# Abstracts Subspecialty Poster Session Neurology and Neurobiology

## S.01
### High resolution imaging of the optic nerve and retina in optic nerve hypoplasia

I. Gottlob, A. Pilat, D. Sibley, R.J. McLean & F.A. Proudlock
*The University of Leicester Ulverscroft Eye Unit, University of Leicester, Leicester, UK*

**Background:** Little is known about optic nerve and retinal morphology in optic nerve hypoplasia (ONH). We investigated optic nerve and macular morphology in patients with ONH using spectral-domain optical coherence tomography (SD-OCT).
**Materials and methods:** High-resolution SD OCT (Copernicus, 3 μm resolution) and hand held SD-OCT (Bioptigen Inc., 2.6 μm resolution) devices were used to acquire horizontal scans in 16 participants with ONH (10 females and 6 males; mean age 17.2 ± 16.22, 6-bilateral involvement) and 16 gender, age and ethnicity-matched healthy controls.
**Results:** Patients with ONH had significantly smaller discs as compared to unaffected eye and healthy controls [($P < 0.03$ for both), horizontal cup diameter ($P < 0.02$ for both), and cup depth ($P < 0.02$ and $P < 0.002$, respectively)]. In the macula significantly thinner retinal nerve fibre layer (RNFL, nasally), ganglion cell layer (GCL, nasally and temporally), inner plexiform (IPL, nasally) and outer nuclear layers (ONL, nasally), inner segment (IS, centrally and temporally) were found in patients with ONH as compared to the control group ($P < 0.05$ for all comparisons). Continuation of significantly thicker GCL, IPL and OPL in the central retinal area (i.e. foveal hypoplasia) was found in more than 80% of patients with ONH. Clinically unaffected eyes of patients with ONH showed mild features of underdevelopment.
**Conclusions:** Our study provides for the first time evidence of retinal changes in ONH. In addition to thinning of retina layers mainly involving RNFL and GCL, foveal maldevelopment was observed in patients with ONH. Optic nerve and foveal parameters measured using OCT showed high sensitivity and specificity for detecting ONH demonstrating their useful for clinical diagnosis.

## S.02
### MicroMRI-based techniques for the detection of normal and cancer stem cells in the nervous system

C. Crivii*, M. Aldea†, L. Crăciun*, A. Fărcăşanu‡ & F. Turcu‡
**Morphology Department, University of Medicine and Pharmacy of Cluj-Napoca, Cluj-Napoca, Romania; †Oncology Department, University of Medicine and Pharmacy of Cluj-Napoca, Cluj-Napoca, Romania; ‡Magnetic Resonance National Center, Babes-Bolyai University, Cluj Napoca, Romania*

**Background:** Neural stem cells (NSC) are prominent elements in the embryonal stage of nervous system development and may also promote glioblastoma development by undergoing oncogenic mutations. Considering the phenotypic resemblance between NSC and glioblastoma stem cells, we aim to optimize a non-invasive method of identifying stem cell populations.
**Materials and methods:** We developed an improved imaging protocol with subsequent 3D reconstruction for central nervous system visualization. We gathered microscopic magnetic resonance imaging (μMRI) images on 3 human embryos from the Embryo Collection of the Morphological Sciences Department (different developmental stages), on cultured cancer stem cells isolated from glioblastoma specimens and on adult brain fragment that included the periventricular zone. All images were obtained by using a 7-T μMRI system.
**Results:** We acquired detailed images of NSC populations that had migrated from the neural crests and outlined peripheral paravertebral nervous structures in different stages of development. By using the same protocol, similar images were acquired from the periventricular zone of the adult brain where NSC are localized and more important, even from glioblastoma stem cell culture. Our imaging acquisition technique also enabled the individualization of NSC from the neighboring structures.
**Conclusions:** Our study develops a visualization technique for neural stem cells. By using a modified imaging protocol and 3D reconstruction, our team obtained a 3D detailed model of the embryonic neural structures, which proved to be comparable with NSC in the adult brain and even with glioblastoma stem cells.

# Abstracts Subspecialty Poster Session Other Topics: Basic Research

## S.03

### Influence of tumor growth on cytotoxic activity of mononuclear splenic leukocytes in mice against tumor cells with different biological properties

I.V. Opeida*, O.G. Fedorchuk†, N.M. Khranovska‡, V.V. Pozur*, M.P. Rudyk*, N.V. Senchilo*, V.V. Shepelevich*, V.M. Svyatetska* & L.M. Skivka*

**Department of Microbiology and General Immunology, Educational and Scientific centre "Institute of Biology", Taras Shevchenko National University of Kyiv, Kyiv, Ukraine; †Department of Pharmacocorrection of Oncogenesis, R.E. Kavetsky Institute of Experimental Pathology, Oncology and Radiobiology, Kyiv, Ukraine; ‡Research Laboratory of Experimental Oncology, National Cancer Institute, Kyiv, Ukraine*

**Background:** Tumor growth is associated with a decrease of quantitative and functional parameters of natural killer cells. The aim of the work was to investigate cytotoxic activity of mononuclear splenic leukocytes in mice with Lewis lung carcinoma (LLC) against low-immunogenic syngeneic, allogeneic and xenogeneic tumor cells.

**Materials and methods:** In the study, C57Bl/6 male mice 2–3 month old were used. LLC cells ($3.5 \times 10^5$ cells/mouse in 0.02 mL physiologic solution) were transplanted subcutaneously in the hind feet. The cytotoxic activity of mononuclear splenic leukocytes was determined by MTT colorimetric assay and characterized by an index of cytotoxicity (IC). Tumor cells of Ehrlich's carcinoma, LLC, and rat C6 glioma were used as target cells.

**Results:** The highest sensitivity to lysis by cytotoxic splenic leukocytes of intact animals was registered for low differentiated allogeneic tumor cells (Ehrlich's carcinoma, IC = 54.5 %). Xenogeneic tumor cells C6 *glioma* were less sensitive (IC = 31.7 %). The lowest sensitivity was observed for syngeneic tumor cells (LLC, IC = 22.4 %), which have a high degree of differentiation. Tumor growth in mice was accompanied by a decrease of cytotoxic activity of splenocytes against xenogeneic tumor cells by 1.5 times, against allogeneic tumor cells by two times and almost four times against syngeneic tumor cells.

**Conclusions:** Growth of LLC was associated with inhibition of cytotoxic activity of mononuclear splenic leukocytes against tumor cells of different degree of foreignness, indicating a negative effect of tumor growth on effector functions of natural killer cells in antitumor immunity, as well as transplantation immunity. The level of tumor-associated suppression of cytotoxic activity of splenocytes against tumor cells was inversely proportional to their degree of foreignness.

## S.04

### Sex hormones coordinate neutrophils immunity in the lower female reproductive tract by controlling chemokine gradients

S. Lasarte*, R. Samaniego†, M.L. Salinas-Muñoz*, E. Mercader*, L.A. Weiss‡, M. Pion§, P. Sanchez-Mateos¶, A. Hidalgo‡, M.A. Muñoz-Fernandez§ & M. Relloso*

**Laboratorio InmunoBiología Molecular, Grupo Fisiopatología Comparada, Hospital General Universitario Gregorio Marañón (HGUGM) and Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain; †Unidad de Microscopía Confocal, Hospital General Universitario Gregorio Marañón (HGUGM) and Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain; ‡Department of Epdidemiology, Atherothrombosis and Imaging, Fundación Centro Nacional de Investigaciones Cardiovasculares (CNIC), Madrid, Spain; §Laboratorio InmunoBiología Molecular, Hospital General Universitario Gregorio Marañón (HGUGM) and Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain; ¶Laboratorio de Inmuno-oncología, Hospital General Universitario Gregorio Marañón (HGUGM) and Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain*

**Background:** Estradiol-based contraceptives and hormonal replacement therapy predispose women to *C. albicans* infections. Moreover, during the ovulatory phase (high estradiol) of the ovarian cycle neutrophil numbers disappear in the vaginal lumen and increase during the luteal phase (high progesterone): therefore, sex hormones control the neutrophil influx to conciliate immunity and reproductive functions. Vaginal secretions contain chemokines that drive neutrophil migration into the vaginal lumen. Chemokines expression during the ovarian cycle or in response to hormonal treatments are controversial and their role in vaginal defense remains unknown.

**Material and methods:** We used *C. albicans* vaginal infection in the presence of female sex hormones. To investigate the hormonal role on the neutrophil transepithelial migration we used adoptive transfer of $CXCR2^{-/-}$ neutrophils and chemokine immunofluorescence quantitative analysis.

**Results:** Our data show that the CXCL1/CXCR2 axis drives neutrophil transepithelial migration into the vaginal and cervical lumen. Estradiol disrupts the CXCL1 gradient and favors neutrophil arrest in the lower female reproductive tract stroma. Progesterone allows the CXCL1 gradient to induce a rapid neutrophil migration and prevents pathogen growth.

**Conclusions:** CXCL1 expression by vaginal epithelial cells drives neutrophil transepithelial infiltration through tightly established gradients. Estradiol-treatment arrests neutrophil migration by disrupting the CXCL1 gradients: as a result, the vagina becomes more vulnerable.

## S.05
## The leukocyte enzyme myeloperoxidase impairs endothelial glycocalyx integrity

K. Manchanda, S. Baldus & A. Klinke
*Department of Cardiology, Heart Center, University Hospital Cologne, Cologne, Germany*

**Background:** It has been shown previously that myeloperoxidase (MPO), a highly cationic heme enzyme with pro-inflammatory properties, reduces the electrostatic repulsion between the negatively charged endothelial glycocalyx (EG) and neutrophils thereby mediating neutrophil-recruitment. We hypothesize that MPO can modulate the EG structure and affect vascular functions.
**Materials and methods:** The murine cremaster-muscle model was used to characterize EG by intravital microscopy. The EG integrity was analyzed by determining the thickness of EG using the FITC-dextran exclusion technique. The carotid artery was used for systemic administration of the various substances. Local inflammation was induced by intrascrotal TNF-α injection, which triggers release of MPO from neutrophils.
**Results:** The EG thickness in cremasteric capillaries was reduced significantly after MPO treatment. A similar effect was also observed after treatment with inactive MPO and the cationic protein protamine. To study this interaction further, heparin was administered in MPO-treated mice, which is known to release the EG-bound MPO. The EG thickness observed was significantly higher than in mice treated only with MPO. Lastly, it was shown clearly that local inflammation does not induce a reduction in the thickness of EG in $MPO^{-/-}$ but in WT mice.
**Conclusions:** The results strongly suggest that systemically administered as well as neutrophil-secreted MPO modulates the EG thickness. This modulation seems to be independent of MPO's catalytic properties but dependent on its surface charge. This strengthens our hypothesis that MPO binds to the negatively charged EG and modifies its structure due to its cationic charge and this effect is reversed when the EG-bound MPO is removed. Further experiments will be performed to investigate the consequence of MPO-dependent EG thickness reduction on vascular function.

## S.06
## Antibacterial effects of resveratrol against oral pathogens

A. Ballini, F.M. Coscia & D. de Vito
*Department of Basic Medical Sciences, Neurosciences and Sense Organs, University of Bari "Aldo Moro", Bari, Italy*

**Background:** Resveratrol (RSV) is a phytoalexin, produced naturally by several plants when under attack by bacterial or fungal pathogens. The present study was undertaken to explore the antibacterial activity of RSV derived from *Vitis vinifera* "Crljenak Kaštelanski" (Vitaceae) against two strains of oral pathogens.
**Material and methods:** The following bacterial strains from the American Type Culture Collection were used: *Streptococcus mutans* (Sm) ATCC 35668 and *Porphyromonas gingivalis* (Pg) ATCC 33277 which are associated respectively to dental caries and periodontal disease.. We investigated the antibacterial activity of RSV against Sm and Pg by minimum inhibitory concentration (MIC) and the determination of inhibition about Glucosyltransferase (GTF) activity.
**Results:** Antibacterial activity was assayed by measuring the diameter of zone of inhibition against Sm and Pg. RSV was significantly inhibited Water-insoluble Glucan (WIG) synthesis by GTF activity test.
**Conclusions:** Generally, these findings suggest that RSV can act as an effective antimicrobial agent against Sm and Pg. Furthermore, we consider that RSV can be used in daily dental products against some oral pathogens.

## S.07
## Paraoxonase 1 genotype – phenotype correlation in patients with metabolic syndrome

L. Ciumarnean*, E. Dronca†, S.C. Vesa‡, D.P. Sampelean* & A. Achimas Cadariu§
**Internal Medicine Department, Iuliu Hatieganu University of Medicine and Pharmacy of Cluj-Napoca, Cluj-Napoca, Romania; †Medical Genetics Department, Iuliu Hatieganu University of Medicine and Pharmacy of Cluj-Napoca, Cluj-Napoca, Romania; ‡Pharmacology, Toxicology and Clinical Pharmacology Department, Iuliu Hatieganu University of Medicine and Pharmacy of Cluj-Napoca, Cluj-Napoca, Romania; §Medical Informatics and Biostatistics Department, Iuliu Hatieganu University of Medicine and Pharmacy of Cluj-Napoca, Cluj-Napoca, Romania*

**Background:** The aim of the study was to investigate the influence of three single nucleotide polymorphisms (SNPs) (−108C>T, −162A>G and −909G>C) from the promoter region of paraoxonase 1 (PON1) gene on the enzyme activity, in patients with metabolic syndrome (MS).
**Patients and methods:** The study group consisted of 61 individuals with MS and the control group of 73 individuals without MS, age and gender matched. For each individual, clinical and genetic parameters with possible influence on PON1 activities (paraoxonase, arylesterase and lactonase) were measured. *PON1* genotyping was performed with PCR-RFLP, using specific primers and restriction enzymes.
**Results:** We found no differences for distribution of *PON1* −108C>T, −162A>G and −909G>C polymorphisms, between the two groups (p-NS). The −108C>T and −909G>C polymorphisms were associated with paraoxonase ($P = 0.03$, $P = 0.006$, respectively), arylesterase ($P < 0.001$, $P < 0.001$, respectively) and lactonase ($P < 0.001$, $P < 0.001$, respectively) activities. The −162A>G polymorphism was not associated with paraoxonase (p-NS) or lactonase (p-NS) activities, but influenced the arylesterase activity ($P = 0.03$).
**Conclusions:** PON1 activities were influenced by all three polymorphisms, regardless of the presence of MS.

## S.08
## Vitamin D improves endothelium-dependent relaxation in aortic rings isolated from streptozotocin-induced diabetic rats

A. Sturza*,†, O. M. Duicu*,†, L. Noveanu*,†, M. Dănilă*,† & D.M. Muntean*,†
**Department of Pathophysiology, "Victor Babeş" University of Medicine and Pharmacy, Timişoara, Romania; †Center for Translational Research and Systems Medicine, "Victor Babeş" University of Medicine and Pharmacy of Timişoara, Timişoara, Romania*

**Background:** An increasing body of evidence suggests that vitamin D has also cardiovascular effects besides the regulation of calcium-phosphate homeostasis. The present study was purported to assess the effect of 1,25-dihydroxy vitamin $D_3$, the

major metabolite of vitamin D, on vascular reactivity of aortic segments harvested from diabetic rats.

**Material and methods:** Aortic rings isolated from streptozotocin-induced diabetic rats (50 mg $kg^{-1}$, single dose, intra-peritoneal) and the non-treated controls were incubated 24 h in the absence or presence of 1,25-dihydroxyvitamin $D_3$ (0.1 μM). Subsequently, the rings were suspended in organ chambers and used for isometric force measurements in the presence of diclofenac (10 μM). The concentration of phenylephrine (Phe) used for preconstriction, was adjusted to obtain an preconstriction level of 80% of the contraction elicited by KCl (80 mM). Endothelium-dependent relaxation to increasing concentrations of acetylcholine (ACh) was recorded together with the vascular contractility to endothelial nitric oxide synthase (eNOS) inhibitor L-NAME (Nω-Nitro-L-arginine-methyl-ester-hydrochloride, 10 μM). The effect of vitamin D on the expression of RAGE (Receptor-for-Advanced-Glycation-Endproducts) was also assessed by quantitative RT-PCR and immunohistology.

**Results:** In arterial samples isolated from diabetic rats, incubation with vitamin $D_3$ modulated the vascular tone by reducing the contractility and improving the endothelium-dependent relaxation by 30%, respectively. Contraction to L-NAME was also significantly increased in diseased vessels and partially normalized by vitamin D treatment.

**Conclusions:** In organ bath studies vitamin D partialy restored the endothelial-dependent relaxation in vascular rings harvested from experimentally-induced type 1 diabetes. Further investigations aimed at characterizing the mechanisms underlying vitamin D action are warranted.

