast cancer. The product of the gene *PSMB7* is a component of the proteasome  $\beta$  subunit. The gene has significantly overexpressed in doxorubicin-resistant MCF7 cell-lines. Since cell-lines indicated resistance to paclitaxel as well, tests have been conducted with the use of both drugs. Our research aims were to examine whether RNAi silencing of the *PSMB7* gene has an impact on the chemoresistance of doxorubicin-resistant cell-lines.

*PSMB7* gene was silenced by RNA interference, which was produced by self designed siRNA oligos and siPORT NeoFX transfection reagent. The validation of the RNA happened with RNeasy Mini kit, the gene expression was measured by

RT-PCR. After silencing the cell vitality was measured. Microarray gene expression of GEO entered raw microarray samples with available progression free survival data was downloaded, and expression of *PSMB7* was used to group samples. After doxorubicin treatment 79.8%±13.3% of resistant cells survived. Silencing of *PSMB7* in resistant cells decreased survival to 31.8%±6.4% ( $p>0.001$ ). A similar effect was observed after paclitaxel treatment. In 1512 microarray samples patients with high *PSMB7* expression had a significantly shorter survival than the patients with low expression ( $p=0.006$ ).

According to our findings, by reducing the overexpression of the *PSMB7* gene via gene silencing the resistant cell's chemoresistance significantly decreased. Consequently the doxorubicin- and paclitaxel-therapy became more efficient. Our findings suggest that high *PSMB7* expression is an unfavorable predictive marker in breast cancer.

**N48 CHARACTERIZATION OF BREAST CARCINOMAS IN WOMEN  $\leq 35$  YEARS OF AGE**

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**Keywords: early-onset breast cancer, BRCA1, molecular subtypes, HER2, immunohistochemistry**

**Background:** Breast cancer is the leading cause of cancer death in young women. Germline mutations in the *BRCA* genes cause ~25% of the cases  $<35$  years. The reason(s) why early-onset breast carcinomas have more aggressive features, are not clear.

**Aims:** To analyze the pathological characteristics of breast cancers among our selected cases. To predict whether these characteristics may be used to predict *BRCA1/2* mutation status. Analysis of the association of these characteristics with disease outcome (OS, DFS).

**Patients&methods:** We have collected breast carcinoma samples (1999-2010) from patients of age  $\leq 35$  at the time of diagnosis. Histological type, grade, ER, PgR and *HER2* status of all tumor specimens were defined. We also gained data regarding family history of malignancies (56 cases). *BRCAPRO* software was used to assess the probability of *BRCA1/2* mutations. The patients' follow-up data were available.

**Results:** The mean age in the cohort was 31,49 years. The proportion of molecular subtypes was the following: 30 cases of luminal A (37,03%), 13 cases of luminal B (16,05%), 15 cases of *HER2* overexpressing (18,52%), and 23 triple negative (28,4%) cases. Summarizing the family history data: there was a high number of malignant tumors, altogether 54 in the 41 families. By *BRCAPRO*, 14 patients showed at least 10% probability of carrying *BRCA1* mutation and 2 women were supposed to be *BRCA2* mutation carriers. A high percentage of deaths revealed in this group of young patients (11 of 83).

**Discussion:** Our results provide additional data in order to make good diagnostic and therapeutic recommendations for this group.

#### **N49 QUADRICUSPID AORTIC VALVE – A CASE REPORT**

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**Keywords: quadricuspid aortic valve, aortic insufficiency, aortic valve preserving, aortic valve replacement**

Quadricuspid aortic valve (QAV) is a rare congenital malformation of the aortic valve. The first known case report was written by Balington in 1862. Since then, there have been anywhere from 129 to 186 case reports, according to recent review articles. A 41-year-old woman presented with a history of dyspnea on exertion. Transesophageal echocardiography showed an enlarged aortic root and ascending aorta, with the presence of quadricuspid aortic valve and severe aortic insufficiency. The incidence of QAV has been reported between .008 and .043 percent making it the rarest malformation of the aortic valve. It is usually found unexpectedly at surgery or diagnosed preoperatively by means of echocardiography or aortography. These QAVs frequently function abnormally; the most common abnormality is valvular insufficiency. Other malformations associated with quadricuspid aortic valve include anomalies of the coronary arteries, stenosis of pulmonic valve, nonobstructive cardiomyopathy, subaortic stenosis, and ventricular septal defect. The QAV is replaced in the majority of patients requiring surgery. At an early stage, however, repairing the valve is possible, although only a few cases of in situ surgical repair have been reported. Previous cases of QAV have already been highlighted by several authors around the world, yet the rarity of the condition means that each case needs to be investigated in depth in order to further increase the understanding of this anomaly. The case I am presenting involved replacement of the aortic valve to an ATS Medical Inc. mechanical prosthesis. The QAV appeared to be type E according to the classification by Hurwitz and Roberts. The patient was discharged 10 days following surgery and made a full recovery. I will be presenting this case of QAV from my research and focusing mainly on the surgical aspects of the problem.

#### **N50 BREAST CANCER: THE EFFECT OF LIFESTYLE AND DIABETES ON THE THERAPEUTIC RESPONSE AND THE DEVELOPMENT OF THE DISEASE.**

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**Keywords: breast cancer, lifestyle, diabetes, risk factors**

Breast cancer is the most common malignant tumor among women. There are several risk factors playing a significant role in the onset of the cancer, such as age, body weight, obesity, etc. This retrospective study is on a small population

of non-diabetic (10) and diabetic women (10), aged 33-75, who were treated for primary breast cancer in the Oncotherapeutic Institute of Pécs. The aim of the study was to examine the differences between the two groups and to see if there is a correlation between diabetes, lifestyle and breast cancer. The results were matched to the internationally published data. A retrospective questionnaire was completed including four main issues: anamnestic data, diet, physical activity and treatment. In addition, a routine blood analysis (AST, ALT, LDH, ALP, CRP, serum iron, protein, albumin, glucose, bilirubin, carbamide, creatinin, CA-15-3 and CEA tumor markers, serum electrolyte levels, quantitative blood count) was performed. The database was compared with the histological diagnosis.

Several specifics and differences were found: tumor markers, LDH, CRP and glucose levels were significantly elevated in diabetic patients. Biopsy results showed significantly more estrogen and progesterone receptor positive cases with a higher tumor stage in the diabetic group. Both groups had an elevated BMI, and compared with the internationally published studies, decreased physical activity.

Moderately increased physical activity, normal body weight and correctly controlled glucose level might decrease the risk of cancer, and improve the therapeutic effect. Due to the small number of patients further studies are needed to confirm our results.

#### **N51 ADIPOPILIN MARKS LIPID DROPLET-ACCUMULATION IN HUMAN DISEASE**

**Benedek Gyongyosi<sup>1,2</sup>**

**<sup>1</sup>Semmelweis University <sup>2</sup>Institute of Pathology, Heidelberg**

**Keywords: adipophilin, lipid droplet, lipid storage, infarction border**

**Introduction:** Lipid droplets (LDs) are dynamic storage compartments for energy-rich fats that are nearly ubiquitously present in eukaryotic cells. LDs are increased in certain conditions following cellular damage or lipid overload such as in atherosclerosis, fatty liver, diabetic kidney and in hypoxia. The structure of LDs is maintained by proteins of the PAT-family with their main constituents perilipin, adipophilin and TIP47. Adipophilin knock-out mice are prevented from fatty liver.

**Aims:** As previous results indicated, adipophilin may be a good general LD-marker in normal tissues of different species, especially in liver. We started to analyze the value of adipophilin immunohistochemistry in human disease.

**Materials and Methods:** Immunohistochemical staining using antibodies against adipophilin were performed on over 70 representative sections of atherosclerotic lesions, cholesteatosis of the gallbladder, adipose tissue necrosis, diabetic kidney, as well as of organ infarctions (heart, liver, kidney, colon; samples provided from Tissue Bank of Institute of Pathology, Heidelberg).

**Results:** Increased lipid storage conditions associated with adipophilin was observed in lipid-laden macrophages in atherosclerotic lesions, in cholesteatosis of the gall bladder

and in necrotic adipose tissue. Adipophilin staining was also enhanced in renal tubules in diabetes in comparison to normal kidney, but was also found in other renal diseases. In organ infarcts, adipophilin-positive LDs marked cells of the border zone of ischemic infarcts of heart, liver, kidney and colon, whereas the cytoplasm of necrotic cells was evenly stained.

**Conclusions:** Adipophilin represents a good and valuable marker for human diseases associated with LD-accumulation in routine pathology.

## NEUROLOGY – PSYCHIATRY SESSION

### **N52 EFFECTS OF EXPANDED TERRITORY AND ENRICHED ENVIRONMENT ON THE NEUROBEHAVIORAL DEVELOPMENT OF NEWBORN RATS EXPOSED TO EXCITOTOXIC LESION**

**Gabor Horvath, Jozsef Farkas, Attila Matkovits, Zsofia Horvath, Julian Zink, Dora Reglodi, Andrea Tamas, Andrea Lubics, Peter Kiss**

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**Keywords: Enriched environment, neurobehavioral development, MSG, newborn rat**

Postnatal neurobehavioral development is well reflected by the appearance of reflexes and performance in motor tasks. This development is affected by various factors, like nutritional state, neurotrophic factors and environmental conditions. Enriched environment increases the level of trophic factors, improves cognitive performance and has profound effects on CNS neurochemistry. Monosodium-glutamate (MSG) is a widespread flavoring substance leading to severe morphological and functional deteriorations in the developing nervous system.