Study funded by the POSDRU postdoctoral grant no.159/1.5/S/136893–DocMed.Net_2.0.

## S.09
## *In vivo* characterization of reactive oxygen species dynamics in rats with unilateral urinary obstruction

A. Vaduva*, C. Glameanu†, D. Muntean‡,§ & A. Dema*
**Department of Microscopic Morphology – Morphopathology, "Victor Babes" University of Medicine and Pharmacy of Timisoara, Timisoara, Romania; †"Pius Branzeu" Center for Flap Surgery and Microsurgery Timisoara, Timisoara, Romania; ‡Department of Functional Sciences – Pathophysiology, "Victor Babes" University of Medicine and Pharmacy of Timisoara, Timisoara, Romania; §Center for Translational Research and Systems Medicine, "Victor Babes" University of Medicine and Pharmacy of Timisoara, Timisoara, Romania*

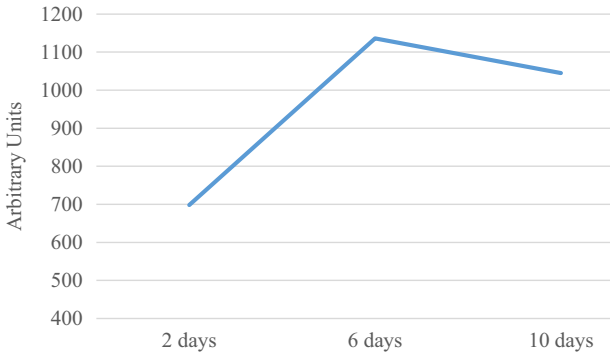
**Background:** As oxidative stress has been systematically associated with the development of acute and chronic kidney diseases (CKD), we aimed to perform a time-dependent characterization of this association in the early phases of experimentally induced CKD.

**Material and methods:** Adult male Wistar rats were subjected to unilateral urinary obstruction (UUO) in order to induce chronic kidney disease, while sham-operated rats were used as control group. Thirty-six rats were randomly assigned into six groups: three UUO and three sham-operated. *In vivo* confocal microscopy was performed 2, 6 and 10 days after UUO or sham surgery. DHE (ex/em 488/610 nm) staining via intravenous injection was used to assess superoxide levels. Image analysis was performed in Icy.

**Results:** UUO rats showed positively stained tubular nuclei, the mean fluorescence intensities being higher on the 6th and 10th day as compared to the 2nd day (Fig. 1). We found a significant difference in DHE staining intensity between UUO and sham rats only in the 10th day post-surgery ($P < 0.01$).

**Conclusions:** *In vivo* confocal microscopy in UUO rats showed the raise in reactive oxygen species production in the early days after ureteral ligation, an observation suggestive for an increase in oxidative stress prior to the previously described timeline for development of morphological changes.

Fig. 1 DHE staining intensity in UUO rats.




## S.10
## MicroRNA modulation renders glioblastoma cells sensitive to chemotherapy

P.P. Cunha*, P. Costa*, R. Costa*, C. Custódia*, R. Branco*, C.M. Morais*,†, A.M. Cardoso*,†, A.L. Cardoso†, A.S. Jurado*,† & M.C.P. Lima*,†
**Department of Life Sciences, Faculty of Science and Technology, University of Coimbra, Coimbra, Portugal; †CNC – Center for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal*

**Background:** Glioblastoma (GBM) is a malignant type of brain tumor, highly resistant to treatment and frequently relapsing, characteristics that have been assigned to a small cell population – the glioblastoma stem-like cells (GSCs). On the other hand, abnormal miRNA expression has been related with GBM aggressiveness, therapy resistance and anaplastic features. We hypothesize that modulation of miRNAs aberrantly expressed, especially those from GSCs, might contribute to enhance GBM susceptibility to chemotherapy.

**Materials and methods:** GSC were isolated from two GBM human cell lines, the commercially available U87 cells and DBTRG-05MG cells, established from a recurrent patient, employing a magnetic bead-based cell separation protocol and using cell surface (CD133) and intracellular (Nestin) markers. miRNA expression was, then, comparatively evaluated through quantitative real time PCR (qRT-PCR) in GSCs and GBM differentiated cells. The effects of modulating deregulated miRNAs by specific delivery of mimic/anti-miR oligonucleotides on cell viability, either *per se* or in combination with chemotherapeutics, were analysed. Anti-tumoral effects from the application of those strategies were also investigated *in vivo* using a GBM orthotropic mouse model.

**Results:** miR-128 and miR-520b were shown to be downregulated and miR-21 was found to be overexpressed in GSCs. Reestablishment of the levels of these miRNAs enhanced GBM cell susceptibility to the multi-tyrosine kinase inhibitor sunitinib, 90% of cell death being reached at low drug concentrations. Importantly, *in vivo* miR-21 silencing using stable nucleic acid lipid particles (SNALPs) targeted to GBM cells, through covalent

coupling of chlorotoxin, and oral administration of sunitinib, decreased tumor malignant features and enhanced animal survival, with negligible systemic toxicity.
**Conclusions:** Our results point towards an interesting and promising multimodal therapeutic approach for GBM based on miRNA modulation.

## S.11
## Comparative characterization of stem cells from human exfoliated deciduous teeth and dental pulp stem cells

A. Desiate
*Department of Interdisciplinary Medicine, University of Bari "Aldo Moro", Bari, Italy*

**Background:** Dental tissues has been identified as a novel and promising stem cell source. This study focused on the characterization of stem cells from human exfoliated deciduous teeth (SHED) in comparison with dental pulp stem cells (DPSCs).
**Material and methods:** In the present study, SHED and DPSCs were assayed for their cell surface antigens and proliferation by measuring the cell cycles, growth rates, and colony-forming units (CFUs). The evaluation of multi-differentiation was performed using alizarin red and oil red O and real-time PCR *in vitro*. The mineralization capability of the cells was examined by Von Kossa staining.
**Results:** SHED showed a higher proliferation rate and differentiation capability in comparison with DPSCs *in vitro*, and the results of the *in vivo* transplantation suggest that SHED have a higher capability of mineralization than the DPSCs.
**Conclusions:** SHED may represent a suitable, accessible and potential alternative source for regenerative medicine and therapeutic applications.

## S.12
## The effect of smoking and age associated lung function decline on the differential white blood cell count

B. Pilden-Sarv*, C. Falten*, R. Jõgi† & S. Sergejeva*
**Institute of Technology, University of Tartu, Tartu, Estonia; †Tartu University Hospital, Tartu, Estonia*

**Background:** Smoking causes airway inflammation and low-grade systemic inflammation. So far, smoking and ageing have been linked to the change in several inflammatory and lung function markers however the results have varied greatly between studies. We aimed to investigate the effect of smoking and age associated lung function changes over a period of 20-years on the differential leukocyte count.
**Materials and methods:** Peripheral blood cytospins from 94 ECRHS (European Respiratory Community Health Survey) stage III participants (64 female, 30 male) were stained by May-Grünwald-Giemsa-method. A differential enumeration of cells was performed using light microscopy (1000× magnification). Smoking and lung function history for each participant was evaluated over a period of 20 years from ECRHS stages I, II and III (1994, 2001–2002 and 2013–2014, respectively).
**Results:** There was a significant loss of FCV (forced vital capacity) per year in female smokers compared to never smokers (30.0 vs. 18.67 mL year$^{-1}$, respectively, $P = 0.01$). This phenomenon was not observed in the male groups. There were no statistically significant differences between the differential cell counts neither in female nor in male groups. There was a weak correlation between the number of eosinophils and the decline in Tiffenau-Pinelli index per year in female never smokers ($P = 0.04$, $r = 0.338$) and a moderate inverse correlation in the male never smokers group ($P = 0.03$, $r = -0.733$).
**Conclusions:** Smoking is associated with exaggerated aging-associated lung function loss. Eosinophils are possibly involved in aging-associated lung function loss. Further studies with more participants are needed to evaluate smoking induced changes in white blood cells and to assess whether these changes are responsible for the observed lung function loss.

# Abstracts Subspecialty Poster Session Other topics: Clinical Research

## S.13
### Reduced vitamin D levels: how much vitamin D is required for the effective replenishment in daily practice?

E. Jungmann & G. Jungmann
*Endocrine and Diabetes Unit, St. Vincent's Hospital Rheda-Wiedenbrück, Rheda-Wiedenbrück, Germany*

**Background:** Reduced vitamin D levels are a prevalent clinical finding that is clearly associated with increased morbidity and mortality. There is considerable controversy, however, as to how much vitamin D is required for the effective vitamin D replenishment in patients with reduced vitamin D levels.
**Materials and methods:** Effectiveness of vitamin D replenishment with 1000 to 3000 U qd of vitamin D and of vitamin D receptor agonists (VDRA) was evaluated in 161 patients with vitamin D levels ≤25 nM (group A) and 104 patients with vitamin D levels of 26–50 nM (group B). Two hundred and nine of the patients were women and 56 men [mean age, 47 ± 1 years (SEM)]. All patients had normal kidney function but GGT was higher in group A (31 ± 3 vs. 21 ± 1 U $L^{-1}$, $P < 0.05$). Reduced vitamin D levels were associated with lactose intolerance (40 % of patients), fructose malabsorption (24 %), pancreatic insufficiency (12 %) and coeliac disease and/or IgA deficiency (11 %). Calcium and phosphate in serum, PTH and 25-OH-vitamin D levels or 1,25-OH-vitamin D levels, respectively, were measured by routine methods.
**Results:** 19 % of the untreated patients had hypocalcaemia and 28 % had secondary hyperparathyroidism (SHPT). 3000 U of vitamin D resulted in vitamin D levels >50 nM in 82 % of the patients in group B but only in 54 % of the patients in group A ($P < 0.01$). Accordingly, SHPT was controlled in 94 % of the patients in group B but only 85 % of the patients in group A. VDRA controlled SHPT in 98 % of patients in group A ($P < 0.05$). In both groups, 1000 and 2000 U of vitamin D were less effective in normalizing vitamin D or calcium levels and in correcting SHPT ($P < 0.001$). There was no case of hypercalcaemia or increased vitamin D or VDRA levels in the course of the study.
**Conclusions:** In patients with reduced vitamin D levels, vitamin D doses up to 3000 U $day^{-1}$ or VDRA, respectively, are required to safely and effectively normalize vitamin D levels, to control prevalent hypocalcaemia and SHPT and to, presumably, prevent its sequelae.

## S.14
### Metformin-associated vitamin B-12 deficiency in patients with type 2 diabetes mellitus: clinical sequelae in daily practice

E. Jungmann & G. Jungmann
*Endocrine and Diabetes Unit, St. Vincent's Hospital Rheda-Wiedenbrück, Rheda-Wiedenbrück, Germany*

**Background:** In recent studies, vitamin B-12 deficiency was observed in 10 % of metformin-treated type 2 diabetic patients, but neurological status of the patients was not defined. Thus, potential consequences of this observation remained subject to controversy. Therefore, we decided to examine to which extent a vitamin B-12 deficiency can be detected in metformin-treated diabetic patients in daily practice and which impact vitamin B-12 deficiency – if present – could have on the development of diabetic neuropathy in these patients.
**Materials and methods:** 88 consecutive type 2 diabetic patients with metformin treatment for ≥1 year [37 females, 51 males, age, 66 ± 2 years (SEM), duration of diabetes, 10 ± 2 years, metformin, 1450 ± 120 mg $day^{-1}$ for 6 ± 2 years] were included in this cross-sectional study. We measured vitamin B-12 levels, folate, 25-OH-vitamin D and PTH by enzyme immunoassay, additionally we performed a routine screening of all patients for signs or symptoms of diabetic neuropathy.
**Results:** 10 % of the patients had vitamin B-12 deficiency, a total of 29 % of the patients had vitamin B-12 levels <200 pM. Patients with decreased vitamin B-12 levels received higher doses of metformin for longer duration than patients with vitamin B-12 levels >200 pM ($P < 0.05$). Moreover, they exhibited an increased prevalence of diabetic neuropathy, had decreased folate levels and decreased vitamin D levels ($P < 0.05$). In patients with decreased vitamin B-12, diabetic neuropathy developed after shorter duration of diabetes and despite better HbA1c levels than in patients with normal vitamin B-12 ($P < 0.05$).
**Conclusions:** In this cross-sectional study in daily practice, there is evidence for neurological consequences of metformin-associated vitamin B-12 deficiency, which therefore must be considered as eventually harmful for metformin-treated patients. Thus, patients should be regularly screened and vitamin B-12 replacement started as early as necessary, together with the replacement therapy of mostly coexistent vitamin D-deficiency.

## S.15
### Impact of age on the cardiovascular event risk conferred by HbA1c in patients with established coronary artery disease

A. Vonbank*,†,‡, C.H. Saely*,†,‡, P. Rein*,†,‡, D. Zanolin†,‡, A. Leiherer†,‡, K.-M. Ebner*,†,‡ & H. Drexel*,†,‡,§
**Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §College of Medicine, Drexel University, Philadelphia, PA, USA*

**Background:** In the present study we tested the hypothesis that age modulates the impact of HbA1c on cardiovascular event risk in patients with established coronary artery disease (CAD).
**Materials and methods:** We prospectively recorded cardiovascular events over a mean follow-up period of 4.4 ± 1.2 years in a large consecutive series of 816 patients with angiographically proven CAD, including 376 subjects <65 years and 440 subjects ≥65 years.

**Results:** During follow-up, the incidence of cardiovascular events was 9.3% among subjects <65 years and 24.8% among subjects ≥65 years ($P < 0.001$). Among the younger patients, HbA1c strongly and significantly predicted cardiovascular events [HR 1.54 (1.06–2.23); $P = 0.022$], but not among in the older patients [HR 1.22 (0.94–1.59); $P = 0.125$]. An interaction term age × HbA1c was statistically significant ($P = 0.007$), indicating that HbA1c was a significantly stronger predictor of cardiovascular events among younger than among older CAD patients.

**Conclusion:** We conclude that HbA1c is a significantly stronger predictor of cardiovascular events in younger patients than in older patients with established CAD.

## S.16

## Albuminuria significantly predicts cardiovascular events irrespective of the metabolic syndrome and the baseline coronary artery state

P. Rein*,†,‡, C.H. Saely*,†,‡, A. Vonbank*,†,‡, D. Zanolin†,‡, A. Leiherer†,‡, K.-M. Ebner*,†,‡ & H. Drexel*,†,‡,§

**Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §College of Medicine, Drexel University, Philadelphia, PA, USA*

**Background:** Albuminuria is an important indicator of cardiovascular risk. Whether albuminuria predicts cardiovascular events independently of the baseline coronary artery state in patients with the metabolic syndrome (MetS) and in subjects who do not have the MetS has not been investigated yet.

**Materials and methods:** We measured urinary albumin and creatinine concentrations in 872 consecutive patients undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease (CAD). Albuminuria was defined as a urinary albumin to creatinine ratio of 30 μg $mg^{-1}$ or greater. Prospectively, we recorded vascular events over 3.1 ± 1.2 years.

**Results:** During follow up, 17.5% of our patients suffered cardiovascular events. In the total study population, albuminuria significantly predicted the incidence of major cardiovascular events after adjustment for age, gender, body mass index, type 2 diabetes mellitus, smoking, blood pressure, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and the estimated glomerular filtration rate [adjusted HR = 1.84 (1.30–2.61); $P = 0.001$]. Further adjustment for the angiographically determined presence of CAD at baseline did not significantly attenuate the predictive power of albuminuria [HR = 1.82 (1.28–2.59); $P = 0.001$]. In analyses with respect to the MetS, the presence of albuminuria strongly and significantly predicted cardiovascular events in patients with the MetS [$n = 390$; HR 1.80 (1.12–2.88); $P = 0.015$] as well as in those without the MetS [2.02 (1.18–3.48); $P = 0.011$]. An interaction term MetS*albuminuria was not significant ($P = 0.619$), indicating that the cardiovascular risk conferred by the presence of albuminuria was not significantly different in subjects with the MetS compared to patients without the MetS.

**Conclusions:** We conclude that albuminuria significantly predicts cardiovascular events both in patients with and in subjects without the MetS independently of established cardiovascular risk factors and of the baseline coronary artery state.

## S.17

## Body mass index significantly modulates the power of C-reactive protein to predict cardiovascular event risk among angiographied coronary patients

A. Vonbank*,†,‡, C.H. Saely*,†,‡, D. Zanolin†,‡, P. Rein*,†,‡, A. Leiherer†,‡, K.-M. Ebner*,†,‡ & H. Drexel*,†,‡,§

**Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §College of Medicine, Drexel University, Philadelphia, PA, USA*

**Background:** Epidemiological studies in various populations show that obesity is associated with inflammation and with increased cardiovascular risk, and that the inflammatory marker C-reactive protein (CRP) strongly predicts the incidence of cardiovascular events. Whether CRP is equally predictive of cardiovascular event risk in obese patients and in non-obese subjects is not known and is addressed in the present study.