We examined the protective effects of the expanded territory and complex enriched environment in MSG-induced lesions in newborn rats. Postnatal development was followed by evaluating various parameters: appearance of eye opening, incisor eruption, negative geotaxis, placing reflexes, grasp reflexes, crossed extensor reflex, sensory reflexes. Motor coordination and behavior were assessed by rotarod, foot-fault and inclined board tests and by open-field test.

We found that 2mg/g MSG administered 3 times on days 1, 5 and 9, induced impairments that could be ameliorated by expanded territory and complex enriched environment. The body weight showed significant differences between the control and the two enriched groups. These groups performed better also in the foot-fault and rotarod tests. In summary, our results suggest that enriched environment can be protective against nervous system injuries in newborn rats.

### **N53 DIFFERENTIAL REGULATION OF HYPOTHALAMIC NEUROPEPTIDE Y HNRNA AND MRNA DURING PSYCHOLOGICAL STRESS AND INSULIN-INDUCED HYPOGLYCEMIA**

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**Keywords: Fasting, Blood glucose, Hypoglycemia, Restraint, Time course**

Many signals reflecting energy balance and stress are integrated at the hypothalamic orexigenic neurons. NPY neurons in the arcuate nucleus play a decisive role in this regulation. Many stress situations result in remarkable changes in food intake and metabolism however, stress-induced changes in the expression of metabolic-related hypothalamic neuropeptides remained unknown. The main interest of our work was to determine transcriptional changes of the NPY gene, related with stress. We have compared two stressors: insulin-induced hypoglycaemia, which is a physiological stressor and restraint as a psychological stressor.

Changes in NPY gene expression, were studied by in situ hybridization histochemistry and real time PCR. We compared the expression of hnRNA and mRNA levels. We followed the time course and our results revealed rapid changes in the expression of the NPY gene in response to both stressors. Overnight fasting did not result in significant elevation of NPY mRNA level. However, after insulin induced hypoglycemia there was a rapid increase of NPY hnRNA. The expression of NPY hnRNA peaked at 1 hour after insulin injection and declined thereafter and run parallel to that of NPY mRNA. Throughout the time course, NPY expressing cells in the medial basal hypothalamus remained localized to the arcuate nucleus. In contrast, during psychogenic restraint, increase of NPY mRNA was detected in spite of decrease of NPY hnRNA up to 2 h after restraint. Our findings support the hypothesis that regulation of stress response and metabolism is coupled at the hypothalamus and orexigenic NPY neurons are involved in the stress-metabolic coupling.

### **N54 COMPARISON NONCONTRAST CRANIAL CT-SCAN FINDINGS WITH SEVERITY OF COMA IN PATIENTS SUFFERED FROM CEREBROVASCULAR DISORDERS**

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**Keywords: CT, cerebrovascular disorder**

**Background:** Raising intracranial pressure leads to disturbance of consciousness. The purpose of our study was to explore the relation between the severity of coma and noncontrast CT-scan findings (roominess of cistern prepons, compression of ventricles, midline shift).

**Material and Methods:** Data of 87 stroke patients, admitted to the Intensive Care Unit of Department of Neurology in

Debrecen, were recorded prospectively (age: 67, SD:14 yrs, male/female: 1.72). The severity of coma was assessed by Glasgow Coma scale and FOUR Score Scale, the seriousness of stroke was estimated by NIH Stroke Scale. Neurological examinations were done within 3 hours after CT-scans were performed. Cisterna, situated between pons and clivus, and midline shift were measured on CT-scans. The extent of early ischemic changes in the middle cerebral artery territory was quantified by ASPECT Score.

**Results:** In point of roominess of cistern prepons (alert: 5.75 mm +/-1.64 mm vs. unconsciousness: 4.21 mm +/-2 mm,  $p<0.0001$ ) and extent of midline shift (alert: 0.3mm +/-0.82 mm vs. unconsciousness: 4.98mm +/-4.9,  $p<0.0001$ ) clear difference was found between alert and unconsciousness patients. The lower the ASPECT Score the higher the odds of obtaining coma.

**Conclusion:** Clear changes can be detected on cranial CT-scan already in the early stage of unconsciousness. The roominess of cistern prepons is inversely proportional, while the extent of midline shift is proportional to the severity of coma. These results point out the importance of performing control CT-scan when the disturbance of awareness deepens and doing clinical examination when severe changes can be detected on images.

#### **N55 EXTERNAL THETA STIMULATION INCREASES THE PERFORMANCE IN A KONORSKI TASK**

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**Keywords: Konorski task, theta, visual memory**

**Introduction:** Memory processes and external audiovisual stimulation in the theta frequency range evoke theta oscillations in the brain (Teplan et al, 2006; Axmacher et al, 2010). We examined the effect of task-irrelevant theta visual stimulation (TVS) on- visual short term memory.

**Methods:** Forty eight subjects of both sexes were studied in a Konorski task (delayed match to sample). 25 control subjects (mean age: 21.4 years) were compared to TVS subjects (n=23, mean age: 25.6 years). All subjects had normal or corrected-to-normal vision and showed no signs of any neurologic or psychiatric disorder. Stimuli were 2, sinusoidal grating patterns (Gabor patch) viewed under 5 degrees of visual angle (exposition time: 100 ms, interstimulus interval: 2000 ms, intertrial interval: 1000-2000 ms). Subjects were instructed to decide whether the second stimulus was turned to the right or to the left compared to the first stimulus by pressing one of two buttons. Correct decisions resulted in a decrease of the orientation differences, while wrong decisions resulted in an increment of the orientation differences (staircase method). In this way every subject reached her/his threshold of orientation discrimination. Subjects had to perform 200 trials. Both groups performed the task in a dark room. For the TVS group a stroboscope generated flashing light stimuli in the theta frequency range, the control group did not receive additional visual stimulation. We registered the reaction times and the

just-noticeable differences (JND) in orientation in the two different groups.

**Results:** There were no significant differences in the reaction times measured between the TVS group and the control. The JND of the control group was 5.3° while the JND of the TVS group was significantly better: 4.3° ( $p<0.05$ ). Tendency in the performance was estimated using linear regression. The control group showed a tendency of getting worse during the experimental session, while the TVS group gradually improved, i.e., the JNDs decreased.

**Conclusion:** We found that external theta stimulation can increase the performance in Konorski task. Further experiments are needed to clarify the underlying neuronal mechanisms.

#### **N56 THE TRANSCRIPTION OF THE AMYLOID PRECURSOR PROTEIN AND TRYPTOPHAN 2,3-DIOXYGENASE GENES ARE INCREASED BY AGING IN THE RAT BRAIN**

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**Keywords: aging, vasopressin, amyloid precursor protein, tryptophan 2,3-dioxygenase, real time PCR**

Aging itself is considered as a major risk factor for dementia. The prevalence of Alzheimer's Disease (AD) increases exponentially after the age of 65 and doubles every 5 years. The major aim of our research was to examine the effect of aging on the transcription of genes associated with neurodegenerative disorders in the rat brain. We also examined the effect of vasopressin (VP) or the lack of the hormone.

Age dependent transcriptional changes of the following four genes were measured in the cortex: (1) the gene of the amyloid precursor protein (APP) was the first one. APP is abnormally cleaved to beta-amyloid fragments, which are the major components of the neurotoxic senile plaques in the AD brain. (2) The mitogen-activated protein kinase (MAPK1) gene was the second one. The MAPK plays role in the hyperphosphorylation of the tau-protein leading to the disintegration of the cytoskeleton and the formation of the neurofibrillary tangles. (3) The product of beta-actin gene is abnormally aggregated in to Hirano-bodies and involved in synaptogenesis, learning, depression and dementias, like AD. (4) The gene of the tryptophan 2,3-dioxygenase (TDO) was the last one. The activity of this enzyme is a rate limiting factor in the metabolism of quinolinic acid and serotonin.

The cortical transcriptional activity of young (2,5 months) and aged (13 months) Brattleboro rats with or without VP production were compared with real time PCR technique.

The amount of the APP and TDO2 mRNA were increased in the aged animals as compared with the transcriptional activity of the young ones. According to our research the presence of VP has no effect on the expression of the four genes. No

changes were found in the MAPK1 and beta-actin mRNA levels.

Our results indicate the importance of certain age dependent transcriptional changes might influence the mechanism of AD and other neurodegenerative disorders.