**Materials and methods:** Cardiovascular events were recorded over a follow-up period of 10 years in a large high-risk population of 1731 consecutive patients undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease (CAD). Obesity was defined as body mass index (BMI) ≥30 kg $m^{-2}$.

**Results:** At baseline, CRP surprisingly was significantly higher in non-obese subjects ($n = 1367$) than obese individuals ($n = 364$) (0.6 ± 1.5 vs. 0.5 ± 0.8 mg $dL^{-1}$; $P < 0.001$). Prospectively, 27.8% of our patients suffered vascular events. CRP proved to be a strong and independent predictor of vascular events in non-obese subjects [HR 1.13 (1.06–1.20); $P < 0.001$] but not in obese subjects [HR 1.08 (0.94–1.235); $P = 0.262$]. An interaction term BMI × CRP was significant ($P < 0.001$), indicating that the mass index weight significantly modulated the power of CRP to predict vascular events.

**Conclusions:** From the results of this large 10-year prospective cohort study we conclude that obesity significantly modulates the power of CRP to predict cardiovascular event risk among angiographied coronary patients.

## S.18

## Plasma chemerin is a strong and independent predictor of cardiovascular event risk

A. Leiherer†,‡, A. Muendlein†,‡, P. Rein*,†,‡, K. Geiger†,‡, P. Fraunberger§, H. Drexel*,†,‡,¶, A. Vonbank*,†,‡, K.I.-M. Ebner*,†,‡ & C.H. Saely*,†,‡

**Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §Medical Central Laboratory, Academic Teaching Hospital Feldkirch, Austria; ¶College of Medicine, Drexel University, Philadelphia, PA, USA*

**Background:** Associations of the adipokine chemerin with the metabolic syndrome (MetS) and with chronic kidney disease (CKD), two important indicators of increased cardiovascular event risk, have been described. However, the power of chemerin to predict cardiovascular events has not been investigated so far and is addressed in the present study.

**Materials and methods:** We measured plasma chemerin in a high-risk cohort of 495 patients undergoing coronary angiography for the evaluation of suspected or established coronary artery disease (CAD) in which cardiovascular events were prospectively recorded over 3.5 ± 1.1 years. Significant baseline CAD was diagnosed in the presence of coronary artery stenoses ≥50%.

**Results:** At baseline, plasma chemerin was significantly higher in patients with the MetS as defined by the current harmonized consensus definition ($n = 147$) than in non-MetS subjects (201 ± 71 vs. 163 ± 62 ng $mL^{-1}$, $P < 0.001$) and was inversely correlated with estimated glomerular filtration rate (eGFR; $r = -0.33$, $P < 0.001$). During follow-up, chemerin significantly predicted cardiovascular events ($n = 82$) univariately, after adjustment for age, gender, body mass index, and eGFR, and also after additional adjustment for the presence of significant baseline CAD, with standardized hazard ratios of 1.83 (1.19–2.83), $P = 0.006$; 1.77 (1.12–2.80), $P = 0.015$; and 1.69 (1.07–2.67), $P = 0.024$, respectively.

**Conclusions:** From this first prospective evaluation of the cardiovascular event risk associated with chemerin we conclude that chemerin is strongly predictive of cardiovascular events independently from standard risk factors, from the MetS, and from the baseline presence of CAD.

## S.19
## Diabetes is not a coronary artery disease risk equivalent among women

C.H. Saely*,†,‡, A. Vonbank*,†,‡, D. Zanolin†,‡, P. Rein*,†,‡, A. Leiherer†,‡, K.-M. Ebner*,†,‡ & H. Drexel*,†,‡,§

**Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §College of Medicine, Drexel University, Philadelphia, PA, USA*

**Background:** Diabetes *per se* is widely considered a coronary artery disease (CAD) risk equivalent, particularly among women. We aimed at investigating the contribution of baseline coronary atherosclerosis to the risk of diabetic women for future vascular events in a prospective cohort study on subjects who were characterized by coronary angiography at baseline.

**Materials and methods:** Vascular events were recorded over 10 years in 598 consecutive women undergoing coronary angiography for the evaluation of established or suspected stable CAD.

**Results:** From our women, 271 had neither type 2 diabetes mellitus (T2DM) nor significant CAD (i.e. coronary stenoses ≥50%) at the baseline angiography, 79 had T2DM but not significant CAD, 152 did not have T2DM but had significant CAD, and 96 had both T2DM and significant CAD. Non-diabetic women without significant CAD had an event rate of 12.5%. The event rate was similar in T2DM women without significant CAD (15.2%; $P = 0.749$), but higher in non-diabetic women with significant CAD (32.9%; $P < 0.001$). Women with both T2DM and significant CAD had the highest event rate (43.8%; $P < 0.001$). Importantly, T2DM women without significant CAD had a significantly lower event rate than non-diabetic women with significant CAD ($P = 0.003$).

**Conclusions:** We conclude that T2DM *per se* is not a CAD risk equivalent among women. Moderate-risk diabetic women without significant CAD and very high-risk diabetic women with significant CAD add up to a grand total of high-risk diabetic women. This is why diabetes seems to be a CAD risk equivalent in many epidemiological studies.

## S.20
## Haemoglobin as a predictor of diabetes incidence in obese and non-obese patients undergoing coronary angiography

A. Vonbank*,†,‡, P. Rein*,†,‡, D. Zanolin†,‡, C.H. Saely*,†,‡, A. Leiherer†,‡, K.-M. Ebner*,†,‡ & H. Drexel*,†,‡,§

**Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §College of Medicine, Drexel University, Philadelphia, PA, USA*

**Background:** The association of blood haemoglobin concentration (Hb) with the incidence of future diabetes in obese patients is unclear. In the present study we therefore addressed this issue.

**Materials and methods:** We prospectively recorded diabetes incidence over a mean follow-up period of 10 years in a large consecutive series of 1479 patients, who did not have previously known diabetes and who underwent coronary angiography for the evaluation of established or suspected coronary artery disease. Obesity was defined as body mass index (BMI) ≥30 kg $m^{-2}$.

**Results:** During follow-up, the incidence of diabetes was 13%. Hb at baseline was significantly higher in obese patients ($n = 331$) than in non-obese subjects (148 ± 12 vs. 145 ± 13 g $L^{-1}$). Prospectively, Hb strongly and significantly predicted diabetes incidence with a standardized adjusted odds ratio (OR) of 1.50 (1.05–2.16); $P = 0.025$ in obese patients but not in non-obese individuals [OR 0.95 (0.75–1.19); $P = 0.658$]. An interaction term BMI × Hb was statistically significant ($P = 0.024$), indicating that the body mass index significantly modulated the power of Hb to predict incident diabetes in this population.

**Conclusions:** We conclude that Hb is a strong predictor of diabetes incidence in obese patients undergoing coronary angiography and that the body mass index significantly modulates the power of Hb to predict incident diabetes in this population.

## S.21
## Impact of gender on the risk of coronary atherosclerosis and cardiovascular events conferred by HbA1c in subjects without known diabetes

C.H. Saely*,†,‡, A. Vonbank*,†,‡, D. Zanolin†,‡, P. Rein*,†,‡, A. Leiherer†,‡, K.-M. Ebner*,†,‡ & H. Drexel*,†,‡,§

**Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §College of Medicine, Drexel University, Philadelphia, PA, USA*

**Background:** Diabetes confers a larger increase in the relative risk of cardiovascular events among women than among men. Whether gender also affects the association of HbA1c with cor-

onary atherosclerosis and cardiovascular events among subjects without known diabetes is unknown.
**Materials and methods:** We enrolled a large consecutive series of 1479 patients undergoing coronary angiography for the evaluation of established or suspected coronary artery disease (CAD), including 495 women and 984 men who did not have previously known diabetes Significant CAD was diagnosed in the presence of significant coronary stenoses ≥50%. Prospectively, we recorded cardiovascular events over 4.4 ± 1.2 years.
**Results:** Among women, 36.4%, 56.2%, and 7.4% and among men 44.2%, 46.6%, and 9.1% had HbA1c values of <5.7% (normal according to ADA criteria), 5.7–6.4% (at risk of diabetes according to ADA criteria), and ≥6.5% (diabetes according to ADA criteria), respectively. The prevalence of angiographically diagnosed significant CAD in these HbA1c categories was 31.2%, 38.2%, and 47.2% among women ($P_{trend}$ = 0.041) and 63.2%, 65.3% and 64.8% among men ($P_{trend}$ = 0.589). An interaction term gender × HbA1c was statistically significant ($P < 0.001$), indicating that the association of HbA1c with CAD was significantly stronger among women than among men. During follow-up, the incidence of cardiovascular events was 21.5% in women and 28.5% in men ($P = 0.002$). Among women, HbA1c strongly and significantly predicted cardiovascular events (adjusted OR for a 1% increase in HbA1c [HR 2.08 (1.24–3.03); $P < 0.001$], but not among men [HR 1.12 (0.94–1.53); $P = 0.145$]. An interaction term gender × HbA1c again was statistically significant ($P = 0.011$), indicating that HbA1c was a significantly stronger predictor of cardiovascular events among women than among men.
**Conclusions:** We conclude that gender significantly modulates the risk of coronary atherosclerosis and cardiovascular events conferred by HbA1c in subjects without known diabetes.

## S.22
## Impaired kidney function is a diabetes risk equivalent in patients with established coronary artery disease

C.H. Saely*,†,‡, D. Zanolin†,‡, A. Vonbank*,†,‡, P. Rein*,†,‡, A. Leiherer†,‡, K.-M. Ebner*,†,‡ & H. Drexel*,†,‡,§
**Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch; Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §College of Medicine, Drexel University, Philadelphia, PA, USA*

**Background:** Type 2 diabetes mellitus (T2DM) is a paramount risk factor for cardiovascular disease, in particular among patients with established coronary artery disease (CAD). Similarly, chronic kidney disease (CKD) confers a high risk of cardiovascular events. We aimed at investigating the single and joint effects of T2DM and of CKD on cardiovascular risk in patients with angiographically proven CAD.
**Materials and methods:** We prospectively recorded cardiovascular events over 10 years in a cohort of 1423 patients with angiographically proven CAD. CKD was defined as an estimated glomerular filtration rate (eGFR) <60 mL $min^{-1}$/1.73 $m^2$.
**Results:** The risk of cardiovascular events was significantly higher in T2DM patients ($n$ = 437) than in non-diabetic subjects (39.1% vs. 28.7%; $P < 0.001$) and also was higher in patients with CKD ($n$ = 246) compared to those with an eGFR ≥60 mL $min^{-1}$/1.73 $m^2$ (47.2% vs. 28.7%; $P < 0.001$). When both, T2DM and CKD were considered, 841 subjects had neither T2DM nor CKD, 336 had T2DM but not CKD, 145 did not have diabetes but had CKD, and 101 had both diabetes and CKD. When compared with the event rate among patients with neither T2DM nor CKD (26.3%), event rates were significantly higher in patients with T2DM who did not have CKD (34.8%; $P = 0.007$) and in non-diabetic patients with CKD (42.8%; $P = 0.020$) and were highest in patients with both, T2DM and CKD (53.5%; $P < 0.001$). Further, patients with both, T2DM and CKD were at a significantly higher event risk than those with T2DM but no CKD ($P = 0.011$) and those without T2DM but with CKD ($P = 0.048$). Event rates were similar in patients with T2DM but not CKD and in non-diabetic patients with CKD ($P = 0.798$).
**Conclusions:** We here report the novel findings that CKD and T2DM contribute synergistically to cardiovascular event risk and that CKD is a T2DM risk equivalent in patients with established coronary artery disease.

## S.23
## Leptin serum levels are independently determined by obesity and by the presence of the metabolic syndrome

D. Zanolin†,‡, C.H. Saely*,†,‡, A. Vonbank*,†,‡, P. Rein*,†,‡, A. Leiherer†,‡, K.-M. Ebner*,†,‡ & H. Drexel*,†,‡,§
**Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §College of Medicine, Drexel University, Philadelphia, PA, USA*

**Background:** Obesity is a major risk factor for the metabolic syndrome (MetS), but some obese individuals do not have the MetS while others have the MetS but are non-obese. The single and joint associations of the adipokine leptin with obesity and the MetS have not yet been investigated and are addressed in the present study.
**Materials and methods:** We measured leptin in four groups of patients: subjects who were non-obese and did not have the MetS ($n$ = 196), non-obese patients with the MetS ($n$ = 149), obese subjects who did not have the MetS ($n$ = 13) and obese patients with the MetS ($n$ = 77). Obesity was defined as a body mass index ≥30 kg $m^{-2}$; presence of the MetS was defined according to the current harmonized consensus definition.
**Results:** Compared to serum leptin in non-obese subjects who did not have the MetS (6.71 ± 7.83 ng $mL^{-1}$), leptin was significantly higher in non-obese subjects with the MetS (9.29 ± 7.53 ng $mL^{-1}$; $P < 0.001$), as well as in obese subjects without (11.15 ± 9.75 ng $mL^{-1}$; $P = 0.016$) or obese patients with the MetS (15.92 ± 11.61 ng $mL^{-1}$; $P < 0.001$), in whom leptin trended ($P = 0.127$) to be higher than in obese patients without the MetS and was significantly ($P < 0.001$) higher than in non-obese patients with the MetS. Analysis of covariance showed that both obesity and the MetS significantly and independently predicted serum leptin, with obesity being the stronger predictor ($F$ = 17.016; $P < 0.001$) than presence of the MetS ($F$ = 7.60; $P = 0.006$).
**Conclusions:** Obesity and presence of the MetS are independent determinants of serum leptin, but obesity explains a larger amount of serum leptin variation than the presence of the MetS.

## S.24
## Lipoprotein (a), type 2 diabetes and vascular risk in angiographied coronary patients

A. Vonbank*,†,‡, C.H. Saely*,†,‡, D. Zanolin†,‡, P. Rein*,†,‡, A. Leiherer†,‡, K.-M. Ebner*,†,‡ & H. Drexel*,†,‡,§

**Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §College of Medicine, Drexel University, Philadelphia, PA, USA*

**Background:** Lipoprotein (a) [Lp(a)] especially in young individuals is an important cardiovascular risk factor. However, data on the long-term vascular risk conferred by Lp(a) in patients with type 2 diabetes mellitus (T2DM) are scarce.

**Materials and methods:** Lp(a) was measured in a cohort of 909 consecutive patients undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease; vascular events were recorded over 10 years.

**Results:** Median Lp(a) at baseline was significantly lower in patients with T2DM ($n = 260$) than in subjects without T2DM [10 (interquartile range 1–34) vs. 16 (1–54) mg $dL^{-1}$; $P = 0.017$]. Prospectively, 27.8% of our patients suffered vascular events. Lp(a) proved to be a strong and independent predictor of vascular events in total population with a standardized adjusted hazard ratio (HR) of 1.15 (1.03–1.27); $P = 0.006$] as well as in subjects without T2DM [HR 1.22 (1.10–1.36); $P < 0.001$] but not in patients with T2DM [HR 0.990 (0.79–1.22); $P = 0.888$]. An interaction term T2DM × Lp(a) was significant ($P < 0.001$), indicating that Lp(a) was a significantly stronger predictor of vascular events in subjects without T2DM than in patients with T2DM.

**Conclusions:** Lp(a) in patients with T2DM is low and is not associated with the incidence of vascular events. The power of Lp(a) as a predictor of cardiovascular events is significantly modulated by the presence T2DM.

## S.25
## Plasma omentin significantly predicts cardiovascular events independently from the presence and extent of angiographically determined baseline coronary artery disease

C.H. Saely*,†,‡, A. Leiherer†,‡, A. Muendlein†,‡, A. Vonbank*,†,‡, P. Rein*,†,‡, K. Geiger†,‡, K.-M. Ebner*,†,‡ & H. Drexel*,†,‡,§

**Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §College of Medicine, Drexel University, Philadelphia, PA, USA*

**Background:** No prospective data on the power of the new adipocytokine omentin to predict cardiovascular events are available. We therefore aimed at investigating (i) the association of plasma omentin with cardiometabolic risk markers, (ii) its association with angiographically determined coronary atherosclerosis, and (iii) the power of plasma omentin to predict cardiovascular events.

**Materials and methods:** We measured plasma omentin in a series of 295 patients undergoing coronary angiography for the evaluation of established or suspected stable CAD; presence of baseline CAD was defined as the presence of any lumen irregularities at angiography; the extent of baseline CAD was defined as the number of significant coronary stenoses ≥50%; prospectively cardiovascular events were recorded over a mean follow-up period of 3.5 years.

**Results:** During this period, 17.6% of our patients suffered cardiovascular events, corresponding to an annual event rate of 5.3%. Plasma omentin did not differ significantly between patients with and subjects without significant CAD ($P = 0.783$), but prospectively omentin significantly predicted cardiovascular events after adjustment for age, gender, BMI, diabetes, hypertension, LDL cholesterol, HDL cholesterol and smoking with a standardized adjusted hazard ratio (HR) of 1.41 (95% CI 1.16–1.72), $P < 0.001$, as well as after additional adjustment for the presence and extent of CAD at the baseline angiography [HR 1.52 (95%CI 1.23–1.86), $P < 0.001$].

**Conclusions:** From this first prospective evaluation of the cardiovascular risk associated with plasma omentin we conclude that elevated omentin is a strong predictor of cardiovascular events independently from the presence of baseline CAD.

## S.26
## ProBNP strongly predicts future macrovascular events in angiographied coronary patients with as well as in those without the metabolic syndrome

P. Rein*,†,‡, C.H. Saely*,†,‡, A. Vonbank*,†,‡, D. Zanolin†,‡, A. Leiherer†,‡, K.-M. Ebner*,†,‡ & H. Drexel*,†,‡,§

**Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §College of Medicine, Drexel University, Philadelphia, PA, USA*

**Background:** Pro-B-type natriuretic peptide (proBNP) is a prognostic biomarker for patients with congestive heart failure as well as in other patient populations. The power of proBNP to predict cardiovascular endpoints in patients with the metabolic syndrome (MetS) is unclear and is addressed in the present study.

**Materials and methods:** We measured serum proBNP in 722 patients undergoing coronary angiography for the evaluation of stable coronary artery disease (CAD). Significant CAD was diagnosed in the presence of coronary stenoses with lumen narrowing of ≥50%. Prospectively, we recorded vascular events over 3.2 ± 1.2 years.

**Results:** ProBNP was significantly higher in patients with ($n = 386$) than in subjects without significant CAD at baseline (711 ± 1287 vs. 663 ± 1565 pg $mL^{-1}$; $P = 0.001$). Prospectively, we recorded 121 cardiovascular events. The incidence of vascular events significantly increased over tertiles of proBNP in patients with the MetS (10.7%, 18.5%, and 28.8% respectively; $P = 0.004$) was well as in those without the MetS (10.4%, 11.5%, and 22.0%, respectively; $P = 0.011$). Similarily, serum proBNP significantly predicted the incidence of major cardiovascular events after adjustment for age, gender, body mass index, smoking, systolic and diastolic blood pressure, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and the estimated glomerular filtration reate both in subjects with the MetS [standardized adjusted HR 1.48 (1.21–1.80); $P < 0.001$] and in those without the MetS [HR 1.21 (1.04–1.40); $P = 0.011$]. These results were not attenuated after further adjustment for the angiographically determined baseline CAD state [HRs 1.50

(1.23–1.83); $P < 0.001$ and 1.26 (1.09–1.47); $P = 0.003$ in subjects with the MetS and in those without the MetS, respectively).
**Conclusions:** Serum proBNP predicts cardiovascular events independently of established cardiovascular risk factors and of the baseline coronary artery state both in patients with and in subjects without the MetS.

## S.27
## Single and joint effects of obesity and of the metabolic syndrome on cardiovascular event risk

C.H. Saely*,†,‡, D. Zanolin†,‡, A. Vonbank*,†,‡, P. Rein*,†,‡, A. Leiherer†,‡, K.-M. Ebner*,†,‡ & H. Drexel*,†,‡,§
*Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §College of Medicine, Drexel University, Philadelphia, PA, USA

**Background:** Obesity is a major risk factor for the metabolic syndrome (MetS), but some obese individuals do not have the MetS while others have the MetS but are non-obese. We prospectively investigated the single and joint effects of obesity and of the MetS on cardiovascular event risk.
**Materials and methods:** Cardiovascular events were prospectively recorded over 10 years in a large cohort of 1705 patients undergoing coronary angiography for the evaluation of established or suspected stable coronary artery disease. Obesity was defined as a body mass index ≥30 kg $m^{-2}$; presence of the MetS was defined according to the current harmonized consensus definition.
**Results:** From our patients, 827 were non-obese and did not have the MetS, 443 were non-obese but had the MetS, 113 were obese but did not have the MetS, and 322 were obese and had MetS. Cardiovascular event risk was 34.1% in non-obese patients with the MetS. It was significantly higher in this patient group when compared to non-obese subjects without the MetS (25.3%; $P < 0.001$), when compared to obese subjects without the MetS (22.1%; $P = 0.036$), and even when compared to obese subjects with the MetS (25.2%; $P = 0.006$).
**Conclusions:** We conclude that non-obese patients with the MetS face a particularly unfavourable cardiovascular prognosis.

## S.28
## Presence of type 2 diabetes mellitus significantly modulates the power of thyroid stimulating hormone to predict cardiovascular mortality

A. Vonbank*,†,‡, C.H. Saely*,†,‡, D. Zanolin†,‡, P. Rein*,†,‡, A. Leiherer†,‡, K.-M. Ebner*,†,‡ & H. Drexel*,†,‡,§
*Department of Internal Medicine & Cardiology, Academic Teaching Hospital Feldkirch, Feldkirch, Austria; †Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria; ‡Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; §College of Medicine, Drexel University, Philadelphia, PA, USA

**Background:** Elevated thyroid stimulating hormone (TSH) is associated with an adverse cardiovascular risk profile, especially in patients with type 2 diabetes mellitus (T2DM). We investigated the association between TSH and cardiovascular mortality in patients with T2DM as well as in non-diabetic subjects.
**Materials and methods:** We measured TSH in a high-risk cohort of 1741 consecutive patients undergoing coronary angiography for the evaluation of established or suspected coronary artery disease (CAD). The incidence of vascular events was recorded over 10 years; T2DM was defined according to current ADA criteria.
**Results:** From our patients, 34% suffered vascular events. TSH proved to be a strong and independent predictor of cardiovascular mortality in subjects without T2DM ($n = 1220$; standardized adjusted hazard ratio (HR) 1.11 [1.00–1.24]; $P = 0.036$), but not in patients with T2DM ($n = 521$; HR 0.99 [0.87–1.14]; $P = 0.934$). An interaction term TSH × T2DM was significant ($P = 0.039$), indicating that TSH was a significantly stronger predictor of vascular events in subjects without T2DM than in patients without T2DM.
**Conclusions:** From the data of this prospective cohort study we conclude that presence of T2DM significantly modulates the power of TSH to predict cardiovascular mortality.

## S.29
## Co-prescribing of renin-angiotensin system (RAS)-acting agents in clinical practice in Romania

A. Farcas*, D. Leucuta†, C. Bucsa*, C. Mogosan*, M. Bojita* & D. Dumitrascu‡
*Drug Information Research Center, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; †Medical Informatics and Biostatistics Department, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; ‡2nd Medical Department, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

**Background:** Due to concerns that combining RAS-acting agents could increase the risk of hyperkalaemia and renal failure compared with RAS-acting monotherapy we conducted an investigation to describe the extent and patterns of co-prescription of RAS-acting agents compared with monotherapy in an electronic health record database.
**Materials and methods:** The descriptive retrospective study included all patients hospitalized during 18 months in 2013–2014 with a prescription of a RAS-acting agent at hospital discharge: angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARBs) or a combination of the two. Variables like demographics, co-morbidities, co-medications and proportion of patients with high creatinine and potassium values before discharge were analyzed.
**Results:** Out of a total number of 10 315 patients, 1003 (9.72%) were prescribed an ACEi, 254 (2.46%) an ARB and 24 (0.23%) were co-prescribed an ACEi and an ARB. There were no differences regarding sex and age between these groups. In patients with diabetes mellitus ($n = 1674$) an ACEi, ARB and a combination of the two were prescribed in 192 (11.47%), 71 (4.24%) and 14 (0.83%) respectively. In patients with renal disease ($n = 609$) an ACEi, ARB and a combination of the two were prescribed in 62 (10.18%), 27 (4.43%) and 5 (0.82%) respectively. Creatinine values (as per the last measurement before discharge) higher than 1.7 mg $dL^{-1}$ and potassium values higher than 5.5 mM were found in 2.64%, 6.88% and 13.04%, respectively in 1.03%, 2.02% and 0% of patients discharged with an ACEi, ARB and a combination of the two.
**Conclusions:** The co-prescription of (RAS)-acting agents is higher in patients with diabetic and renal disease comparing

to overall population, being prescribed in more patients with altered creatinine values compared to patients receiving monotherapy.

**Acknowledgements:** This paper was published under the frame of European Social Found, Human Resources Development Operationl Programme 2007–2013, project no. POSDRU/159/1.5/136893.

## S.30
## Clinical investigation of quality-of-life data among laryngectomized patients

M. Chirila*, C. Ţiple*, F.V. Dinescu* & S.D. Bolboacă†
**Department of Otorhinolaryngology, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania; †Department of Medical Informatics and Biostatistic Department, Iuliu Haţieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania*

**Background:** The objective of our study was to find thresholds for health-related quality-of-life (HRQL) that laryngectomees consider to be clinically relevant 1 year after surgery (i.e., the level of HRQL that patient's rate as satisfactory).

**Materials and methods:** We performed a retrospective case-control study between October 2013 and November 2014. We included patients diagnosed with laryngeal or hypopharyngeal cancer and surgical treated with total laryngectomy at the ENT Clinic of Cluj-Napoca. We used the European Organisation for Research and Treatment of Cancer core questionnaires (QLQ-C30) and the head and neck cancer module (QLQ-H&N35).The target values for the QLQ-C30 and QLQ-H&N35 were defined on a sample of 80 patients at 1 year following laryngectomy and 20 healthcare professionals (HCPs).

**Results:** On the functional scales, patients accept most problems in emotional functioning (37.75) and cognitive functioning (50.25). Patients are the most accepting of sensory impairments (49.49), coughing (38.38), and dyspnea (25.25), whereas diarrhea (4.55) and nausea/vomiting (8.33) were rated as being the most troublesome symptoms. Difficulties in social contact (28.48), social eating (22.10), and pain in the mouth (30.30) were also judged as being very hard to live with. HCPs assessed more of the studied complaints as being tolerable than patients did, especially in psychosocial domains.

**Conclusions:** For some domains, we found large discrepancies between desired quality-of-life levels and reality, with a large proportion of the laryngectomized patients not reaching the desired cutoff values. A remarkable result of the study is the observation that symptoms, resulting directly from disease or therapy, are easier for patients to accept than general, nonspecific symptoms.

## S.31
## Effect of ablative treatment of hepatocellular carcinoma (HCC) on the genomic expression in circulating peripheral blood mononuclear cells (PBMC)

D. Santovito, S. D'Amore, A. Mele, A. Gesualdo, V.O. Palmieri & G. Palasciano
*Department of Biomedical Sciences and Oncology, University of Bari, Bari, Italy*

**Background:** Genomic profiling of HCC have significant clinical and prognostic role.

The aims are: to find out role of gene expression profile of PBMCs as a surrogate approach for assessment of local HCC-infiltrating mononuclear inflammatory cells; to find out whether ablative treatment of HCC may affect genomic expression in circulating PBMCs.

**Methods:** Twenty-five patients affected by HCC, classified on Child Class, staged by BCLC criteria, underwent to ablative treatment (radiofrequency 13, chemoembolization 11); its effect has been evaluated by mRECIST criteria. Blood samples have been collected at time 0, before treatment, and at time 1, 3 months after procedure. Microarray expression profiling on PBMCs has been performed to identify upregulation and/or down-regulation of gene expression pathways by means high-throughput iSCAN illumina facility. The genomic analysis has been completed for 14 subjects, seven complete response (CR); seven partial response (PR).

**Results:** At time 0, the gene HLA-DBR4 is overexpressed in patients with PR in comparison to subjects with CR (3328 + 1280vs2660 + 651 signal avg, $P < 0.005$). In patients with CR, one gene is overexpressed (ERH) and seven genes (HNRNPL, H1FX, STARD3, FOS, RNU1–5, RNU1G2, SNORD3C, RN5S9, JUN) are underexpressed after treatment. In patients with PR, seven genes are up-regulated (C22orf27, FYCO1, PSMC4, ZNF217, SYT11, RAB8B, MLKL) and 11 are down-regulated (SESN1, SETD1A, GDPD5, FAM100B, C2orf24, SH3BP1, CYBASC3, CIC, PLIN2, SLC35A4, DNM2).

Further evaluation has enclosed the comparison among genes expression at time 1 among CR and PR patients and identification of pathways and possible networks related to tumor progression.

**Conclusions:** Genomic analysis of PBMCs by microarrays is important for the study of genomic profiling of HCC and for clinical and prognostic effects on gene expression of the ablative treatment.

## S.32
## How intrauterine growth restriction influence anthropometry and morbidities of pre-term and respectively term infants?

M.G. Hăşmăşanu*, M.I. Baizat†, S.D. Bolboacă‡, T.C. Drugan‡, M. Matyas* & C.G. Zaharie*
**Department of Neonatology, Iuliu Haţieganu University of Medicine and Pharmacy Cluj-Napoca, Cluj-Napoca, Romania; †Department of Neonatology, Emergency Clinical County Hospital Cluj-Napoca, Cluj-Napoca, Romania; ‡Department of Medical Informatics and Biostatistics, Iuliu Haţieganu University of Medicine and Pharmacy Cluj-Napoca, Cluj-Napoca, Romania*

**Background:** The aim of our study was to investigate if intrauterine growth restricted (IUGR) infants had different anthropometry and morbidities in preterm and term subgroups compared to controls.

**Materials and methods:** A retrospective study was conducted in the Emergency County Hospital, Cluj-Napoca on infants admitted to the 1st Gynecology Neonatal-Ward during 2.5 years. The medical charts were reviewer and preterm (gestational age, GA < 37 weeks) as well as term (GA ≥ 37 weeks) infants with IUGR (birth weight for GA < 10th percentile) were included in the sample. A matched healthy control in terms of GA and gender was identified in a ratio of 1:1 and included in the study.

**Results:** One-hundred-forty-two newborns were investigated in each group (IUGR and control), 51 preterm and 91 term

infants. A significantly higher percent of subjects in both preterm and term subgroups proved baby-girls (F:M = 2.00 (preterm), 1.53 (term), $P < 0.0001$). Caesarean delivery proved more frequent in both preterm and term subgroups among IUGR group compared to controls ($P < 0.005$). The birth height as well as cranial perimeter proved significantly lower in both preterm and terms IUGR compared to controls ($P < 0.001$). A significantly higher percentage of IUGR preterm infants had cerebral hemorrhage and respectively hypoglycemia ($P < 0.02$) compared to controls while a significantly lower percent of preterm IUGR infants had obstetrical trauma. A significantly lower percent of IUGR term infants had obstetrical trauma and respiratory distress compared to term controls ($P < 0.05$) while a significant higher percent of IUGR term infants had hypoglycemia compared to term controls ($P < 0.0001$).

**Conclusions:** IUGR infants proved smaller compared to controls. Hypoglycemia proved a characteristic of all IUGR infants while cerebral hemorrhage is a characteristics of preterm IUGR infants.

## S.33
## Retrospective analysis of serum creatinine and potassium monitoring in patients prescribed with angiotensin-converting enzyme inhibitors, non-steroidal anti-inflammatory drugs and diuretics

C. Bucsa*, D.C. Moga[†,‡,§], A. Farcas*, C. Mogosan*, M. Bojita* & D.L. Dumitrascu[¶]

**Drug Information Research Center, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; [†]Department of Pharmacy Practice and Science, College of Pharmacy, University of Kentucky, Lexington, KY, USA; [‡]Institute for Pharmaceutical Outcomes and Policy, University of Kentucky, Lexington, KY, USA; [§]Department of Epidemiology, College of Public Health, Lexington, KY, USA; [¶]2nd Department of Internal Medicine, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania*

**Background:** To evaluate in retrospective data the extent of serum creatinine and potassium monitoring in patients prescribed with angiotensin-converting enzyme inhibitors (ACE-I) and non-steroidal anti-inflammatory drugs (NSAIDs) or ACE-I/NSAIDs and diuretics and to determine the prevalence of laboratory values above the upper normal limit (UNL) in monitored patients.