### **N57 “ME AND MY NURSE”- THE CASE OF FRIDA KAHLO**

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**Addictology Research Center, Budapest, Hungary**

**Keywords: borderline, interpersonal addiction, alcoholism**

**Background:** on the painting tilted Me and My Nurse the nurse's head is a stone mask, Frida Kahlo's body is a body of a child, her head is a head of an adult and they don't look at each other. This picture perfectly mirrors the painter's basic experience of emotional deprivation that causes her later addictions. In Frida's case the inadequate mother-child connection may lead to Borderline personality disorder. (Chessick 1977)

From the diagnostic criterions Frida matches the following criteria:

1. mid-life crisis, 2. fear of abandonment (huge efforts to prevent it), 3. unstable intensive connection with extreme feelings (her husband, Diego Rivera), 4. emotional unsteadiness (serious mood disturbance), 5. impulsivity (alcohol, drugs, smoking), 6. dissociative symptoms triggered by stress, paranoid thoughts

**Main points:**

I. I intend to understand the background of her personality fragmentation and her sexual identity disturbance

II. I detail her defensive efforts so as to keep a sense of being cohesive. According to Heinz Kohut the borderline patient use twinship-, idealizing- and mirroring self objects as a help to create a stronger self of sense. Frida's twinship selfobjectum: a perfect imaginary friend created at the age of six during her polio, later her self-portraits, her idealizing and mirroring self objects: her father, later her husband, Diego and the art community

III. Fear of abandonment: Apparently Frida isn't able to fight with her impulsivity. Her alcoholism become regular after her husband created sexual connection with her sister. Alcohol will become the symbol and instrument of self-destruction, jealousy and amorous frustration.

To sum up: the case of Frida Kahlo perfectly shows the interlocking of different behavioral and chemical addictions, cause and effect relationship, as well as the dilemma of the artistic idioms and creative processing.

### **ANATOMY SESSION**

#### **K36 ISCHEMIC KIDNEY INJURY IN PACAP KNOCKOUT AND WILD-TYPE MICE**

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**Keywords: kidney, ischemia, PACAP**

**Introduction:** We have previously shown that a single bolus of intravenous PACAP (pituitary adenylate cyclase activating polypeptide) significantly ameliorates the ischemic damage in the kidney. We have also described the presence of endogenous PACAP in the kidney.

**Aim:** The aim of the present study was to investigate the role of endogenous PACAP in ischemic kidney injury.

**Methods:** PACAP knockout and wild-type mice were investigated in our study. They underwent 45 or 60 minutes of renal ischemia followed by a 2-weeks reperfusion. Kidneys were processed for histological analysis. Sections stained with PAS-haematoxylin were graded for the following parameters: dilatation of the Bowman's capsule, tubular dilatation, thyreoidisation, lymphocyte and macrophage infiltration, disappearance of the PAS-positive glycocalyx along the brush border.

**Results:** PACAP knockout mice had a worse histological outcome, with significantly higher histological scores for most of the tested parameters.

**Conclusion:** In conclusion, the lack of endogenous PACAP leads to higher susceptibility to in vivo renal ischemia/reperfusion, suggesting that PACAP has an endogenous renoprotective effect.

#### **K37 CLINICAL ANATOMICAL EXAMINATION OF THE EXTRAHEPATIC ARTERIAL BLOOD SUPPLY OF THE LIVER**

**Karoly Nemeth<sup>1,2</sup>, Jimmy Hu<sup>1</sup>, Andras Szuak<sup>1</sup>, Agnes Nemeskeri<sup>1</sup>, Laszlo Kobori<sup>2</sup>, Matyas Kiss<sup>1</sup>**

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**Keywords: Liver, anatomy, extrahepatic, arteries, variations**

**Aim:** Detailed knowing of the extrahepatic arterial variations is essential for the preoperative planning of liver surgeries, especially for liver transplantation. According to available data the incidence of extrahepatic arterial variations alters between 10.5% and 55%. We investigated the variations of the extrahepatic arterial blood supply of the liver in the Hungarian population.

**Methods:** We analyzed 33 human organ complexes consisting of the liver, stomach, pancreas, spleen and the bowels, the abdominal aorta (AA) from the origin of the inferior phrenic artery (IPA) until below the origin of the superior mesenteric artery (SMA). Twenty-one organ complexes were injected with methylene blue through the SMA. If the blue color appeared under the Glisson's capsule, it indicated that an accessory liver artery exists arising from the SMA. Thereafter we injected the arteries through the AA with resin and then the organ complex was immersed into concentrated hydrochloric acid to corrode the parenchyma. The other 12 organ complexes were corroded without the previous methylene blue injection.

**Results:** The cast preparations were macroscopically analyzed, and the arterial variants were categorized by using Michels' classification. We found extrahepatic arterial variations in 24.24% of cases (8/33).

**Conclusions:** Precise knowledge of the different types of extrahepatic arterial variations is crucial for surgeons to safely perform liver resections, organ harvesting, intestinal surgeries and particularly during liver transplantation. Our data can contribute to the safer performance of surgical interventions of not only the liver, but the pancreas, the extrahepatic bile ducts and the intestines as well.

## DERMATOLOGY SESSION

### K38 NOVEL, *IN VIVO* METHOD FOR MONITORING TRANSDERMAL PENETRATION OF DRUGS

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**Keywords:** monitoring, transdermal, drug

**Introduction:** the transdermal penetration of pharmaceutical agents is a highly important, alternative way of drug intake, therefore the enhancement of the penetration is the goal of several on-going studies. The aim of our study was to establish a novel method for *in vivo* simultaneous monitoring of the penetration and the absorption.

**Method:** on the back of the anesthetized, hairless SKH-1 mice a skinfold was created and clamped with two symmetrical titanium plates with windows. On one side of the skinfold a circular wound was cut and a metal cylinder was tightened to the wound. Then the metal cylinder was filled with phosphate buffer. The other side of the skinfold was treated with 5% ibuprofen gel. Buffer and blood samples were collected for 6 hours after treatment, and the concentration of the active agent was determined using HPLC. The microcirculation of the skinfold was monitored by intravital videomicroscopy and histological examination was also carried out.

**Results:** according to the data of the microcirculatory and histology analyses the skinfold remained functionally and morphologically intact. The concentration of the active agent was continuously increasing in the buffer and reached its maximum level 3 hours after treatment in the sera.

**Conclusion:** Our model might be appropriate to carry out *in vivo* examinations on kinetics of the penetration and absorption of drugs.

### K39 EPIDERMAL (ETG) AND TISSUE (TTG) TRANSGLUTAMINASE ELISA STUDIES THROUGH THE FOLLOW UP OF DERMATITIS HERPETIFORMIS PATIENTS

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**Keywords:** Epidermal transglutaminase, Tissue transglutaminase, gluten sensitivity

Dermatitis herpetiformis, an autoimmune blistering skin disease, characterized by granular IgA eTG at the tips of the papillary dermis. There is growing evidence, that DH should be considered as gluten sensitivity of the skin developing only in certain patients with gluten sensitive enteropathy (GSE) who produce eTG autoantibodies of high avidity and affinity. Endomysium antibodies (EMA), similarly to tTG autoantibodies are sensitive and specific markers of GSE associated with the skin condition. Although there is a body of information on changes of EMA and tTG autoantibodies in GSE under gluten-free diet, there are still limited data available on the correlation between changes of eTG, tTG IgA and EMA in long-term studies. Aim: to study parameters of DH patients followed through years of treatment, counseling and follow up. 19 DH patients followed and monitored for 5 or more years were selected for this study. In all cases the diagnosis has been confirmed by skin immunofluorescence and histology. Archived and collected samples were assayed on heTG ELISA. In all patients eTG IgA levels were elevated, while two of the DH patients were EMA and tTG negative. Introduction of gluten free diet slowly reduced the EMA, lowered the tTG and gliadin IgA levels, whereas eTG showed a slower decrease in titer. In 17 cases although tTG IgA autoantibodies became normal under the GFD or treatment, eTG IgA autoantibodies remained elevated. IgA type eTG autoantibodies seem to be sensitive markers of DH and are more characteristic for the skin disease than for the GSE.

### K40 RESEARCHING A POLYMORPHISM OF THE PTCH GENE IN PATIENTS WITH ATYPICAL BASAL CELL CARCINOMAS

**Kende Kalmán Lorincz<sup>1</sup>, Reka Farkas<sup>1</sup>, Norbert M. Wikonkal<sup>2</sup>**

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**Keywords:** PTCH, basal cell carcinoma, loss of heterozygosity, single nucleotide polymorphism

**Introduction:** The PTCH gene is a tumor suppressor gene, which is involved in the development of nearly all basal cell carcinomas (BCCs). A single nucleotide polymorphism within PTCH exon 22 at codon 1315 modifies the suppressor activity of the gene.

**Objectives:** Our intention was to analyze the mentioned polymorphism of the PTCH gene, at patients with unusually numerous basal cell carcinomas according to the age.

**Methods:** 102 patients with multiple BCCs were examined, beside 63 control patients with negative anamnesis for skin cancers. A number of patients were heterozygous, enabling allelic loss studies. In 7 cases we isolated the gene from the tumor tissue itself, and analyzed it for the polymorphism.

After the isolation the DNA samples were amplified with PCR technique and sequenced with an automated sequencer.

**Results:** 48 of the 102 patients were heterozygous, 42 homozygous with the allele combination Leu/Leu and 12 with Pro/Pro. Among the control group 26 patients were heterozygous, and 37 homozygous. In 7 cases we found the combination Leu/Leu and in 30 cases Pro/Pro. 7 tumors were examined for loss of heterozygosity (LOH). 6 showed the phenomenon.