**Materials and methods:** Hospitalized patients with ACE-I in their therapy at discharge were included in three groups as follows: ACE-I, DT (double therapy with ACE-I and NSAIDs) and TT (triple therapy with ACE-I, NSAIDs and diuretics) groups. We evaluated differences on demographic characteristics, comorbidities, medications, laboratory monitoring and quantified the patients with serum creatinine and potassium levels above the UNL using descriptive statistics.

**Results:** Of 9960 admitted patients, 1214 were prescribed ACE-I, 40 were prescribed ACE-I/NSAIDs and 22 were prescribed ACE-I/NSAIDs/diuretics (3.13% and 1.72%, respectively, of the patients prescribed with ACE-I). Serum creatinine and potassium were monitored for the great majority of patients from all groups (75% and 93%, respectively, of patients in ACE-I group; 87% and 75%, respectively, in DT group and 91% and 82%, respectively, in TT group). The highest percentage of hyperkalemia was found in the DT group (10% of the patients) and of serum creatinine above UNL in the TT group (45.45%).

**Conclusions:** The monitoring of patients receiving DT/TT was relatively high. Still, an important percentage of patients were prescribed triple therapy even though the serum creatinine levels were above the UNL. Further studies are needed to determine the exact values of creatinine for which the combinations are prescribed and to improve physicians' knowledge on specific risks posed by these combinations.

## S.34
## Clinical management and risk of amputation among patients with critical lower limb ischemia

R.A. Ciocan*[,†], S.D. Bolboacă[†], T.C. Drugan[†], Ş. Rădulescu* & C.D. Gherman*[,‡]

**Department of Vascular Surgery, County Clinical Hospital Cluj-Napoca, Cluj-Napoca, Romania; [†]Department of Medical Informatics and Biostatistics, Iuliu Haţieganu University of Medicine and Pharmacy Cluj-Napoca, Cluj-Napoca, Romania; [‡]Department of Surgery II, Iuliu Haţieganu University of Medicine and Pharmacy Cluj-Napoca, Cluj-Napoca, Romania*

**Background:** Our study aimed to analyze the clinical management of patients admitted with critical limb ischemia (CLI) at Second Surgical Clinic, Clinical County Hospital Cluj-Napoca and to identify the risk factors for amputation.

**Materials and methods:** A 2 years retrospective study was conducted on subjects hospitalized for critical lower limb ischemia at 2nd Surgical Clinic, Clinical County Hospital Cluj-Napoca. The medical charts of patients with critical lower limb ischemia as principal diagnosis were reviewed.

**Results:** Four hundred and forty-one patients with mean age of 66.22 ± 10.40 years were included in the study. A significantly higher percentage of patients were male (M:F = 4.25, $P < 0.0001$). Smoking was positive on 67.12% of subject with significant higher percentage among men compared to women (76.75% vs. 26.19%, $P < 0.0001$). Diabetes (F vs. M: 47.62% vs. 31.65%) and presence of ischemic heart disease (F: M = 64.29:47.34%) proved significantly higher in women compared to men ($P < 0.01$). Ninety-nine bypasses were performed [22.45% (18.59 26.76), values in square brackets are 95% confidence interval lower and upper bounds] and more than a half were at femoro-popliteal level [62.62% (52.54 71.71)]. Other interventions included lumbar simpathectomy (1.81%), disarticulation (12.24%), amputation (17.01%) and soft tissues necrectomy (17.46%). Majority of patients received vasodilator (91.38%) and respectively anticoagulant (67.57%) treatment. Sepsis [5.22% (3.40 7.71)], bypass thrombosis [3.17% (1.81 5.44)], and hemorrhage [0.45% (0.00 1.81)] were the main complications. Favorable discharged status was observed on 89.12% of patients. The mean of hospitalization stay was 11.94 ± 7.34 days, with no significant differences among different discharged statuses ($P = 0.103$). Smoking proved a significant risk factors for amputation [OR = 1.98 (1.06 3.70)].

**Conclusions:** Bypass was the most frequent treatment strategy, with fairly small percent of complications while medical treatment included vasodilator and anticoagulant drugs. Smoking proved a significant risk factor for amputation.

## S.35
## Corticotropin and cortisol kinetics in chronic HBV infection

I. Lupaşco
*Scientific Laboratory of Gastroenterology, State University of Medicine and Pharmacy "N.Testemitanu", Chisinau, Republic of Moldova*

**Introduction:** HBV infection remains enigma of hepatology despite is widespread and involves estimated 13.3 million adult people in important social and economic consequences.
**Aim of the study:** In the context of the functioning mechanisms of adaptation to chronic stress, such as chronic HBV infection was considered important to study pituitary-adrenal axis.
**Material and methods:** One hundred and ten patients with chronic hepatitis (CH) HBV have been evaluated during the study, in dependence on the viral infection phase were formed three groups: I – HBeAg+ (21), II – antiHBe+, minimal activity (56), III – antiHBe+, moderate/maximum activity (24). Thirty healthy individuals served the control group. The corticotropin and cortisol kinetics was studied in all groups fasting and in the dynamics of the authors' glucose and euphylline stimulation test at 60 and 120 min.
**Results:** Corticotropin level in patients of I group after 60 min of stimulation presented an impaired appearance without characteristic burst featured for healthy individuals, ($P < 0.01$). III group differed from control data from the very beginning ($P < 0.05$), having the exactly opposite ACTH pattern at 2 point of the test ($P < 0.01$). In HBeAg + group observed a significant increase in cortisol initial data ($P < 0.01$), with an inversion of the response to stimulation at 2 point ($P < 0.01$) with no return to normal values ($P < 0.01$). The same pattern was observed in II group, that differs in hormonal lower values at 2 and 3 points of the test ($P < 0.01$, $P < 0.01$, $P < 0.01$). The III group presented significantly higher cortisol values at all points of the study ($P < 0.01$, $P < 0.01$, $P < 0.01$).
**Conclusions:** ACTH and cortisol kinetics impairment was found in relation to the viral infection phase and disease activity.

## S.36
## Comparative effects on the muscular system of native vitamin D and alphacalcidol

C. Capatina*,†, M. Carsote*,†, M. Berteanu*,‡ & C. Poiana*,†
**"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; †"C.I.Parhon" National Institute of Endocrinology and Metabolism, Bucharest, Romania; ‡Emergency Hospital Elias, Department of Physical Medicine and Rehabilitation, Bucharest, Romania*

**Background:** VD deficiency is associated with the atrophy of muscle fibers (predominantly type II), which is reversible with normalization of the VD status. We aimed to analyse the differential effects of native VD and alphacalcidol treatment on the muscular system in women with either postmenopausal low bone mass or proven VD deficiency.
**Material and methods:** We analysed 185 women (80 postmenopausal with low bone mass – group A, 105 with a serum concentration of 25 hydroxyD (25OHD) below 30 ng $mL^{-1}$ – group B). We recorded the grip-strength the results of the chair-rise test (CRT) and timed-up-and go test (TUG). We randomised the patients to receive colecalcipherol 1000 IU daily or alphacalcidol 1 mcg daily, for 6 months.
**Results:** The mean baseline 25OHD concentration was $12.68 \pm 5.77$ ng $mL^{-1}$ (mean $\pm$ SD) and $18.41 \pm 8.2$ ng $mL^{-1}$ in group A and B, respectively. After treatment the serum 25OHD level was $23.93 \pm 7.7$ and $17.2 \pm 8.9$ ng $mL^{-1}$ in group A and B, respectively, significantly higher in cases supplemented with cholecalciferol compared to those treated with alphacalcidol ($P = 0.000$). After treatment, TUG and CRT test results improved significantly ($P = 0.000$ compared to baseline). Gripstrength also increased slightly but significantly (6.07% compared to baseline in group A, 9.8% in group B). The benefit was more significant in cases treated with alphacalcidol for gripstrength ($P = 0.000$) and TUG ($P = 0.012$ in group A, $P = 0.000$ in group B).
**Conclusions:** Improvement of VD status is associated with improvement of the muscular performance in women with VD deficiency or postmenopausal low bone mass. Alphacalcidol exerts similar but more significant positive effects, which appear not to be mediated by an increase in serum 25OHD concentration.

## S.37
## The relation between myometrial relative expression of *ERAP2, LILRA3* and *OXTr* genes and functional dystocia

O. Munteanu*, E. Bratila†, C. Berceanu‡ & M.M. Cirstoiu*
**Department of Obstetrics and Gynecology, University Emergency Hospital Bucharest, Bucharest, Romania; †Department of Obstetrics and Gynecology, "Sfantul Pantelimon" Emergency Hospital Bucharest, Bucharest, Romania; ‡Department of Obstetrics and Gynecology, University of Medicine and Pharmacy Craiova, Craiova, Romania*

**Background:** Dystocia is defined as difficult labor that requires in most cases extraction of the fetus by Cesarean section. The causes of dystocic labor are either anatomic – cephalopelvic disproportion, or functional – anomalies of intensity, frequency and duration of uterine contractions. This study was undertaken in order to determine the relation between myometrial relative expression of endoplasmic reticulum aminopeptidase 2 (*ERAP2*), leukocyte immunoglobulin-like receptor subfamily A member 3 precursor (*LILRA3*) and oxytocin receptor (*OXTr*) genes and functional dystocia.
**Materials and methods:** We analyzed myometrial biopsies obtained from the lower segment of 40 patients who underwent Cesarean section. Two groups were formed. In group D ($n = 20$) we enrolled patients diagnosed with functional dystocia, while in group C ($n = 20$) patients with other indications for Cesarean section, who had demonstrated efficient uterine contractions during the first stage of labor. Total RNA was extracted from biopsies and tested qualitatively using small volume spectrometry. We determined the relative abundance of mRNA for the *ERAP2, LILRA3* and *OXTr* genes by qPCR. Data analysis was conducted using the software of real-time PCR system by comparing the levels of *ERAP2*, *LILRA3* and *OXTr* to genes with constant expression.
**Results:** *ERAP2*, *LILRA3* and *OXTr* genes were down-regulated in group D. The gene *OXTr* was down-regulated in 12 patients enrolled in group C.
**Conclusions:** Genes *ERAP2*, *LILRA3* and *OXTr* are down-regulated in patients with functional dystocia. Therefore, functional dystocia may by predicted by determining the serum levels of proteins encoded by genes *ERAP2*, *LILRA3* and *OXTr*.

## S.38
## Colposcopy – a mandatory procedure for the diagnosis of premalignant cervical lesions

M.M. Cirstoiu*, E. Bratila†, C. Berceanu‡ & O. Munteanu*
*Department of Obstetrics and Gynecology, University Emergency Hospital Bucharest, Bucharest, Romania; †Department of Obstetrics and Gynecology, "Sfantul Pantelimon" Emergency Hospital Bucharest, Bucharest, Romania; ‡Department of Obstetrics and Gynecology, University of Medicine and Pharmacy of Craiova, Craiova, Romania*

**Background:** Cervical cancer is the third most frequent type of cancer in female population, a condition with increased mortality. Appropriate screening allows the detection of premalignant cervical lesions in most patients. However, a consensus regarding the patients who require colposcopy has yet not been established. This study was undertaken in order to determine if colposcopy is mandatory in patients with Pap smear result atypical squamous cells of undetermined significance (ASCUS) or only in those with high risk types of human papilloma virus (HPV).
**Materials and methods:** We evaluated 60 patients with Pap smear result ASCUS. Two groups were formed. In group A we enrolled 30 patients who underwent direct colposcopic examination and biopsy. Group B was formed of 30 patients who were screened for high risk types of HPV; only the ones that were positive underwent colposcopic examination and biopsy. After histopathological examination we analyzed and compared the number of patients diagnosed with cervical intraepithelial neoplasia 2 (CIN2) or more severe premalignant cervical lesions.
**Results:** In group A we detected colposcopic lesions that required biopsy in 11 cases; following histopathological examination the diagnose was CIN2 in three cases and CIN3 in one patient. In group B we detected high risk types of HPV in nine patients – colposcopic lesions were encountered in three cases, who were biopsied and diagnosed with CIN2 after histopathological examination.
**Conclusions:** Colposcopy is a mandatory procedure for the diagnosis and adequate management of patients with premalignant cervical lesions.

## S.39
## Can pain level after uterine artery embolization for uterine leiomyoma predict the effect of this procedure?

M.M. Cirstoiu*, E. Bratila†, C. Berceanu‡ & O. Munteanu*
*Department of Obstetrics and Gynecology, University Emergency Hospital Bucharest, Bucharest, Romania; †Department of Obstetrics and Gynecology, "Sfantul Pantelimon" Emergency Hospital Bucharest, Bucharest, Romania; ‡Department of Obstetrics and Gynecology, University of Medicine and Pharmacy of Craiova, Craiova, Romania*

**Background:** Uterine leiomyoma is one of the most frequent gynecological benign conditions. Uterine artery embolization is a minimally invasive angiographic procedure that induces ischemia, fibrosis and slow resorption of uterine leiomyoma. The acute ischemia causes pain in the first 8 h after the selective embolization of the uterine arteries. In some cases, due to variant anastomoses between the uterine and ovarian arteries this procedure is inefficient. This study was undertaken in order to determine if pain level after uterine artery embolization for uterine leiomyoma can predict the effect of this procedure.
**Materials and methods:** We evaluated 50 patients who underwent uterine artery embolization for uterine leiomyoma. All participants recorded the level of pain in the first 8 h after the procedure using a 10 point visual analog scale with the value of 10 meaning 'worst imaginable pain' and 1 'absence of pain'. In group A ($n$ = 25) we enrolled patients who claimed levels of pain between 1 and 4 on the visual analog scale, while the rest formed group B ($n$ = 25). All patients were reevaluated after three respectively 6 months after the procedure in order to determine the effect of uterine artery embolization on the uterine leiomyoma.
**Results:** Uterine artery embolization has been effective (reduced tumor size and decreased blood supply) in four patients enrolled in group A and 22 pertaining to group B.
**Conclusions:** Pain level after uterine artery embolization for uterine leiomyoma can predict the effect of this procedure. The absence or low levels of pain correlate with a poor response of this technique.

## S.40
## Correlations between seric VEGFR2-values, immunocytochemistry testing of p16ink4a, histopathological diagnosis and immunohistochemistry test for VEGFR2 to predict progressive cervical lesions

R. Stanculescu*, E. Torac†, E. Bratila*, V. Bausic*, D. Comandasu* & B. Manolescu†
*Department of Obstetrics and Gynaecology, Carol Davila Medicine University, Bucharest, Romania; †Department of Biochemistry, Carol Davila Medicine University, Bucharest, Romania*

**Background:** The research contributes to a betterment of the panel of predictive markers for cervical progression lesions by correlating the significance of different parameters of cervical lesions diagnosis.
**Material and method:** Our original study includes 64 cases positive for human papilloma virus high risk types that were multiple modes investigated by seric levels of Vascular Endothelial Growth Factor (Seric-VEGFR2-values), immunocytochemistry testing (ICC) of $p16^{INK4a}$, colposcopy with biopsy, histopathological diagnosis (HP) and immunohistochemistry (IHC) for VEGFR2. The used methods were based on ELISA – R&D Systems (UK), ICC-CINtec $p16^{INK4a}$ ready-to-use cytological kit (clone E6H4), IHC by indirect three-stages ABC-Hsu, modified by Bussolati and Gugliotta, (A-20): sc-152 clone, source Santa-Cruz, 1:50 dilution. The statistical interpretation was performed using the correlation matrices between mentioned diagnostic parameters. The IHC-VEGFR2 expression was evaluated in percentages, through the number of positive cells, as very low reactivity (VLR), low reactivity (LR), moderate reactivity (MR), intense reactivity (IR).
**Results:** The seric-VEGFR2-values were statistically associated to ICC-$p16^{INK4a}$ diagnosis group but the analysis reveals that there isn't a crisp differentiation for corresponding parameter domains. So the seric-VEGFR2-value can not differentiate cytological diagnosis, but on average there is a correlation between seric-VEGFR2-value and cytological diagnostic groups. Correlation matrix between HP (using 2014 classification), and IHC-VEGFR2 reveals a total correlation between HP-cancer diagnosis and IHC-VEGFR2-IR, a strong correlation between HP-High-Grade Lesions and IHC-VEGFR2-MR but just a weak correlation

with IHC-VEGFR2-IR. The HP-Low-Grade Lesions associates a significant correlation for IHC-VEGFR2-LR.
**Conclusions:** The seric-VEGFR2-value is not a serum marker for cervical cancer but has the capacity to reveal the development of a proliferative angiogenesis tumoural process. IHC-VEGFR2 testing offers the objective opportunity to disclose the cervical lesion progression.

## S.41
## How to combine multiple seric parameters in order to forecast the preeclampsia and HELLP Syndrome disease

R. Stanculescu, E. Bratila, M. Russu, V. Bausic & C.A. Coroleuca
*Department of Obstetrics and Gynaecology, Carol Davila Medicine University, Bucharest, Romania*

**Background:** The fact that under the circumstances of development of preeclampsia and HELLP syndrome the laboratory modifications precede the clinic symptoms justifies the necessity to identify more seric parameters able to pinpoint the risk of further evolution towards severe vascular endothelial damage during pregnancy and next 6 weeks.

Our study purpose is to conclude about the seric parameters which could stand for an investigation panel able to early warn about the risk of preeclamsia and HELLP syndrome.
**Material and method:** A literature search was conducted as regards accepted parameters-seric able to relieve the risk for preeclampsia and HELLP syndrome development.
**Results:** The literature search shows controversial results about the prognostic value of the seric values of soluble fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PIGF) measured in serum samples on an automated platform. Recent studies proved that the plasma levels of circulating cell-free DNA (c-f DNA) has a sensitivity and specificity of 0.93 for detecting HELLP syndrome. Parameters like oxidized low-density lipoprotein (oxLDL) measured by enzyme-linked immunoassay (ELISA), serum paraoxonase (PON1) activity and malondialdehyde (MDA) concentrations measured by spectophotometric methods at 15–20 weeks are able to early ascertain the risk to develop sever preeclampsia. Studies relieve that the elevated maternal sFlt-1/PlGF ratio, increased c-f DNA levels, higher value of PON1 activity at the midgestational age could be predictive values concerning the preeclampsia and HELLP syndrome.
**Conclusions:** The data obtained by the literature review highlights the necessity to thoroughly analyze the correlation between the parameters aforementioned with purpose to discover if these parameters could compose a panel diagnostic test providing higher accuracy for early detection of the risk of preeclampsia and HELLP syndrome.

## S.42
## Determination of pulse-oximetry efficiency as a noninvasive method of assessing dental pulp vitality in children

D. Esian, A. Jurca & C. Bica
*Paediatric Dentistry Department, University of Medicine and Pharmacy of Tirgu-Mures, Tirgu-Mures, Romania*

**Background:** The study is focused on the innovative assessment of dental pulp status by means of pulse-oximetry, that is based on exploring the pulp vascular function which is a more objective method and less traumatic for children than traditional sensitivity tests.
**Materials and methods:** One hundred and sixteen children and young people aged 8–30 years old were examined, from which were selected for testing a number of 229 teeth that includes upper central incisors, upper lateral incisors and upper canines. Thus, there were formed five study groups, based on tooth integrity (caries, fractures and restorations) and vitality (vital teeth and teeth without vitality). Examination of oxygen saturation ($SpO_2$) in pulp teeth was achieved with a small sensor OxiMax'Dura Y D-YS Multisite (Nellcor) adapted on an acrylic support specially created for this purpose. In addition, control tests were performed consisting of cold thermal test, radiographic examination and determination of $SpO_2$ from the systemic circulation.
**Results:** The results emphasized a statistically significant association between the measurements made by pulse-oximetry and those performed by cold thermal test. Also, the results show a reduction of $SpO_2$ in teeth that have cavities, fractures and restorations.
**Conclusions:** Although the method has proved to be extremely effective, the limits of pulse-oximetry as a method of assessing pulp vitality are related currently with the absence of a sensor specifically designed to adapt to the anatomical surface of all temporary and permanent teeth.

## S.43
## Incidental thyroid findings identified by 18F-fluorodeoxyglucose positron emission tomography/computed tomography

E.A. Bonci*, E. Barbus*,†, A. Irimie*,† & D. Piciu*,†
**"Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; †Department of Nuclear Medicine, "Prof. Dr. Ion Chiricuta" Institute of Oncology, Cluj-Napoca, Romania*

**Background:** The incidental thyroid findings on positron emission tomography integrated with computer tomography (PET/CT) have become a part of the reporting results due to the increasing number of PET/CT examinations with 18F-fluorodeoxyglucose (18F-FDG). We aimed to see if the discovered thyroid incidentalomas correlate with subsequent disease of the thyroid gland.
**Materials and methods:** We used a retrospective study to investigate the 18F-FDG PET/CT scan reports for 435 patients who underwent this examination for non-thyroid disease during 2014. The thyroid findings were reported as: focal uptake (part of the thyroid gland) or diffuse uptake (the entire thyroid gland). Maximum standard uptake value in lean body mass unit (SUV lbm Max) was calculated for every thyroid uptake described in the reports. Patients with incidental thyroid findings were sent to further investigation to define the thyroid pathology.
**Results:** In 19 out of 435 patients (4.36%) an uptake in the thyroid bed was described. The incidence of focal uptake was 1.1 % (five patients, two men and three women) with a mean age $\pm$ standard deviation (SD) of $55 \pm 26.3$. The SUV lbm Max reported on focal uptake was between 2.45 and 7.79, in three patients the thyroid malignancy being confirmed (0.68%) and was correlated with SUV higher than 3. Chronic thyroiditis was confirmed in all the 14 patients reported as diffuse uptake with a high level of thyroid peroxidase antibodies.
**Conclusions:** Thyroid incidentalomas discovered on 18F-FDG PET/CT seem to predict a subsequent thyroid malingnancy

and further clinical investigation is required in every case, but the low incidence (<1%) does not justify the PET/CT scan as screening for this pathology.

## S.44
## Management and outcomes in women with hereditary thrombophilia during pregnancy

I. Rotar*,†, A. Breban†, F. Stamatian*,† & D. Muresan*,†
*Department of Obstetrics and Gynecology, University of Medicine and Pharmacy Cluj Napoca, Cluj Napoca, Romania; †1st Clinic of Obstetrics and Gynecology, Emergency Clinical County Hospital, Cluj-Napoca, Romania

**Background:** Inherited thrombophilia induces a hypercoagulative status in pregnant patients leading to potential complications including maternal death, pregnancy loss, preeclampsia, intrauterine growth restriction and placental abruption that can be prevented by early screening and therapy. The aim of this study was to investigate the pregnancy outcomes in women with hereditary thrombophilia.
**Materials and methods:** A retrospective analysis was performed in the 1st Clinic of Obstetrics and Gynecology, Cluj-Napoca, Romania including 76 deliveries in thrombophilic patients that took place between 2013 and 2014. For each patient were noted parameters related to the pregnant women: age, gravidity, parity, delivery route, gestational age at delivery, type of inherited thrombophilia, treatment (type, dose and duration of treatment, maternal or fetal side-effects), personal history, delivery related complications respectively for the neonates (weight, Apgar score, sex).
**Results:** From the total number of 76, 74 where singleton deliveries. Birth weight ranged between 700 g and 4700 g, at gestational age between 27 and 41 weeks. A higher rate of cesarean section was encountered 63.16%. Fifteen deliveries were preterm. A history of spontaneous pregnancy loss was recorded in 72.36% of patient's, 6.66% of them being encountered in second trimester. Moreover five women had suffered a stillbirth, and 10 had history of a preterm delivery. Almost all of the patients (98.68%) were treated: most of them used folic acid supplementation; 43.42% used low-dose aspirin during pregnancy, 73.68% were treated with low-molecular-weight heparin. No complications in anticoagulant administration have been reported. There was one case of deep vein thrombosis during pregnancy. Five patients developed preeclampsia.
**Conclusions:** Treatment with low-molecular-weight heparin in selected patients represents a safe option for women with hereditary thrombophilia allowing an improved pregnancy outcome.

## S.45
## Adverse fetal metabolic phenotyope programming induced by maternal obesity – a new concept

D.E. Comandaş*, E. Brătilă*, R. Stănculescu*, M.M. Cârstoiu†, D. Miricescu‡, D. Lixandru‡, B. Vîrgolici‡ & M. Mohora‡
*Department of Obstetrics and Gynecology, "Saint Pantelimon" Emergency Clinical Hospital Bucharest, Bucharest, Romania; †Department of Obstetrics and Gynecology, University Emergency Hospital Bucharest, Romania; ‡Department of Biochemistry, "Carol Davila" University of Medicine and Pharmacy Bucharest, Bucharest, Romania

**Background:** Obesity epidemic is a concern of the modern world, its prevalence continously rising. Besides the increased gestational risks, it has been recently described that maternal obesity has long-term metabolic consequences for the offspring. Metabolic programming appears during early life and has major impact on physiological outcome.
**Materials and methods:** Using an animal model, we showed that maternal obesity induces fetal inflammation resulting in accelerated adipogenesis in the offspring of rats. In order to predict an adverse outcome for these we established associations between maternal diet and fetal metabolic status using biomarkers (leptin, cytokines, histopathological findings). We searched a possible metabolic reprogramming process by submitting obese rat females to interventional therapies, like dietary changes or anti-inflammatory supplements.
**Results:** Environmental alterations like overnutrition, lead to organogenesis dysfunctions and altered metabolic status, predisposing the offsping to childhood and later adult obesity, cardiovascular disease and diabetes. The underlying cause seems to be a chronic low grade inflammation status caused by obesity, which has been given the description of metainflammation, leading to epigenetic changes with the imprinting at the genome level of irreversible alterations.
**Conclusions:** Our article proves that early life exposure to maternal metainflammation is a mediator for programming insulin tissue resistance in the fetus with metabolic phenotype manifestations in adult life.

## S.46
## Recurrent obstetric rectovaginal fistula treated by Surgisis graft: a case report

E. Brătilă*, C.P. Brătilă†, R. Stănculescu*, M.M. Cârstoiu‡, D.E. Comandaşu*, C. Berceanu§ & O. Munteanu‡
*Department of Obstetrics and Gynecology, "Saint Pantelimon"Emergency Hospital Bucharest, Bucharest, Romania; †Gynecologic and Pelvic Reconstructive Surgery Department, Euroclinic Hospital, Bucharest, Romania; ‡Department of Obstetrics and Gynecology, University Emergency Hospital Bucharest, Romania; §Department of Obstetrics and Gynecology, University of Medicine and Pharmacy of Craiova, Craiova, Romania

**Background:** Obstetrical trauma is the most common cause of rectovaginal fistulas. Although it has an incidence of 0.5–1% of all vaginal births, rectovaginal fistulas produce a devastating effect on women's quality of life. We present the romanian experience in the treatment of recurrent rectovaginal fistulas using a tissue interposition graft of acellular biological second generation Surgisis.
**Materials and methods:** We present the case of a 33 years patient who gave birth vaginally to a 3200 g child 10 years before, after a precipitate labor for which an episiotomy was performed, followed by the appearance of rectovaginal fistula with numeous attempts of reconstruction. Following a process in which we used biological graft interposition was cured the rectovaginal fistula.
**Results:** We present the principles we consider important in the treatment of recurrent rectovaginal fistulas to achieve maximum success rate. In this case with multiple treatment attempts in history that led to major alterations in the anoperineal and vulvovaginal region we used the technique of episioproctotomy with sphincter reconstruction and interposition of acellular tissue graft. Favorable postoperative course proved the method's efficacy.
**Conclusions:** Recurrent rectovaginal fistulas associated with sphincter lesions can be addressed by epsioproctotomy

technique. Biological tissue graft interposition is an alternative that can solve recurrent rectovaginal fistulas.

## S.47
## Inflammatory markers of vascular changes in type 2 diabetes mellitus

V. Negrean*,†, M.V. Milaciu*, A.L. Vele*, T. Micul*, C. Lupu* & T. Alexescu†
**4th Medical Clinic, Cluj-Napoca, Romania; †Department 5 – Internal Medicine, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania*

**Background:** Type 2 diabetes mellitus's (T2DM) prognosis is described by vascular affectation. C reactive protein (CRP), tumor necrosis factor α (TNF-α), interleukin 6 (IL-6) and interleukin 8 (IL-8) are inflammation markers with abnormal values in the serum of diabetic patients. The purpose of this study was to evaluate the vascular affectation and the alteration of these markers in patients with or without T2DM.
**Materials and methods:** Without selection, we enrolled a group of 35 consecutive patients that gave their consent for participating in the study. The patients were admitted for check-up in the 4th Medical Clinic, Cluj-Napoca, during October 2014. There were 28 patients with T2DM and seven non-diabetic patients with no chronic diseases; for each patient we noted the anamnesis, the complications/commorbidities and values of CRP, TNF-α, IL-6, IL-8, fibrinogen, cholesterol, triglycerides and glycemia. Statistical analysis was performed using MedCalc.
**Results:** In the T2DM group, 38% of the patients had polyneuropathy, 38% had retinopathy and 24% had nefropathy. The Mann-Whitney *U*-test applied on the T2DM group vs. non-diabetic group showed that CRP, TNF-α, IL-6, IL-8, and fibrinogen values were raised in the T2DM group. We used the Spearman test to evaluate the relationship between these markers and glycemia levels; for each parameter we found difference with statistical significance level ($P < 0.05$), except for IL-8 ($P = 0.302$). In the T2DM group, only the presence of retinopathy and neuropathy were close to the statistical significance level ($P = 0.088$ and $P = 0.088$, respectively).
**Conclusions:** In our study, all the markers of inflammation were raised in the T2DM group, including the IL-8. For this interleukin we didn't find a strong association with the gycemia levels.

## S.48
## 18Fluor-fluorodeoxyglucose positron emission tomography evaluation in patients with thyroid carcinoma with negative iodine scan and increased thyroglobulin

C.P. Căpreanu*, E. Bărbuş*,†, C. Peştean*,†, A. Başa*, A. Piciu*,† & D. Piciu*,†
**Nuclear Medicine Department, Institute of Oncology "Prof. Dr. Ion Chiricuţă", Cluj-Napoca, România; †University of Medicine and Pharmacy "Iuliu Haţieganu", Cluj-Napoca, România*

**Background:** Differentiated thyroid cancer has a favorable outcome through multidisciplinary management. A small number of patients develop persistent disease, with clinical and ultrasound negative status and elevated thyroglobulin (Tg), with negative iodine scan (TENIS syndrome); they should be reevaluated for optimal treatment decision. We analyzed how 18fluor-fluorodeoxyglucose positron emission tomography/computer tomography (18F-FDG PET/CT) can change the therapeutic strategy.
**Material and methods:** We have done a retrospective study by analyzing a total of 533 patient who performed 18F-FDG PET/CT scans during 1 year, 2014. Among them, we identified 94 patients with TENIS syndrome. Data regarding age, sex, primary diagnostic, thyroid stimulating hormone, Tg and Tg antibodies, previous CT scans, surgical treatment, radio iodine treatment (RIT) and hormonal substitutive treatment were analyzed. Patients fasted for 6 h before 18F-FDG PET/CT examination and blood glucose levels were measured. Whole body scans were acquired 60 min after intra venous injection of 18F-FDG (specific dose calculation per patient).
**Results:** The 18F-FDG PET/CT examination found physiological uptake in 64 patients (68.08%) and pathological uptake in 30 patients (31.92%) suggesting recurrence or persistent disease. Most frequent sites of the pathologic uptake were: in the neck (27 patients) followed by mediastinum (five patients), lungs (five patients), bones (three patients) and other sites (four patients). Follow-up was recommended for the normal uptake 18F-FDG PET/CT scan group and therapeutic strategy was changed for the pathological uptake 18F-FDG PET/CT scan group. Patients were referred to surgical treatment, chemotherapy or RIT.
**Conclusions:** 18F-FDG PET/CT examination changed the therapeutic strategy in more than 1/3 of cases with TENIS syndrome patients through tumor identification that guided the physician in choosing optimal treatment.

## S.49
## Prognostic significance of CCND1 PIK3C3 and ATM in bladder cancer: a pilot study

A. Truta*,†,‡, C. Braicu*, L. A. Pop*, M.A. Jurj*, O. Zanoaga*, S. Chira*, L.Z. Raduly*, B. Petrut‡, L. Ghervan§, I.V. Pop† & I. Berindan Neagoe*,‡
**Research Center for Functional Genomics Biomedicine & Translational Medicine, "Iuliu Hatieganu" University of Medicine & Pharmacy, Cluj-Napoca, Romania; †Department of Medical Genetics, "Iuliu Hatieganu" University of Medicine & Pharmacy, Cluj-Napoca, Romania; ‡Institute "I Chiricuta", "Iuliu Hatieganu" University of Medicine & Pharmacy Oncology, Cluj-Napoca, Romania; §Clinical Institute of Urology & Kidney Transplant, "Iuliu Hatieganu" University of Medicine & Pharmacy, Cluj – Napoca, Romania*

**Background:** Bladder cancer is a highly heterogeneous cancer originated from the urothelium of the urinary bladder. Until present there are available only a limited number of prognostic biomarkers used in bladder cancer. The deregulated gene expression level shared among tumours and normal tissues might have a significant clinical implication. The aim of the present study was to evaluate the prognostic value of a panel of four genes (CCND1, PIK3C3, ATM, p53) in a set of matched samples of normal and tumour tissues of bladder cancer.
**Materials and methods:** In this study, we evaluated the expression level by using TaqMan qRT-PCR approach by using specific primers and UPL probes in normal and bladder cancer tissue, followed by correlation with clinical and pathological characteristics. As housekeeping gene were used β-actin and GAPDH. Relative gene expression level was calculated by applying ΔCt method.
**Results:** Relative gene expression level for CCND1, PIK3C3, ATM and p53 was evaluated in a set of 12 tumor samples and normal bladder tissue. Our data reveals a statistically increased level for *CCND1*, *PIK3C3* and *ATM* when it was done the

comparison between tumour samples vs. non-tumour matched sample. In our study, we obtained differences in level of expression of CCND1,PIK3C3 and ATM between tumour and normal tissues, indicating them as potential candidates as biomarkers for further validated studies.