**Conclusions:** According to our results there is a significant difference between the patients with multiple BCCs and the control group. We presuppose that carrying the Leu/Leu allele variation is predisposing to unusually juvenile BCCs. The LOH examination of the samples from the tumor tissue confirms the biological relevancy of the locus.

## EXPERIMENTAL SURGERY SESSION

### K42 THE EFFECTS OF PRE- AND POSTCONDITIONING ON LIVER IN EXPERIMENTAL ISCHEMIC REPERFUSION ANIMAL MODEL

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**Keywords: Ischaemic-reperfusion injury, preconditioning, postconditioning, liver surgery**

**Introduction:** By surgical vascular clamping ischemic-reperfusion injury occurs in the liver. In the clinical setting it is fundamental to decrease the damage, as the level of injury is essential for viability and the long-term survival of the liver. According to several studies, the ischemic preconditioning (IP) and postconditioning (IPo) have been proved to be protective against reperfusion injury.

**Aims:** In our animal experimental model postconditioning was applied in the beginning of reperfusion after prolonged ischemia. The results were compared with the outcomes found in our earlier ischemic preconditioning experiments.

**Methods and materials:** 45 and 90 minutes long segmental liver ischemia was induced in male Wistar rats followed by 6 hours of reperfusion. The animals (n=10) were divided into 3 groups: sham, I-R damaged control and ischemic postconditioned (IPo) groups. The circulation was registered with Laser-Doppler-flowmeter in the first hour of reperfusion. Serum necroenzymes (AST, ALT) were analyzed from the blood samples. The damaged liver segments were inspected under conventional light microscope.

**Results:** In case of 45 minutes clamping the ischemic preconditioning and the postconditioning provided significant improvement in the circulation compared to the control group. (PM p=0.03; p=0.00019, RT p=0.039; p=0.00032). After 90 minutes of ischemia no upgrade could be detected either in the pre- or in the postconditioned group compared with the control group. (PM p=0.075; p=0.81; RT p=0.079; p=0.61) The histological sections confirmed the protecting effects against I-R damages in both groups.

**Conclusion:** Postconditioning used after the 45 minutes clamping offered similar degree of protection against I-R

injuries as preconditioning. Neither of the techniques could lessen the harming effects of 90 minutes I-R damages. In the attenuation of I-R injury the length of ischemia is likely to be more deciding than the applied technique itself.

### K43 POSTOPERATIVE INCISIONAL HERNIA; LATE COMPLICATION OF LIVER TRANSPLANTATION

**Adrienn Lukacs, Petra Agota Szukovics**

**Department of Transplantation and Surgery, Semmelweis University, Budapest**

**Keywords: Postoperative incisional hernia; late complication of liver transplantation**

**Introduction:** Incisional hernia is a late complication of liver transplantation (LT). The literature provides few data, but it reports a 5-17% incidence.

**Objective:** The aim of our study is analyzing the appearance and treatment of incisional hernia after liver transplantation, performed in the Semmelweis University, *Department of Transplantation and Surgery*.

**Patients and method:** Our retrospective study contains the data of 159 patients, who underwent liver transplantation between 2005 and 2009. 17 patients were excluded from the study. We compared the group of postoperative hernia with the "hernia-free" group considering the average age, sex distribution, body mass index (BMI), type of the surgical incision, intraoperative blood needs, and the need for postoperative steroid shot.

**Results:** Incisional hernia occurred at 21 of 142 (14.8%) patients. The average age was 48 years, sex index was 15 male/6 female, (no difference from control group). The incidence of incisional hernia was significantly higher after applying Mercedes incision, versus bilateral subcostal incision (25% vs. 5.5%; p<0.001). BMI and intraoperative blood needs turned out to be significantly higher in the group with hernia (28.5 kg/m<sup>2</sup> vs. 26.1 kg/m<sup>2</sup>; p=0.04 and 15 U rbc vs. 10 U rbc; p=0.004). Reoperation in the early postoperative stage was shown to be different between the two groups (52% vs. 37%), but was not statistically significantly different. The average time from the transplantation till the hernia surgery was 15.5 months (0.5-49). Average hospital stay for hernia treatment of was 11 days per patient (6-23). Surgery was performed on 20 patients because of incisional hernia, mesh repair was used in 8 cases. Complications: wound infection in one case, and recurrence in 2 patients in case of reconstruction without mesh implant.

**Conclusion:** The higher BMI, Mercedes incision, and large blood transfusion requirements increase the risk of developing an incisional hernia after LT significantly. Mesh repair was proved to be more durable solution.

## ORTHOPEDICS SESSION

### K44 WRIST PROPRIOCEPTION – WHAT DO WE KNOW ABOUT IT?

**Noemi Szakacs, Rita Kiss**

**Clinic of Orthopedics, Semmelweis University**



**Keywords: wrist, proprioception, biomechanics**

The aim of this presentation is to summarize the basic knowledge regarding wrist proprioception. We would like to present our study for the improvement of wrist proprioception. Although various concepts of carpal kinetics and kinematics have been studied extensively, little is yet known about the proprioceptive characteristics of the wrist. However, to treat wrist injuries it is essential to clearly understand the anatomy, the biomechanics and the function of the wrist. The proper skeletal alignment, passive restraint from ligaments and the muscular structure are working together to ensure an anatomically, kinetically and kinematically stable joint. It is important to have a knowledge regarding the distribution of mechanoreceptors in wrist ligaments and in the joint capsule, this was published in 2008, and the wrist proprioceptive reflex in 2010. The mechanoreceptors react to changes of joint angle, joint velocity, mechanical distortion and changes in intraarticular pressure and through the nervous system send message to the efferent muscles. For the training of these neuromuscular reflexes the effectiveness of Powerball was proven in one study (Balan, 2008). The Powerball is a gyroscope, that generates random multidirectional forces to the forearm and wrist.

With the creation of wrist proprioceptive training program we use the Powerball together with physiotherapy and our aim is to minimize to risk of wrist injuries on forward falls occurring in sports activity or in the everyday life, and to improve the rehabilitation of our patients.

Recent years have brought new research findings on the wrist joint proprioception, that we should incorporate and apply in the clinical field to improve the rehabilitation of our patients, emphasizing the necessity of physiotherapy beside surgical treatment on carpal disorders.

(There is no interest in commercialization with the product (250 Hz NSD Powerball) by the authors and no financial association)

**K45 IMPROVEMENT IN THE SURGERY METHODS OF HALLUX VALGUS TREATMENT**

**Petra Agota Szukovics, Adrienn Lukacs**

**Department of Orthopedics, Semmelweis University, Budapest, Hungary**

**Keywords: hallux valgus, Schede, Wilson, Ludloff, Keller-Brandes**

**Introduction:** Hallux valgus is one of the static foot diseases. It occurs from young age to older ages as well, but its prevalence is higher in women. It usually hurts, makes wearing shoes uncomfortable and walking harder. Conservative treatment exists in early stages (orthosis, arch-support, orthopedic shoes). The improved-stage deformity that causes complaints can only be solved surgically.

**Objectives:** We would like to determine the change and its cause in the surgical treatment of hallux valgus in our clinic, using a ten-year covering retrospective statistical study.

**Materials and methods:** We collected the details of hallux valgus surgeries from the register performed from 1998 to 2007 in the Department of Orthopedics, Semmelweis University. We analyzed the frequency of each of ten different types of surgical methods, both cumulatively and in one-year sections, and we determined the average age of the patients who underwent any of these operations.

**Results:** The method of Schede completed with capsule plastic has been performed from 2003 in force (17.6% of all the methods, averaging in 7 years). In the same term, the method Op. Sec. Ludloff disappeared almost completely (0.36% in 7 years). The performing of the more drastic method of Wilson - involving bones - has decreased significantly ( $p=0,001$ ). There is no correlation among average ages. The reason being that the main consideration in choosing the surgical method is the rate of deformity.

**Conclusion:** The new techniques - just as adopting the gentle instruments used in hand surgery into foot surgery - made it possible, that the expanded soft tissue surgery could gather ground in the face of the methods involving bones. But naturally it is professionally essential to consider the stage, the age, the lifestyle and the co-operation of the patient when we select the appropriate method.

**K46 IS PELVIC INCIDENCE A CONSTANT ANATOMIC PARAMETER?**

**Mate Nagy, Mate Burkus, Miklos Tunyogi-Csapo, Szabolcs Somoskeoy, Tamas Illyes**

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**Keywords: pelvic incidence, Duval-Beaupere, EOS 2D/3D, scoliosis, reconstruction**

**Introduction:** Among sagittal pelvic parameters introduced by Duval-Beaupere in 1998 [1], pelvic incidence (PI) is known to be individually characteristic and independent of postural positional changes. However, information published by others [2] and earlier observations made by us on patients operated with scoliosis suggest that in some cases PI might adjust to changes in spinopelvic balance after scoliosis correction.

**Aims:** We compared PI values of the same patient in standing and sitting positions and tried to show clinically significant differences.