**Conclusions:** A major pathway engaged in bladder cancer progression is mis-regulated in muscle-invasive tumors that mainly contain mutations in the TP53 gene: *CCND1*, *PIK3C3* and *ATM* might have prognostic significance and the data should be extended on a higher number of cases.

**Acknowledgments:** Dr Truta Anamaria acknowledges financial suport from an POSDRU grant no 159/1.5/S/138776 grant with title: 'Model colaborativ institutional pentru translatarea cercetarii biomedicale in practica clinica – TRANSCENT'. This study was financed by the PN-II-PT-PCCA-2011-3.1-1221: 'Intelligent Systems of Prediction of Recurrence and Progression in Superficial Bladder Cancer Based on Artificial Intelligence and Microarray Data: Tumor mRNA and Plasmatic microRNA-IntelUro'. AT received a fellowship financed by Grant 159/1.5/S/138776.

## S.50
## Detection of hepatic metastasis using 18F-Fluorodeoxyglucose positron emission tomography/computed tomography in patients with colorectal cancer

A. Basa*, E. Barbus*,†, C.P. Capreanu*, C. Pestean*,†, A. Piciu*,† & D. Piciu*,†

**Department of Nuclear Medicine, Institute of Oncology "Prof. Dr. Ion Chiricuta", Cluj-Napoca, Romania; †University of Medicine and Pharmacy "Iuliu Hatieganu", Cluj-Napoca, Romania*

**Background:** The 18F-Fluorodeoxyglucose positron emission tomography/computer tomography (18-FDG PET-CT scan) has proven to be of great benefit for the assessment of colorectal cancer (CRC), mainly in the detection of occult metastases, particularly intra- or extrahepatic sites of disease. Accurate preoperative staging is essential to estimate prognosis and institute appropriate therapy in CRC.

**Materials and methods:** This is a retrospective study within 1 year of 47 patients diagnosed with CRC. We analyzed the 18-FDG PET-CT scans according to gender and age distribution, initial site of the tumor, maximum standard uptake value lean body mass (SUV lbm), the level of carbohydrate antigen 19-9 (CA 19-9) and carcinoembryonic antigen (CEA) and results of the computer tomography (CT) scans with/without contrast.

**Results:** 18FDG PET-CT confirmed the presence of metastases in the liver in 12 patients out of 47 cases (25.5%), having the primary tumor located as follows: sigmoid (6), rectum (5) and transverse colon (1). Gender distribution was equal. The mean age range was 59 year old and the SUV lbm in the liver metastasis ranged between 2.44 and 10.6. In this group only two patients (16.6%) had suspicious CT images for secondary hepatic tumors, all others being diagnosed at PET/CT. The final histology obtained either by biopsy or liver resection confirmed in all cases the malignancy and changed the therapeutic strategies.

**Conclusions:** PET-CT imaging may be particularly useful in patients with several hypodense or hypoenhancing liver lesions that are not clearly characterized by CT alone and in patients in whom standard CT fails to detect metastases in the setting of a rising serum tumor marker.

## S.51
## Association between fatty liver disease and carotid atherosclerosis in patients with history of stroke

L.D. Rusu, M.L. Rusu & L. Poantă

*Medical Semiology Department, University of Medicine and Pharmacy Iuliu Hatieganu, Cluj Napoca, Romania*

**Background:** Hepatic steatosis (HS) is associated with obesity, dyslipidemia, diabetes and atherosclerosis. Carotid intima-media thickness (IMT) increase indicates atherosclerosis. Our goal was to determine the prevalence of HS in patients with history of stroke, and to evaluate their carotid IMT.

**Materials and methods:** Fourty six patients mean aged 61 years, with a history of stroke in the last 3 years were enrolled. All the patients had transient ischemic stroke and were evaluated by contrast enhanced computer tomography. HS and IMT were evaluated by ultrasonography. Plasma liver function tests and other biochemical blood measurements were determined. Demographic and vascular risk factors were detailed for all subjects. We also enrolled a control group of 42 patients without stroke, age and sex matched.

**Results:** HS was found in 28 patients (60.8%) with stroke and only in 23% of controls ($P = 0.002$). By adjusting sex and age, odds ratio for HS was 2.20 (95% confidence interval: 1.27–3.81) that was statistically significant ($P = 0.003$). Subjects with HS had higher values for body mass index, diastolic and mean blood pressure, triglycerides, and lower HDL cholesterol concentration, but there were no differences regarding IMT between stroke patients with or without HS ($P = 0.09$). Behavioral variables (smoking, diet, sedentarism), fasting plasma glucose, and LDL cholesterol levels in subjects with HS did not differ significantly from those without HS ($P = 0.08$).

**Conclusions:** Stroke patients with HS in our study showed a cluster of cardiovascular risk factors but non-significant carotid atherosclerosis. The detection of HS by abdominal ultrasound should alert about the existence of higher cardiovascular risk. The association between IMT and HS in stroke patients is still under debate, results in the literature being controversial.

## S.52
## Reconstruction of soft tissue defects in elbow using propeller perforator flaps

D.I. Dumitrascu & A.L.V. Georgescu

*Department of Plastic Surgery and Reconstructive Microsurgery, UMF "Iuliu Hatieganu", Cluj-Napoca, Romania*

**Background:** Soft tissue defects in the elbow region represent a challenge for the plastic surgeon. Not only due to the abundance of noble anatomical structures that are usually exposed during injuries of this area, but also due to the importance of the elbow joint. The elbow joint is very sensitive to immobilization, usually required after free flaps surgery. A useful alternative to the classical free tissue transfer is the propeller perforator flaps. The study presents a series of elbow reconstruction using this technique.

**Materials and methods:** Twelve patients having large elbow region soft tissue defects, and were operated in our department in 2014 were included in the study. The etiology of the defect was traumatic or surgical. The coverage was performed with 90° to 180° rotation of the flap, based on perforators from recurrent ulnar and radial arteries. Descriptive statistics was used.

**Results:** The survival rate of the flaps was 100%. Only in three cases a superficial marginal necrosis was observed. The mean value of the perforator vessels diameter was 1.1 mm ($P < 0.05$) while the mean surface of the flaps was 85 $cm^2$ ($P < 0.05$). The mobilization was started in the 1st postoperative day in all 12 cases. The patients and surgeons satisfaction for both cosmetic and functional results was high.
**Conclusions:** The propeller perforator flaps are a very efficient alternative for covering soft tissue defects in the elbow region. They offer best functional and aesthetic results. As opposed to free flaps, immobilization of the elbow joint is not needed.
**Acknowledgement:** This paper was published under the frame of European Social Fund, Human Resources Development Operational Programme 2007–2013, project no. POSDRU/159/1.5/S/138776

## S.53
## Erythropoietin – marker for perinatal complications of the low birth weight infants

G. Zaharie*, B. Ligia*, M. Matyas*, S. Bolboaca†, S. Nicoara‡ & M. Hasmasanu*
**Neonatology Department, UMF Iuliu Hatieganu, Cluj-Napoca, Romania; †Department of Medical Informatis and Biostatistics, UMF Iuliu Hatieganu, Cluj-Napoca, Romania; ‡Oftalmology Department, UMF Iuliu Hatieganu, Cluj-Napoca, Romania*

**Background and aim:** IUGR may complicate 7–10% of pregnancies and is a major cause of perinatal morbidity and mortality. The aim of the study was to evaluate the plasmatic erythropoietin levels on intrauterine growth restriction and preterm infants compare to the newborns at term and the perinatal complications at each group.
**Material and methods:** A retrospective study was done in newborns hospitalized in 1st Gynecology Clinic, Emergency County Hospital Cluj-Napoca between 2008 and 2011. The groups were: infants with intrauterine growth restriction (group1), preterm (group2) and full-term (group3). We evaluated anthropometric data, APGAR score, type of delivery, Astrup parameters, plasma erythropoietin (EPO) level, earlier complications (resuscitation need, neonatal asphyxia, respiratory distress). The study has been approved by the Ethical Committee of the hospital.
**Results:** The study included 91 infants : 33 IUGR, 42 preterms and 16 healthy controls. EPO values varied from 2.4 to 256.1 mIU $mL^{-1}$ in IUGR, from 0.9 to 212 mIU $mL^{-1}$ in preterm, and from 20.8 to 84.5 mIU $mL^{-1}$ in controls ($P < 0.0001$). Astrup parameters revealed hypoxia and metabolic acidosis in IUGR group compare to prematures or term babies ($P = 0.002$). The IUGR group proved to have significantly higher proportion of pulmonary hemorrhage (18%) compared to preterm (2%) (Z-statistic = 2.2766, $P$ -value = 0.0228). Mortality was five times higher in IUGR compared to preterm (Z-statistic = 2.1086, $P$ -value = 0.035). Only for IUGR group, Epo plasma level proved significantly correlated with type of delivery, hemoglobin level and hyperbilirubinemia.
**Conclusions:** Epo seric level is higher for preterm infant and IUGR infant comparative with term newborn. The high EPO level could be a marker for the risk of pulmonary hemorrhage, hyperbilirubinemia, metabolic acidosis and perinatal asphyxia.

## S.54
## The influence of genes polymorphisms of inflammatory markers in allergic diseases

I.C. Bocsan*, R. Pop*, I.A. Muntean†, D. Nicoară*, S.C. Vesa*, A. Trifa‡ & A.D. Buzoianu*
**Department of Pharmacology, Toxicology and Clinical Pharmacology, University of Medicine and Pharmacy, Cluj Napoca, Romania; †Department of Allergology and Clinical Immunology, University of Medicine and Pharmacy, Cluj Napoca, Romania; ‡Department of Genetic, University of Medicine and Pharmacy, Cluj Napoca, Romania*

**Background:** Genetic polymorphism may influence the diseases severity and response to specific treatment. This study investigated IL-6 174G/C polymorphism in patients with allergic rhinitis and asthma, regarding the genotypes frequency and their correlation with diseases severity and type of sensitization.
**Material and method:** Thirty patients with allergic rhinitis and 30 patients with asthma were included in the study. The patients were clinically evaluated regarding disease severity (total symptoms score in patients with rhinitis and presence of the symptoms and exacerbations in patients with asthma), type of treatment and sensitization. IL-6 174G/C polymorphism was determined using PCR-RFLP technique. The results were statistically analyzed, with significance at $P < 0.05$.
**Results:** GC genotype is more frequent in female (83.3% vs. 16.7%), while CC genotype was observed frequently in male patients (75% vs. 25%, $P = 0.001$). In patients with allergic rhinitis, GG genotype was observed in 33%, while GC genotype in 40%, and CC in 26.7% of them. In asthma patients, GC genotype is more frequently observed, while CC genotype is more rare (13.3%) compared to rhinitis, but the differences are not statistically significant ($P = 0.25$). The presence of C allele was correlated with high severity in patients with rhinitis: higher symptoms score in patients with GC ($11.67 \pm 3.25$) and CC ($10.13 \pm 2.53$) vs. GG ($7.9 \pm 2.18$) genotype ($P = 0.01$). In patients with asthma, C allele was observed in patients with moderate and severe forms of disease and was correlated with an increased number of exacerbation ($P = 0.05$). G allele was correlated with sensitization to house dust mites ($P = 0.019$) and C allele with pollen sensitization ($P = 0.045$).
**Conclusions:** The polymorphism of IL-6 gene 174G/C is correlated with severe forms of respiratory atopic diseases and different types of sensitization.

## S.55
## Perceptions of occupational stress in secondary education employees

D Triff* & Z. Triff†
**Occupational Medicine Section of Professional Diseases, "Constantin Opris" Emergency Hospital of Baia Mare, Baia Mare, Romania; †The Faculty of Psychology and Educational Sciences, "Vasile Goldis" Western University of Arad, Arad, Romania*

**Background:** We aimed to study the workers' perception of stressors in undergraduate education starting from the syllabus of the European Agency for Work Safety and Health
**Methods:** The workers' perception on occupational stress was assessed on basis of questionnaires distributed to 137 employees from a high school and three secondary schools. The questionnaires targeted the workers' individual socio demographic and organizational factors, according to the European Agency for Work Safety and Health syllabus. Emotional exhaustion was

evaluated using Maslach Burnout Inventory, anxiety by Spielberger State/Trait Anxiety Inventory and perceived self-efficacy using the general self-efficacy scale.

**Results:** Significantly increased sources of stress in female employees in secondary education vs. male workers are: working extra hours for carrying out duties ($P = 0.01$), relationships and communication with colleagues ($P = 0.00$) as well as monotonous work tasks ($P = 0.02$). Also the anxiety-trait level is significant ($P = 0, 02$) in the female employees in the study group.

For secondary education employees, the level of education significantly increases the feeling of self-efficacy ($P = 0.049$) but it does not favor emotional exhaustion ($P = 0.00$) while anxiety-state level decreases as well as the level of anxiety-trait ($P = 0.00$).

**Conclusions:** There are no significant differences of self-efficacy, emotional exhaustion and anxiety state in terms of gender. Educational level was higher in younger employees, and is correlated with income level. Emotional exhaustion and anxiety level in undergraduate education do not show significantly high values. The means of preventing and fighting occupational stress in teachers is of equal concern for the community as a whole and each employee.

## S.56
## The use of serotonin assay in menopausal women skeleton evaluation (with or without osteoporosis)

M. Carsote*,†, C. Capatina*,†, A. Caragheorgheopol‡, D. Manda‡, R. Baloescu§, A.M. Stefanescu‡, D. Paun*,† & C. Poiana*,†

**Department of Endocrinology, "C.Davila" University of Medicine and Pharmacy, Bucharest, Romania; †"C.I.Parhon" National Institute of Endocrinology, Bucharest, Romania; ‡Department of Laboratory, "C.I.Parhon" National Institute of Endocrinology, Bucharest, Romania; §Department of Pituitary and Neuroendocrine Diseases, "C.I.Parhon" National Institute of Endocrinology, Bucharest, Romania*

**Background:** The peripheral serotonin has pro-resorptive effects, yet its use in menopausal skeleton assessment is limited. We aim to analyse the serotonin levels in relationship to the Bone Mineral Density (BMD) as evaluated by lumbar Dual-energy X-ray Absorptiometry (DXA), and to the Bone Turnover Markers (BTM).

**Material and method:** A cross-sectional study included menopausal females without any history of bone pathology or carcinoid syndrome. DXA is assessed by Prodigy device. The serotonin (ELISA) and BTM were assessed: blood CrossLaps (resorption marker, ELISA), blood osteocalcin (bone formation marker, ELISA). Statistical significance is at $P < 0.05$.

**Results:** Two hundred and two subjects were included: mean age of 57.34 ($\pm$7.77), mean serotonin of 176.54 ($\pm$105.92) ng mL$^{-1}$ (normal between 40 and 400 ng mL$^{-1}$). Seven of 203 patients had serotonin above the normal limit. 110 patients (group A) had T-score of $\leq -1$ (osteopenia+osteoporosis); 92 (group B) had T-score of $> -1$ (normal DXA). The lumbar BMD is statistically significant lower in group A (mean of 0.9 g cm$^{-2}$) vs. group B (mean of 1.17 g cm$^{-2}$). The BTM were not statistically significant between group A and B (OC of 0.47 vs. 0.13 ng mL$^{-1}$, $P = 0.3$; CL of 24.21 vs. 21.82 ng mL$^{-1}$, $P = 0.2$). The serotonin is statistically significant higher in group A vs. group B (group A: 187.07 $\pm$ 115.08 ng mL$^{-1}$, median: 166 ng mL$^{-1}$; group B: 163.93 $\pm$ 92.8 ng mL$^{-1}$, median: 151 ng mL$^{-1}$). The linear regression coefficient between either OC or CL and serotonin in group A or B proved no correlation.