**Methods:** We examined sagittal pelvic parameters in 22 patients (mean age  $17.93 \pm 9.42$  years) using standing and sitting X-ray images made by the EOS 2D/3D ultra-low radiation dose full-body X-ray scanner [3]. We used clinical parameters automatically calculated by sterEOS 3D software after a precise three-dimensional (3D) reconstruction of the spine and pelvic using EOS 2D full-body anteroposterior and lateral images. Results represented average values based on 3 independent measurements by 4 experienced examiners. Statistical analysis employing descriptives and independent samples t-test was carried out by SPSS 16.0.

**Results:** Difference in standing and sitting PI values of 5 patients were found to be greater than 6 degrees while other 3 patients showed differences of 3 to 6 degrees, all 8 results were statistically significant ( $p < 0.05$ ). In 4 other cases the difference was 1-3 degrees but was considered clinically not significant.

**Conclusion:** PI values could adjust to a simple change in body position as standing and sitting. This indicates that in some individuals PI is not an anatomical constant, behaving more like a positional pelvic parameter. This behavior could be connected to a slight movement in the sacroiliac joint. Our observation could be important for considerations of the compensatory role of sagittal pelvic parameters in maintaining sagittal spinopelvic balance, especially before and after surgical correction of spine deformities.

References:

1. J. Legaye, G, Duval-Beaupère J, Hecquet CM (1998). Pelvic incidence: a fundamental pelvic parameter for three-dimensional regulation of spinal sagittal curves. *Eur Spine J*, 7: 99-103.
2. Skalli W, Zeller RD, Miladi L, et al. (2006) Importance of Pelvic Compensation in Posture and Motion After Posterior Spinal Fusion Using CD Instrumentation for Idiopathic Scoliosis. *Spine*, 31: 359-366.
3. Dubousset J, Charpak G, Dorion I, Skalli W, Lavaste F, Deguise J, Kalifa G, Ferey S. (2005) [A new 2D and 3D imaging approach to musculoskeletal physiology and pathology with low-dose radiation and the standing position: the EOS system]. *Bull Acad Natl Med.*, 189(2):287-97.

#### **K47 IN VITRO ANTIBIOTIC RELEASE FROM PMMA-SORBITOL BASED CAPSULES**

**Dorottya Frank<sup>1</sup>, Gellert Cseh<sup>2</sup>, Balazs Borsiczky<sup>2</sup>, Bela Kocsis<sup>3</sup>, Attila Miseta<sup>1</sup>**

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**Keywords:** PMMA, antibiotic, chronic osteomyelitis

Local delivery of antibiotics via polymethylmethacrylate (PMMA) has been widely and successfully used in the treatment of chronic osteomyelitis for more than 40 years. Unfortunately, PMMA is completely water insoluble, which seriously limits the delivery of antibiotics. In addition the PMMA polymerization temperature is high, consequently only heat stable antibiotics can be used. In order to avoid these drawbacks, our aim was to develop a more effective antibiotic delivery system which can be loaded with a wide variety of antimicrobial agents, and deliver the molecules in a time-dependent-manner. We created a PMMA-sorbitol based capsule system. The preliminary results proved that the release kinetic of the capsules strongly correlated with the sorbitol content and wall thickness.

In this study we aimed to monitor the in vitro antibiotic release (gentamycin, amikacin, tobramycin) from the capsules showing optimal release kinetic. We found that by adjusting the sorbitol content and wall thickness we can control the antibiotic release and achieve an effective and relatively even drug concentration at the site of the infection. In conclusion our data suggests that PMMA-sorbitol capsules are potentially superior local drug delivery device compared to antibiotic-laden bone cements. Elongated and effective drug concentrations can be achieved for 42 days by selecting the appropriate capsule for the desired drug.

#### **K48 DEVELOPMENT OF KNEE FUNCTION FOLLOWING HAMSTRING LENGTHENING IN SPASTIC DIPLEGIA – A LONG-TERM OUTCOME STUDY**

**Dora Vegvari<sup>1</sup>, Thomas Dreher<sup>2</sup>, Sebastian Wolf<sup>2</sup>, Andreas Geisbusch<sup>2</sup>, Petra Armbrust<sup>2</sup>, Waltraut Schuster<sup>2</sup>, Wolfram Wenz<sup>2</sup>, Frank Braatz<sup>2</sup>**

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Increased knee flexion during stance phase of gait is one of the most common gait abnormalities in patients with spastic diplegia. Hamstring tightness was accused to be one main factor leading to crouch gait. For the correction of increased knee flexion during stance phase hamstring lengthening is considered as a standard procedure. According to various studies satisfactory short term-results after hamstring lengthening could be achieved with improved knee extension during stance phase. Problems in treatment are increased pelvic tilt and high incidence of genu recurvatum. Therefore, surgical strategy for the correction of crouch gait is seen controversial. There are no studies existing, which report long-term results of adult patients who were treated in childhood by hamstring lengthening.

39 children (age at surgery: 10yr±3yr) with spastic diplegia and functional disturbing increased knee flexion during stance phase were treated with medial (77 legs) or combined medial and lateral (18 legs) hamstring lengthening in the context of multilevel surgery. All subjects were evaluated by a standardized protocol with clinical exam and instrumented three-dimensional gait analysis pre- (E0), 1 year (E1), 2-4 years (E2) and 6-12 years (E3) post-operatively. The examined parameters were: mean knee flexion instance, peak knee extension in mid stance, mean pelvic tilt, Gillette Gait Index, popliteal angle.

The gait analysis parameters and popliteal angle showed initial significant improvement in E1 compared to the pre-operative values. These parameters deteriorated significantly in the long-term follow-up. The popliteal angle nearly reached the pre-operative value.

Newer investigations address the femoral extension osteotomy in combination with patellar advancement as an alternative surgical strategy. Future studies should compare this strategy with hamstring lengthening.

## CARDIOLOGY SESSION

### **N58 HEART FAILURE – AN ALZHEIMER HEART**

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**Semmelweis University**

**Cardiovascular Institute, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston MA**

**Keywords: heart failure, dilated cardiomyopathy, presenilin genes, protein misfolding**

The second most frequent cause of heart failure after ischemic origin is the 'idiopathic' dilated cardiomyopathy (iDCM), in which the cause of the disease is still unknown. Recently more diseases have been associated with protein misfolding and the accumulation of cytotoxic proteins, such as amyloidosis or various neurodegenerative disorders such as Alzheimer disease. Preliminary evidences suggest that iDCM may have a similar origin, however the exact mechanism is still unclear.

It has been shown, that mutations in the same genes causing Alzheimer disease can also be at the origin of iDCM. Currently we were investigating the role of presenilin 1 in the etiology of heart failure. We used three different types of Alzheimer disease model transgenic mice with the PSΔE9 mutation, the APP Swedish mutation and presenilin gene overexpression (PSOE). With ultrasound measurements at 3, 6 and 9 months of age we determined the cardiac function and cardiac dysfunction has been found at the PSΔE9 mutated mice at 9 month of age compared to same age wild type mice. However, these mice did not show amyloid deposits in electromicroscopic images. As it is known that presenilin binds to SERCA, the main calcium pump involved in the excitation-contraction coupling, it has been suggested that the cardiac dysfunction derives from changes in the intracellular calcium handling caused by the mutation of the presenilin gene. In order to investigate this hypothesis, we isolated myocytes from the mice mentioned above and using a cell length and cell calcium recording system we investigated the contractility of the single myocytes.

### **N59 CRYOBALLOON CATHETER ABLATION FOR TREATMENT OF ATRIAL FIBRILLATION. A CASE REPORT**

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**Division of Electrophysiology, Department of Cardiology, Institute of Augusztá, University of Debrecen, Debrecen, Hungary**

**Keywords: atrial fibrillation, pulmonary vena potentials, catheter ablation, cryoablation**

Atrial fibrillation is the most common sustained arrhythmia in humans associated with significant morbidity and increased mortality. Antiarrhythmic medications have been found of low yield therapy in long-term maintenance of sinus rhythm. Transcatheter ablation procedures have been introduced to electrically isolate all pulmonary veins known to be common triggers of atrial fibrillation from the rest of the left atrium. Originally, radiofrequency energy has been used for these

procedures. We report on use of cryoballoon catheter, a novel technique for safe and more simple isolation of the pulmonary veins.

Ablation was performed on a 54-year-old man with symptomatic paroxysmal atrial fibrillation since 2000. In light sedation together with local anaesthesia, transeptal catheterization was performed. All 4 pulmonary veins were identified and successfully isolated using cryoballoon energy. Electrical isolation was evidenced by disappearance of pulmonary vein potentials recorded by a special, circumferential catheter positioned within the ostia of these veins. No complication was encountered, procedure time was 158 min and fluoroscopy time 25 min. Patient was discharged in sinus rhythm and no atrial fibrillation occurred during 10 months follow-up.

### **N62 ROLE OF ENDOTHEL MARKERS IN THE PLANNING OF A CORONARY ANGIOGRAPHY**

**Eniko Plozer<sup>1</sup>, Eva Bartha<sup>2</sup>, Sandor Keki<sup>3</sup>, Tihamer Molnar<sup>4</sup>**

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**Keywords: ADMA, SDMA, coronary angiography, endothelial marker**

Coronary angiography plays an important role in the diagnosis of cardiovascular diseases. We investigated whether a non-invasive test combined with biomarker measure could predict the need of elective coronarography in patients with coronary artery disease (CAD).

We prospectively examined 44 patients with scheduled dipyridamol-stress myocardium perfusion scintigraphy. Blood samples were collected two times from each patient (prior to test and at 5th post-stress minute) and vital parameters were checked in every minute. Blood gas analysis, asymmetric- and symmetric dimethylarginine (ADMA, SDMA) levels were measured from venous blood samples. We analyzed the results of MIBI scans in all patients and the results of coronarography if they were available. For statistical analysis independent sample test, Mann-Whitney U-test and ROC analysis were used.

Coronarography was performed in fifty percent of patients (n=22) with a total of 17 positive results. A positive MIBI scan was found in 31/44 cases. A significant correlation was found between MIBI scan and coronary angiography. MIBI positive cases had significantly higher levels of post-stress SDMA (p=0.007), but as a predictor of positive coronarography the post-stress ADMA level seems to fit (p=0.03). We also found significant increase in the basal levels of ADMA and SDMA compared to healthy subjects. Post-stress ADMA ≤ 0.706 (Area:0.857, p=0.034) can predict a

negative result of coronary angiography with 100% sensitivity and 65% specificity.

Non-invasive tests like MIBI scans are useful for the screening of susceptible patients, but it is desirable to improve their sensitivity with complementary measures. Our results suggest that MIBI scans combined with biomarkers of endothelial dysfunction like ADMA can help in selection of high-risk patients with CAD. However, further prospective studies are needed with higher sample size and other biomarkers as well.

### **N63 EXAMINATION CARDIAL STATE OF PATIENTS HAVING HEREDITARY ANGIOEDEMA**

**Erika Szabo, Zsuzsanna Zotter, Andras Zsary, Henriette Farkas**

**3rd Department of Internal Medicine, Semmelweis University Budapest, Hungary**

**Keywords: HANO, danazol, diastolic dysfunction**

**Background:** Hereditary angioedema (HAE) is an illness what gets into C1 inhibitor deficiency, which comes together with paroxysm of subcutaneous and submucous angioedema. Bradykinin plays a role in coming into existence angioedema. The number of acute paroxysm can be decreased by danazol prophylaxis. For the effect of treatment lipid profile can be changed towards atherogenic direction. By patients having hypercholesterolemia endothelial dysfunction can be showed, what can come together with decreasing of diastolic function of heart. Investigating cardiac state of patients having HAE. Comparing cardiac state of patients having HAE getting danazol prophylaxis to patients getting NO danazol prophylaxis.

**Methods:** 32 patients having HAE were examined (age: 33.5 year (21-58) men: 16 women: 16). From among these 16 patients get danazol prophylaxis. The patients filled in questionnaire about their basic illness and cardiac state. We have made physical examination, EKG and measured metabolic parameters. We have made echocardiography examinations, where we have observed systolic and diastolic parameters.

**Results:** EF= 70 % (65-76) patients getting danazol prophylaxis while 69 % (65-74) by patients getting NO danazol prophylaxis ( $p=0.4851$ ). DT value by getting danazol prophylaxis is 250 ms (208-293), the DT value of other group is 232 ms (182-279) ( $p=0.4061$ ). Comparing the other parameters diastolic function disorder could not be compared by both of the patients groups.

**Conclusion:** We expected a decrease in systolic and diastolic heart function resulting from Danazol treatment due to lipid profiles resulting in now a more atherogenic state. However, we did not show a difference between the two examined groups. Further studies are in progress to confirm our hypothesis.

### **N64 CARDIOPROTECTIVE EFFECT OF EXOGENOUS BIGLYCAN: THE ROLE OF NITRIC OXIDE**

**Tamas Baranyai, Timea Szegi, Aniko Gorbe, Erika Bereczki, Andrea Szunyog, Eda Aypar, Melinda E. Toth, Zoltan V. Varga, Csaba Csonka, Ferenc Fulop, Miklos Santha, Tamas Csont, Peter Ferdinandy**

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**Keywords: cardiocytoprotection, biglycan, nitrogen-monoxide**

Biglycan is an extracellular proteoglycan which plays a crucial role in the assembly of the extracellular matrix, but it is also important for the activation and inactivation of several cytokines. We have recently shown that biglycan has a cardioprotective effect. The aim of our study was to investigate the role of nitric oxide (NO) in the cardiocytoprotective effect of biglycan. In order to investigate the effect of biglycan on ischemia/reoxygenation injury, neonatal primary rat cardiomyocyte cultures underwent 20 h pre-treatment with biglycan (30nM), followed by 150 min hypoxia and 120 min reoxygenation. Viability assay was performed by using Trypan blue staining. After 20 h pre-treatment with biglycan cardiomyocyte cultures were used for the measurement of mRNA-expression of NO-synthases (NOS2, NOS3) by polymerase chain reaction, NOS2 and NOS3 proteins with Western-blot, and cellular NO level by electron spin resonance spectroscopy. For the elucidation of the role of NO in the biglycan-induced cytoprotection the cultures were treated with NOS-inhibitor (N-nitro-L-arginin methyl ester: L-NAME; 0,1mM). Exogenous biglycan (30nM) decreased cell death from 41.3% to 17.3%. The administration of biglycan significantly elevated mRNA-expression of NOS3, NOS2- and NOS3-protein levels, and cellular NO-level when compared to the control group. L-NAME significantly attenuated the protective effect of biglycan, but the protection was not ceased. In conclusion, the exogenous biglycan has a cardiocytoprotective effect which is partially mediated by nitric oxide signalling.

### **N65 EFFECTS OF CORONARY REVASCULARIZATION WITH OR WITHOUT CARDIOPULMONARY BYPASS ON PLASMA LEVELS OF THE ENDOGENOUS NITRIC OXIDE SYNTHASE INHIBITOR ADMA**

**Zsafia Lenkey<sup>1</sup>, Attila Cziraki<sup>1</sup>, Adam Nemeth<sup>1</sup>, Zeno Ajtay<sup>1</sup>, Nasri Alotti<sup>2</sup>, Sandor Szabados<sup>1</sup>**

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<sup>2</sup>Department of Cardiac Surgery, Zala County Hospital

**Keywords: endothelial dysfunction, ADMA, coronary bypass**

**Objective:** The concentration of asymmetric dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide synthase, is increased in patients with endothelial dysfunction. The present study was designed to measure and compare serum ADMA, symmetric dimethylarginine (SDMA) and L-arginine levels in blood samples obtained from coronary sinus and from

peripheral vein in patients undergoing coronary revascularization with or without cardiopulmonary bypass.

**Patients and methods:** Two groups of patients with coronary heart disease (CHD) were selected for elective coronary bypass graft surgery (CABG). Patients were subjected to CABG surgery with cardiopulmonary bypass (CPB) (n=20) or with off-pump CABG surgery (OPCAB) (n=21). Blood samples for measurements of ADMA, SDMA and L-arginine were withdrawn from the coronary sinus (CS) and from the peripheral vein (P) at baseline; three times during CABG surgery and on the first and fifth postoperative days. Plasma levels of L-arginine, SDMA, ADMA were determined with liquid chromatography-tandem mass spectrometry (LC-MS-MS).

**Results:** Based on the intraoperative (CS) samples, the post-hoc ANOVA did not reveal a discernible increase of ADMA in the OPCAB group. In contrast ADMA levels rose in the CPB group (F=0.416, p<0.685 and F=14.751, p<0.001 for OPCAB and CPB groups respectively). A similar significant increase of ADMA was observed in the peripheral blood (F=30.738, p<0.001) during CPB, while ADMA levels remained largely unchanged in the peripheral blood during OPCAB. The time-course of L-arginine levels was significantly different in the blood samples from coronary sinus (F=3.255, p<0.05), when compared to samples from the peripheral blood. (F=3.255, p<0.05). In the OPCAB group repeated measures ANOVA did not reveal a significant intrasubject time effect of L-arginine, either in blood samples from coronary sinus or in the samples from the peripheral vein. The values of the L-arginine/ADMA ratio were significantly higher in the OPCAB group at baseline and on the first postoperative day as compared to results of the CPB group ( $178.29 \pm 11.56$  vs.  $136.28 \pm 13.72$  and  $129.43 \pm 7.08$  vs.  $106.8 \pm 6.9$  for OPCAB and CPB groups respectively).

**Conclusion:** Plasma levels of ADMA, SDMA, L-arginine and L-arginine/ADMA ratio are reliable and feasible markers of an early ischaemia-reperfusion injury. During CPB operation (but not during OPCAB), the plasma concentration of ADMA increased significantly and remained elevated until the first postoperative day due to extensive ischemia-reperfusion injury caused by CPB.