**Conclusions:** The serum serotonin is statistically significant higher in menopausal women with low Bone Mineral Density (osteoporosis + osteopenia) than in subjects with normal DXA, and it is not correlated to bone turnover markers as CrossLaps or osteocalcin.

## S.57
## Myocardial perfusion assessment in patients with radically treated, differentiated thyroid carcinoma, with medium and high probability of coronary disease

M. Saftencu*, A. Piciu*,† & D. Piciu*,†

**Faculty of Medicine, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; †"Prof. Dr. Ion Chiricuţă" Institute of Oncology, Cluj-Napoca, Romania*

**Background:** In patients radically treated for differentiated thyroid carcinoma, we assessed the response of highly sensitive C-reactive protein (hsCRP), an inflammatory biomarker for cardiovascular risk, after thyroid hormone withholding, and then we performed a myocardial perfusion scintigraphy to observe the myocardial tissue perfusion.

**Materials and methods:** We included 30 adults, mean age 42.2 years (min 32, max 61), who were disease free after total thyroidectomy, radioiodine ablation and chronic thyroid hormone therapy. They were life-long non-smokers without apparent inflammatory comorbidity, cardiovascular history beyond pharmacotherapy-controlled hypertension, anti-dyslipidemic medication, or C-reactive protein >10 mg L$^{-1}$in any study measurement. The index deprivation lasted >2 weeks, elevating serum thyrotropin >40 mIU L$^{-1}$ or >100$\times$ the individual's suppressed level. We determined the serological levels of hsCRP and we performed a myocardial perfusion scintigraphy using the radiopharmaceutical Technetium-99 m sestamibi. We analyzed the relationship between age, gender, number of prior deprivations, post-deprivation hsCRP levels and myocardial perfusion.

**Results:** Post-deprivation, C-reactive protein reached intermediate and high cardiovascular risk levels (based on general population studies involving chronic elevation). In male patients >50 years old that have undergone more than six hormonal withdrawals and hsCRP >2.5 the global myocardial perfusion was lower than the control group, male patients >50 years old having two or less hormonal withdrawals ($P < 0.024$).

**Conclusions:** Thyroid hormone withdrawal frequently elevated C-reactive protein to moderate and high-risk levels and decreased the myocardial perfusion due to the inflammatory state of the coronary circulation, increasing the cardiovascular risk.

## S.58
## Is low birth weight a risk factor for calcium and magnesium homeostasis disturbances in early neonatal period?

L.D. Blaga*, M. Matyas*, M. Muresan†, C. Vidra† & G. Zaharie*

**Neonatology Department, University of Medicine and Pharmacy, Iuliu Hatieganu, Cluj Napoca, Romania; †Second Neonatology Department, Emergency County Hospital of Cluj, Cluj, Romania*

**Background:** Althought there are a lot of studies about calcium and magnesium homeostasis, there are a lot of controversies

over their physiological low limits. Calcium and magnesium values smaller than those which are biostatistic classified, without any clinical and electrocardiographic changes, are they normal or patological for ontogenetic age? The aim of this paper is to evaluate the incidence of early hypocalcemia and hypomagnesemia in term and preterm small for gestational age infants and the risk factors that require framing them in a screening program.

**Material and method:** this is a prospective study on 120 newborns [term and preterm infants small for age (SGA) and appropriate for gestational age (AGA)], born in our service during 2 years. Calcium was determinated with the Beckman flam photometric method and magnesium with colorimetric method at 48 h of life. The statistical analysis was done using the SPSS program.

**Results:** Hypocalcemia was detected in 16% of term SGA with ponderal index 1.2–1.8 and 16% of preterm SGA with gestational age below 32 weks and birth weight below 1500 g. In five cases hypocalcemia was asymptomatic. Hypomagnesemia was detected in 4% of term SGA and 16% of preterm SGA. Symptoms were present only in those cases who associated hypomagnesemia and hypocalcemia.

**Conclusions:** severe intrauterine growth retardation and extreme prematurity with low birth weight are high risk factors for early mineral homeostasis disturbances. Hypocalcemia is more frequent than hypomagnesemia. Screening is useful in SGA infants with low ponderal index and prematures under 1500 g.

## S.59

## Adiponectin and atherosclerosis related cardiovascular events in type 2 diabetes dialysis patients

I.M. Kacso*, A.R. Potra*, C.I. Bondor†, D. Moldovan*, C. Rusu*, I.M. Patiu‡, S. Racasan‡, R. Orasan‡, D. Vladutiu*, C. Spanu§, A. Rusu§, C. Nita§, R. Moldovan¶, B. Ghigolea¶ & G. Kacso**

**Department of Nephrology, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, Cluj-Napoca Romania; †Department of Informatics and Biostatistics, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, Cluj-Napoca, Romania; ‡NephroCare Dialysis Center Cluj-Napoca, Cluj-Napoca, Romania; §RenaClinic Cluj Napoca, Romania; ¶Nefromed Dialysis Center Alba Iulia, Alba Iulia, Romania; **Department of Oncology, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, Cluj-Napoca, Romania*

Dr. Alina Ramona Potra is a fellow of POSDRU grant no.159/1.5/S/138776 grant with title: 'Model colaborativ institutional pentru translatarea cercetarii stiintifice biomedicale in practica clinica – TRANSCENT'.

**Background:** Adiponectin is an anti-inflammatory adipokine, insulin-sensitizing with anti-atherogenic actions in the general population. In dialysis patients it is not certain if adiponectin keeps its protective role or is leading to a worse prognosis. We assessed the predictive value of adiponectin for atherosclerosis related cardiovascular events in type 2 diabetic dialysis patients.

**Materials and methods:** Dialysis patients with type 2 diabetes from three dialysis units ($n = 77$ were enrolled in a 3 years' prospective observational study. These patients were also assessed after 2 years of following up, with promising results (data presented at BANTAO Congress 2013). Serum adiponectin, clinical and laboratory parameters were determined at baseline; new occurrence of atherosclerosis related events (coronary events, atherosclerosis obliterans, and stroke) was recorded.

**Results:** Baseline adiponectin was 17.25 (9.53–31.97) μg $mL^{-1}$ and significantly correlated to HDL cholesterol ($r = 0.29$, $P = 0.01$, triglycerides ($r = -0.40$, $P = 0.0004$), ferritin ($r = -0.29$, $P = 0.02$), transferrin ($r = -0.28$, $P = 0.02$), uric acid ($r = -0.24$, $P = 0.04$). In multivariate analysis association to triglycerides ($P = 0.001$), HDL cholesterol ($P = 0.01$) and ferritin ($P = 0.04$) remained significant. Thirty-six new fatal and non-fatal new cardiovascular events occurred, 29 patient died. Cox proportional regression analysis showed that adiponectin below or above a ROC-derived cut-off of 27.33 μg $mL^{-1}$ significantly influenced event-free survival: hazard ratio (HR) 2.48, 95% confidence interval (CI) (1.09–5.66), $P = 0.031$ along with fasting glucose HR 1.01, 95% CI (1.00–1.02), $P = 0.01$ and history of cardiovascular events at inclusion HR 3.16, 95% CI (1.36–7.32), $P = 0.007$. In multivariate analysis baseline adiponectin HR 5.02, 95% CI (0.98–25.06), $P = 0.05$ and glycaemia HR 1.01, 95% CI (1.00–1.02), $P = 0.01$ influenced event-free survival. Adiponectin also predicted cardiovascular events in patients without cardiovascular disease at inclusion but was not associated to overall mortality.

**Conclusions:** In type 2 diabetes dialysis patients low adiponectin is associated to atherosclerosis related cardiovascular events.

## S.60

## Presence of bile acids in human follicular fluid and their relation with embryo development in modified natural cycle *in vitro* fertilisation

R.A. Nagy*,†, A.P.A.van Montfoort*,‡, A. Dikkers†, J.van Echten-Arends*, I. Homminga*, J.A. Land*, A. Hoek* & U.J.F. Tietge†

**Department of Obstetrics and Gynaecology, Section Reproductive Medicine, University of Groningen University, Medical Centre Groningen, Groningen, The Netherlands; †Department of Paediatrics, Centre for Liver, Digestive, and Metabolic Diseases, University of Groningen, University Medical Centre Groningen, Groningen, The Netherlands; ‡Department of Obstetrics & Gynaecology, GROW School for Oncology and Developmental Biology, Maastricht University Medical Centre, Maastricht, The Netherlands*

**Background:** Bile acids (BA) are increasingly recognized to possess intrinsic endocrine activities. Thus far the synthesis of BA from cholesterol is a function exclusively attributed to hepatocytes. We recently recognized that also granulosa cells in the ovary express key enzymes of the BA synthesis pathway. However, the biological significance of this observation is unclear. We therefore aimed to investigate (i) the presence of BA in follicular fluid (FF) and (ii) the potential relevance of FF-BA for embryo development.

**Materials and methods:** Total BA and BA subspecies were determined by liquid chromatography-mass spectrometry in FF and matching serum samples from 156 patients undergoing a first cycle of modified natural cycle *in vitro* fertilisation and were subsequently related to parameters of oocyte and embryo quality.

**Results:** Levels of total BA were two-fold higher in FF compared to serum ($P < 0.001$). Embryos with eight cells on day three after oocyte retrieval were more likely to originate from follicles with a higher level of ursodeoxycholic derivatives than those with fewer than eight cells ($P < 0.05$). Moreover, FF corresponding to top quality embryos contained a significantly higher

level of ursodeoxycholic derivatives compared to FF from embryos that were not of top quality ($P = 0.002$). Furthermore, FF levels of chenodeoxycholic derivatives were higher and deoxycholic derivatives were lower in the group of embryos with fragmentation compared to those without fragmentation (each $P < 0.05$).

**Conclusions:** (i) Significantly higher BA levels in serum than FF indicate a previously unrecognized local production of BA in the ovary. (ii) Specifically UDCA derivatives in FF are positively associated with the development of top quality embryos, while chenodeoxycholic and deoxycholic derivatives have a negative impact on fertility.

## S.61
## Risk factors for recurrent deep vein thrombosis

Ş.C. Vesa*, S. Crişan†, A.P. Trifa‡ & A.B. Buzoianu*
**Department of Pharmacology, Toxicology and Clinical Pharmacology, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; †Department of Internal Medicine, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; ‡Department of Medical Genetics, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania*

**Background:** Deep vein thrombosis (DVT) is a frequent disease with an important morbidity and mortality rate. Recurrent DVT (RDVT) is common, especially in patients with unprovoked DVT. There are studies showing that a polymorphism of the gene encoding vitamin K epoxide reductase (VKOR) is associated with DVT. This study investigated several risk factors for a RDVT.

**Materials and methods:** We recruited 144 patients (age 61.1 ± 14 years; 78 (54.2%) men, 66 (45.8%) women) diagnosed with acute DVT with duplex ultrasonography and admitted to the internal medicine and geriatrics wards of a city hospital, between January 2010–April 2011. We recorded the presence of factors known to increase the risk for DVT: history of DVT, cancer, exacerbation of chronic obstructive pulmonary disease (COPD), heart failure, obesity, bed rest for more than 3 days, major surgery in the previous month, varicose veins, and autoimmune diseases. Using PCR-RFLP technique we determined the factor V Leiden mutation, prothrombin G20210A mutation and the genotype for *VKORC1* gene indicating c.-1693 G>A polymorphism.

**Results:** RDVT was present in 63 (43.1%) patients. The AA genotype of the *VKORC1*-1693 G>A polymorphism was found in 5 (8.1%) patients with RDVT and in 9 (11%) patients without RDVT. The difference was not statistically significant ($P = 0.2$). We did not find differences regarding age ($P = 0.4$), gender ($P = 0.3$), heart failure ($P = 0.4$), obesity ($P = 0.4$), bed rest ($P = 0.06$), major surgery ($P = 0.1$), varicose veins ($P = 0.4$), autoimmune diseases ($P = 0.1$), factor V Leiden mutation ($P = 0.3$), prothrombin G20210A mutation ($P = 0.7$). Cancer and exacerbation of COPD were more frequent in patients with RDVT (11 (17.7% vs. 5 (6.1%), $P = 0.05$; 6 (9.7% vs. 1 (1.2%), $P = 0.04$).

**Conclusions:** The *VKORC*-1693 G>A polymorphism was not associated with RDVT.

## S.62
## Oral sucrose effect for pain relief in premature infants

S. Andreica, G. Zaharie & A. Kis
*Mother and Child Department, University of Medicine and Farmacy "Iuliu Haţieganu" Cluj Napoca, Cluj Napoca, Romania*

**Background:** Pain in neonates is known to cause adverse short and long-term effects. We decided to evaluate the effect of oral sucrose for relieving the procedural pain in premature neonates.

**Materials and methods:** This is a prospective cross-over study which evaluated the pain after heel lance interventions. Oral sucrose 25% (0.5 mL) was administrated before the second heel lance intervention. The first intervention was performed without sucrose administration and we compared the intensity of pain perception. The interventions and the behavior of the patients were video recorded to improve the accuracy of the evaluation. PIPP (Premature Infant Pain Profile) score was used for assesment of pain after pain stimulus.

**Results:** Twenty-four premature neonates were included in this study. PIPP score was 6.42 when was used oral sucrose towards 13 when sucrose wasn't used ($P = .005$).

**Conclusions:** Oral sucrose administration is a simple and efficient methode for pain relief in case of premature infants.

## S.63
## A forgotten method used in preventing vascular spasms and hyper permeability of capillary endothelium: the role of Reticuline-M

C. Barsu
*Department of History of Medicine, Social Sciences and Humanism, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania*

**Background:** Reticuline-M was a drug invented in 1923 by Professor Iuliu Moldovan (1882–1966), from the Cluj Medical Faculty. He chose this name, because he considered that this substance was produced by the so-called reticulo-endothelial system (mononuclear phagocyte system). The usefulness of this drug in different diseases having vascular spasms and hyper permeability of capillary endothelium was demonstrated by many clinicians of the same faculty. The aim of our poster is to present the role of this drug in the treatment of different internal diseases.

**Materials and methods:** Moldovan obtained Reticuline-M as a result of his studies focused on the fact that the intravenous injections of China ink at horses blocked their reticulo-endothelial system. This blockage was followed by the appearance in the animal blood of a protective substance against the anaphylactic shock.

**Results:** Reticuline-M had a protective effect on the endothelium of blood capillaries, maintaining or restoring the normal capillary permeability and prevented vascular spasms. This drug had no toxicity and proved to have therapeutic effect in allergic manifestations, such as bronchial asthma, in some pathological conditions which were accompanied by neuro-vegetative unbalance, in only few cases of arterial hypertension, in some local and general reactions on therapeutic serum testing.

**Conclusions:** Our paper summarizes the knowledge of Reticuline-M in preventing vascular spasms and hyper permeability of capillary endothelium in different diseases, accompanied by neuro-vegetative unbalance.

S.64

## The study of oxidative stress in preterm neonates: lipid and protein peroxidation

M. Matyas, L.D. Blaga, M. Hasmasanu & G. Zaharie
*Neonatology Department, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj Napoca, Romania*

**Background:** The oxidative stress is produced by the harmful effects of free radicals. Several neonatal conditions are correlated with oxidative stress : bronchopulmonary dysplasia, periventricular leucomalacia, retinopathy of prematurity, intraventricular haemorrhage, necrotizing enterocolitis. The harmful effect of free radicals are linked to their capacity to react with polyunsaturated fatty acids of cell membranes, proteins and nucleic acids.
**Material and method:** We conducted a prospective, non-randomized study. In the study group were included 14 preterm neonates with different pathologies: respiratory distress, asphyxia, cerebral hemorrhage. The control group consist in 13 healthy, late preterm neonates. For all patients family's consent was obtained. For the study of the oxidative stress we measured the malonildyaldehide (MDA) by Satoh's method and the protein peroxidation was determined spectrophotometrically as described by Reznick and Packer . For neonates from the study group we performed two determination on the first and third day of life. For control we performed one measurement on first day of life. The statistical analysis was done with SPSS program .
**Results:** Five neonates of the study group presented sever asphyxia and ten neonates respiratory distress. The median value of MDA in the study group was higher on the third day of life than on the first day (5.12 vs. 4.87 nmol $mL^{-1}$). The protein peroxidation process presented the same behaviour (5.57 vs. 4.91 nmol $mL^{-1}$). The protein peroxidation was significantly higher in the study group than at the control ( $P < 0.05$).
**Conclusions:** The oxidative stress at preterm neonates is more severe when different pathologies are associated which are leading to overproduction of free radicals than in healthy condition. The knowledge of oxidative stress could be useful to implement antioxidant defenses strategies for preterm neonates.