## IMMUNOLOGY-CELL BIOLOGY SESSION

### N66 SYSTEMS PHARMACOLOGY AND COMPUTATIONAL BIOLOGY

**Andras Falus, Andras Gerzsi, Peter Antal**

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An enigmatic change in research paradigm as *systems biology* is related primarily to the development of bioinformatics and computational biology. Clinical science translates achievements of basic research to medically relevant applications, that is prediction, prevention, diagnosis and therapy

A major driver for the advancement of pharmacology is the expansion of knowledge of genetic and functional elements of the xenobiotic metabolism. The key enabling technologies of genomics, proteomics, and computational biology (such as genomic pathway analysis, gene set enrichment analysis) provide large quantities of data describing molecular profiles of various physiological and pathological states.

This lecture introduces a network model for genetic prediction for possible effectiveness of doxorubicin in acute lymphoid leukemia. Translation of technological and scientific advances into actual clinical solutions remains a huge task and pharmacogenomics offers means for systematic analysis and speeding-up the selection, discovery, design and validation of new diagnostic and therapeutic products for 21<sup>st</sup> century.

### N67 EFFECTS OF THE ABSENCES OF NKX2-3 HOMEODOMAIN TRANSCRIPTION FACTOR AND LYMPHOTOXIN BETA RECEPTOR ON THE LYMPHOID CELL CONSTITUTION OF SPLEEN

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**Keywords: LTbR, Nkx2-3, 2xKO mouse, spleen**

Both the LTbR and the Nkx2-3 homeodomain transcription factor play important roles in the development of peripheral lymphoid organs. In the absence of the LTbR, lymph nodes do not develop, the white pulp of the spleen is disorganized, while the red pulp remains normal. The absence of the Nkx2-3 results in a lymph node-like vasculature of the spleen with missing red pulp vessels, while lymph nodes develop. This complementary lesion suggested studying the influences that these factors have on each other. In our work we created a 2xKO mouse by crossing the LTbR KO and the Nkx2-3 KO mice. Their genotype was verified by simultaneous triple PCR examinations. We performed macroscopic, fluorescent microscopic, and flow cytometric experiments to examine their peripheral lymphoid tissues, and compared them to normal, LTbR KO, and Nkx2-3 KO lymphoid tissues. We found no lymph nodes and Peyer's patches in the 2xKO mice. The spleen showed disorganization of the T- and B-cell areas. Besides deterioration in the arrangement of marginal zone macrophages, follicular dendritic cells were also absent. The T/B cell ratio in the spleen of the 2xKO mouse showed a moderate T-cell dominance, which differed from both the LTbR KO mouse and from the Nkx2-3 KO mouse. The CD4/CD8 cell ratio was close to normal. Marginal zone B cells, identified by their C21hi and CD23lo expression, were scarce in number. Based on our results, the 2xKO mouse may be a valuable model for identifying the stromal elements taking part in the peripheral B cell development.

### N68 PRESENCE OF PITUITARY ADENYLATE CYCLASE ACTIVATING POLYPEPTIDE-38 IN HUMAN PLASMA AND MILK

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**Keywords:** PACAP, radioimmunoassay, plasma

**Objective:** Pituitary adenylate cyclase activating polypeptide (PACAP) is a pleiotropic and multifunctional neuropeptide widely distributed throughout the body. It is involved in the regulation of various physiological and pathophysiological processes, such as reproduction, thermoregulation, motor activity, brain development, neuronal survival, inflammation and pain. Since little is known about its distribution in humans, our aim was to examine PACAP-38 in human plasma. Furthermore, based on the presence of vasoactive intestinal peptide, structurally the closest to PACAP, in milk and PACAP and its receptors in the mammary gland, our aim was to study PACAP-38 in human milk.

**Design and methods:** The presence of PACAP-38 was determined by mass spectrometry in plasma samples from healthy male and female volunteers (age: 20-40), as well as in plasma and milk samples from lactating women (age: 20-35). PACAP concentration was measured with a specific and sensitive RIA.

**Results:** Our results revealed that PACAP-38 is present in human plasma, its concentration is relatively stable in healthy volunteers and it is not significantly altered by gender, age, food intake or hormonal cycle in females. However, PACAP-38 plasma levels significantly increased in lactating women having 1-6 month-old babies. Moreover, this study is the first which provides evidence for the presence of PACAP-38 in the human milk with levels 5-20-fold greater in the milk whey than in the respective plasma samples.

**Conclusions:** We found PACAP-38 in human plasma and its increase during the first 6 months of the lactation period. A prominent, nearly 10-fold higher concentration of this peptide was detected in human milk. Based on the literature, several important actions of milk-derived PACAP-38 can be suggested such as mammary gland proliferation, nutrient transfer as well as regulation of growth/differentiation of certain tissues of the neonates. The novelty of the present descriptive data provides a basis for further investigations on the mechanism of PACAP-38 secretion in human milk and its functional significance.

#### **N69 CHARACTERIZING A TET-REPRESSIBLE ERBB2-EXPRESSING FIBROBLAST LINE AS A POSSIBLE MODEL FOR TESTING ERBB2 TARGETED THERAPIES**

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**Keywords:** ErbB2, transfected, therapy, characterization

ErbB2 is a receptor tyrosine kinase underlying bad prognosis in several human malignancies. Trastuzumab, a humanized anti-ErbB2 antibody is a specific targeted therapy against these tumors, with a history of both success and a high rate of therapy resistance. The SADR cell line is a derivative of NIH3T3 fibroblasts stably transfected with the ErbB2 gene under the negative control of tetracycline.

We studied the age dependent (3<sup>rd</sup>, 10<sup>th</sup> and 20<sup>th</sup> passages) sensitivity of native and ErbB2-deprived (tetracycline treated) SADR cells to short (5 minutes) and long (3 days) treatments with 0.1 mg/ml trastuzumab in terms of proliferation, cell cycle, ErbB2 expression and phosphorylation, as well as apoptosis.

The proliferation rate upon ErbB2 deprivation by tetracycline decreased at all passages, coherent with the proliferation advantage from excess ErbB2. In these cells, trastuzumab did not decrease the proliferation further, nor did it affect the cell cycle, thus confirming specific trastuzumab action targeting ErbB2. In native SADR not treated with tetracycline, trastuzumab caused a G1-block that was correlated with the passage number, also enhanced short term ErbB2 phosphorylation, and decreased ErbB2 expression in the long run. While in the earliest passage minimal effects were observed upon trastuzumab treatment, by the 20<sup>th</sup> passage all ErbB2-related effects have manifested.

It is likely that the complete signaling and regulatory system around the ectopic ErbB2 evolves in time, resulting eventually in addition to the oncogene and sensitivity to its targeting. The experiments also draw attention to the stability problems of transfected cellular systems.

#### **N71 THE COMPLEMENT REGULATORY PROTEINS CD55 AND CD59 ARE ACTIVE COMPONENTS OF THE LYPOPOLISACCHARIDE RECOGNIZING COMPLEX OF DENDRITIC CELLS**

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**Keywords:** CD55, CD59, LPS, dendritic cell, TLR4

Lipopolysaccharide (LPS) is the characteristic microbe-associated molecular pattern of Gram(-) bacteria that is recognized by CD14 as an LBP-LPS complex and signals through TLR4-MD2. Despite the low expression of membrane CD14 in conventional dendritic cells (DCs), LPS induces DC activation however, the cell type-specific pathway of LPS stimulation is still enigmatic.

**Objective:** The primary function of the CD55 and CD59 glycosylphosphatidylinositol (GPI)-linked membrane proteins is the inhibition of the complement system to protect antilogous cells from complement-mediated damage. However, CD55 is also part of the LPS receptor complex in Monocytes (Heine et al. Eur J Immunol 2003) and CD59 is involved in LPS-mediated signal transduction of oral keratinocytes (Yamamoto et al. Cell Signal 2003). The goal of

our work was to study the role of the complement proteins CD55 and CD59 in LPS signaling of monocyte-derived DCs.

**Methods:** The gene expression of CD55 and CD59 was measured by real time Q-PCR, protein expression was detected by flow cytometry. The expression and function of CD55 and CD59 proteins was inhibited by specific silencing RNA (siRNA) transfected to developing DCs by electroporation. The level of secreted cytokines in LPS-activated moDCs supernatants was measured by ELISA, the migration of mature moDCs was tested in Boyden chamber.

**Results:** Our results show that as compared to monocytes the expression of CD59 increases in the course of DC differentiation, whereas the expression of CD55 decreases parallel with that of the LPS-recognizing CD14 receptor. Inhibition of CD55 and CD59 expression or function significantly reduces the degree of LPS-induced activation of DCs monitored by the membrane expression of CD83, the secretion of inflammatory cytokines TNF- $\alpha$ , IL-6, IL-12, and the migratory capacity of mature moDCs.

**Conclusion:** These results show that the complement regulatory proteins CD55 and CD59 play an important role in LPS-mediated DC signaling, activation and effector functions. Moreover, the composition of the LPS-recognizing complex is reorganized during monocyte to DC transition. As both innocent and pathogenic microbes can trigger DCs through TLR4, the cell type-specific composition of the LPS receptor complex may transduce different stimulatory signals in various cell types.

## N72 HEAT SHOCK-INDUCED REARRANGEMENTS OF YEAST PROTEIN-PROTEIN INTERACTION NETWORK

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**Keywords: network, heat shock, yeast, module, adaptation**

In recent years biological data sets became exceedingly complex. Since most of these datasets have a high medical significance, their adequate interpretation is of high priority for potential therapeutic purposes. The analysis of the topology of the cellular networks constructed from these datasets may show novel changes at the systems biology level. We investigated the topological changes of yeast (*S. cerevisiae*) protein-protein interaction (PPI) network after heat shock. Overlapping modules of the yeast interactome were determined using NodeLand method developed recently in our research group ([www.linkgroup.hu/modules.php](http://www.linkgroup.hu/modules.php)). Changes in link weights of the exponentially growing yeast cells after heat shock were modeled using mRNA microarray data and converting the changes in mRNA levels to changes in the probability of protein-protein interactions.

Our results showed a partial disintegration of PPI network: protein modules having distinct functional annotations became more separated, and the integration of network skeleton decreased. Molecular chaperones (heat shock proteins)

emerged as key organizing centers, which may have a role in the reintegration of PPI network after stress.

Our work uncovered novel features of the stress response at the systems biology level. The method we developed may be useful in the investigation of systems level alterations of PPI networks in human diseases.

## N73 INVESTIGATING POSSIBLE NEW LIGANDS OF CHEMOTACTIC DRUG TARGETING (CDT): MET-ENKEPHALIN AND ITS DERIVATIVES

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**Keywords: Chemotaxis, enkephalin, drug targeting, opioid, cytokine**

Enkephalins are neurotransmitters of opioid origin. In this presentation we sum up our results of the chemotactic effect of Met-enkephalin and its derivatives.

The CDT theory offers a reasonably selective drug targeting by special signal molecules attached to a drug and carrier complex, inducing the migration of the object cell and finally resulting in the drug endocytosis.

**Aims:**(i) To describe the chemotactic effects of Met-enkephalin and its derivatives on inferior cilium cells and on higher monocytes. (ii) To find such potent chemo-attractant enkephalins which can be proper new signal molecules of CDT in the future.

**Material and Methods:** Met-enkephalin (YGGFM) and its synthetic elongated versions (by 1-3 amino acids on the C terminal). *Tetrahymena pyriformis* GL model cell was examined by chemotaxis in a 2-chamber capillary-assay; the human MonoMac6 monocytes (MM6) cell line was observed in a NeuroProbe® chamber, both between  $10^{-12}$  –  $10^{-6}$ M. The role of *PI3 kinase* was studied by consequent chemotaxis assays after LY-294,002 and Wortmannin inhibitor treatment.

**Results:** Modification of the original YGGFM peptid causes notable variations of chemotactic potential, while there are some homology in the reactivity of the two models. The most effective derivatives in *Tetrahymena* model were: **-V** (168%), **-KF** (161%), **-RSI** (183%); *MM6*-on a **-KF** (192%), the most effective concentrations in **-D** model ( $10^{-9}$ - $10^{-6}$ M) were found. In *PI3K assay* both of the inhibitors could eliminate the chemotactic effect.

**Conclusion:** Some derivatives of Met-enkephalin can act as chemoattractants in both model cells. The 2 or 3 aminoacid elongation, may significantly improve chemotactic potential. Based on the results of Monocyte assays, we can suggest that **-D** and **-KF** derivatives as new ligands of CDT.

## N74 LITHIUM TREATMENT INDUCES UNFOLDED PROTEIN RESPONSE AND INCREASES O-GLCNA6 MODIFICATION OF PROTEINS IN JURKAT CELLS GROWN ON GALACTOSE

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University of Pécs, Pécs, Hungary**

**Keywords: O-GlcNAc, lithium, unfolded protein response, galactose**

Lithium is a traditional mood stabilizer in the treatment of patients with bipolar disorder, although its exact molecular mechanism is still not clarified. By replacing  $Mg^{2+}$  on the binding sites of many proteins, lithium may influence several metabolic and signaling pathways of a cell. In this study, we have assessed the impact of lithium on O-linked  $\beta$ -N-acetylglucosamine (O-GlcNAc), a dynamic post-translational modification that participates in the regulation of numerous signaling events.

Lithium's targets include phosphoglucomutase (PGM) and glycogen synthase kinase-3 (GSK-3), both involved in galactose/glucose metabolism, therefore we incubated Jurkat cells in glucose or galactose containing media with or without lithium treatment. While lithium slightly decreased and growth properties of Jurkat cells in both media, O-GlcNAc was increased by lithium only in galactose containing media. Furthermore, while UDP-Galactose/UDP-Glucose levels increased, we have found that the elevated O-GlcNAc was not a direct consequence of an increased flux through the hexosamine pathway since UDP-GlcNAc, the donor substrate of O-GlcNAc even decreased upon lithium treatment while galactose was present. Finally, confirmed by induced mRNA splicing of X-box binding protein 1 (XBP1), unfolded protein response (UPR) was greatly elevated in Jurkat cells treated by both galactose and lithium. Taken together, our results suggest that lithium treatment, by inhibiting both PGM and GSK-3, significantly influences galactose downstream metabolite levels, which in turn cause endoplasmic reticulum (ER) stress and UPR followed by the subsequent activation of O-GlcNAc as a stress response.

**N75 NEW FETAL AND PREGNANCY'S OUTCOME  
RISK SCREENING PROTOCOL I.**

**Karoly Szili, Edit Ferencz, Janos Tamas Szabo**

**Department of Medical Genetics, University of Szeged**

**Keywords: fetal, embryo, HR, CRL, outcome**

**Objective:** The most important tool of fetal medicine is the ultrasound diagnostics by which we can receive information about the current status of the embryo/ fetus. To follow up the embryonic development, one of the most appropriate parameter is the embryonic heart rate.

**Aim of study:** To define the normal reference range of the embryonic heart rate during the first trimester between 5-13 weeks calculated by the last menstrual period (LMP).

**Methods:** We studied the embryonic heart rate (EHR), the crown-rump length (CRL) and the age of the embryo calculated by the LMP in euploid gestations with normal outcome in non-invasive ultrasound examinations. These parameters both literally and empirically were studied. We created a protocol for the data processing. The data was

analyzed by Shapiro-Wilk statistical test. The results were imaged on diagram showing the normal and limit curves.

**Results:** The embryonic heart rate in the early first trimester gradually increases, then it reaches the maximum for the 10th week and after a slow decrease it sets a relatively constant value until the end of pregnancy. However, the embryonic age calculated by the last menstrual period does not give reliable results, therefore the embryonic heart rate was reliably and accurately evaluated by the crown-rump length, since the CRL shows the real age of the embryo.

**Conclusion:** We would like emphasize the importance of measuring the fetal heart rate in fetal medicine, as it is a relatively easily measured parameter and it can give us important information about the outcome of pregnancy.

**SPECIAL SESSIONS**

**O1 THE PROPER RESEARCH PRESENTATION**

**Tamas Peredy**

**President of HMAA**

**Medical Director, Northern New England Poison Center**

**Assistant Medical Director York Count Center for Wound**

**Assistant Professor of Emergency Medicine, Maine**

**Medical Center, a Tufts University School of Medicine**

**Affiliate**

**Introduction:** The proper written and oral presentation of original research is an important process in the advancement of clinical knowledge. Mistakes in the presentation despite impeccable attention to scientific validity can lead to audience misinterpretation or apathy.

**Methods:** As an academic physician, I have suffered through innumerable poor performances and other stuff despite this and after reviewing every article about everything mistakes continue to be made. Through example, I wish to highlight some of the COMMON mistakes !!!

**Results:** Failure of a research presentation may be from an innumerable of reasons including flaw in the underlying research itself and will not be discussed further. The research question may be of no importance, not answered or the conclusion is not supported by the data. The presentation may drag on exceeding the time and space allowed because of inappropriate detail like the time I lost my puppy and spent hours looking for it. It may not be geared for the audience or have inadequate explanation. Visual display either through slides or on a poster may be distracting or offensive to really tall beanpole people.

**Conclusion:** A proper research presentation is unnecessary unless you have an audience, readership or you are not alone in the auditorium.

**O2 QUIZ BOWL**

**Tamas Peredy**

**President of HMAA**

**Medical Director, Northern New England Poison Center**

**Assistant Medical Director York Count Center for Wound**

**Healing and Hyperbaric Medicine**



**Assistant Professor of Emergency Medicine, Maine Medical Center, a Tufts University School of Medicine Affiliate**

**Aims:** The goal of this talk is to identify those with superior intellect while humiliating others who have progressed less far up the evolutionary ladder.

**Methods:** Countless hours (because they weren't counted) were spent scouring the Index Medicus Inconsequentia to identify those bits of medical knowledge completely detached from basic science, irreproducible experimentally and utterly irrelevant to clinical practice. These factoids were gathered and placed in question format.

**Conclusions:** It remains possible by traditional methods of reward and shame to identify those students who will do just about anything for personal reward.

**EDITOR'S NOTE**

All abstracts available to the Editorial Office as of July 27, 2010 are included in this edition of the Archives of the Hungarian Medical Association of America.

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

With questions or suggestions, please contact the Editor at [ssomkuti@abington-repromed.com](mailto:ssomkuti@abington-repromed.com) or personally at the conference.

Thank you,

Istvan Somkuti MD PhD

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