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Târgu Mureș

BOOK OF ABSTRACTS

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CONSEQUENCES OF ALLOXAN DIABETES UPON CERTAIN PHYSIOLOGIC PARAMETERS UNDER THE INFLUENCE OF HERBAL (PHYTO) MEDICINE (FASSC- V)

Bacalov I[1], Crivoi Aurelia[1], Chirita Elena[1], Gherman I[2], Croitori C[2], Casco Doina[2]

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Background: Phytotherapy is now widely applied in different medical specialities and diseases. One of them in which phytotherapy was proposed as a possible alternative is diabetes. **Objective:** Our research presents the results of experimental investigations concerning the influence of plant extracts (FASSC-V) on some hematologic indicators and hormonal status. **Results:** Our results showed hypoglycemic effect of plant extracts (FASSC-V) and some efficient effects upon the indicators of blood. In the first tentative it was estimated that plant extracts FASSC-V display physiological action upon reproductive system function, characterized by the rise of sexual hormones on the level of gonads, as well as an action on endocrine pancreas and thyroid gland. **Conclusions:** The plant extracts FASSC-V may actively influence the functions of endocrine system and thus the reaction of the body and the metabolic processes.

Keywords: diabetes, medical plants, hormones

PARTICULARITIES OF THE FIBRINOLYSYS AT BIRTH

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Background: The influence of pregancy on the clotting-fibrinolysis equilibrium was already investigated, but comparative studies on mother-newborn couple are still necessary. More, the newborn is characterized by an impaired platelet aggregation,a reduced synthesis of clotting factors and inhibitors and molecular abnormalities in some proteins of blood coagulation. The role of fibrinolysis is, however, less studied. **Objective:** We have assessed the fibrinolytic activity in fullterm/preterm newborns. The present paper is devoted to the study of the plasma fibrinolytic activity at birth in mother and newborn. **Methods:** The euglobulin lysis time (ELT) was evaluated in several groups of newborn, according to their weight at birth as main criterion. Other criteria were APGAR score at birth and gestational age. We also recruited for study the corresponding groups of mothers. **Results:** The resulted data indicate a significantly reduced ELT in full-term newborn comparative to maternal values. We also described a significantly increased of the same parameter in premature newborn versus full term newborn group.

Keywords: fibrinolysis, euglobulin lysis time, newborn

CITOGENETIC ABNORMALITIES AND EVOLUTION OF A LOT OF PATIENTS WITH MULTIPLE MYELOMA

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Objective: The cytogenetical examination in Multiple Myeloma (MM) presents difficulties created by the low proliferation rate of the malignant clone, the used techniques, and not at least, by the diversity interpretation of results. **Methods:** Our study was made on 44 patients with MM at diagnosis. 75% of patients are in the III stage of illness at diagnosis. **Results:** The cytogenetical examination was positive in 29.54% cases, most frequent were involved chromosomes 1 and 14. In 83.33% the cytogenetic abnormalities are complex, including both structural and numerical lesions. For a bone marrow plasma cell infiltration is less than 30%, the rate of cytogenetic abnormalities was 12.5% and for greater than 30% the rate was 39.28%. The incidence of the cytogenetic abnormalities it becomes to increase for the lot with plasmablastic and immature MM (50%) Vs lot of patients with intermediate and mature MM (21,87%) - Greipp. The 24 month survival rate is 61.53% for the patients with cytogenetic abnormalities and 87.1% for the patients without cytogenetic abnormalities. The 36 month survival is 33.07% Vs 64.45% for the same groups mentioned before. 38.46% of patients maintain plateau phase at 12 month for the lot with cytogenetic abnormalities and 67.74% for the patients without cytogenetic abnormalities. For the patients with plateau phase longer than 18 months the percentage was 23.07% Vs 58.06% (with Vs without abnormalities cytogenetical). **Conclusions:** The cytogenetical examination was positive in approximately 30% by the patients with MM untreated before. The cytogenetic lesions are complex and heterogeneous. The presence of cytogenetical abnormalities seams to be correlated with the plasma cell infiltration degree, with the morphological subtypes and with a sever prognostic, too. Our statement must be taken by cautious, regarding the reduced studied lot and the impossibility of making PCLI and univariational statistically analysis.

Keywords: multiple myeloma, cytogenetic abnormalities, prognosis

FACTORS THAT DETERMINE MYELOMATOSIS TUBULOPATHY IN MULTIPLE MYELOMA

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Objective: The study of the renal lesions in multiple myeloma (MM) has a particular importance both pathophysiologically considering the great complexity of the mechanisms involved, and clinically for their prognostic implications. **Methods:** The study proposes the review of the pathophysiological mechanism involved in the renal lesions in MM and their impact in a group of 44 patients pertaining to the Clinic of Hematology, Hospital Filantropia, Craiova. The renal lesions in MM can affect any segment of the nephron (contort tubes, glomerules, intertice), the tubular affection being the most frequent. The renal anomalies may be functional or organic (from minimal disturbances of the concentration, to renal failure). **Results:** Renal failure in patients with MM is determined in most cases (47.42%) by myelomatosis tubulopathy which is characterized by: increased chance in patients presenting Bence-Jones proteinuria (23.80% compared to 8.69%); increased chance in patients in disease progression (95.56%) of those in advanced stage (95.46%); the close correlation between creatinin level and hypercalcemia (r = 0.54; 0.34–0.74) which determines the initiation of a vicious cycle that may induce the decease if it is not stopped in time. **Conclusion:** Anomalies of the renal concentration are frequent in MM patients with light chains excretion (65.9%), but the tubular transport functions disturbance is rarely evidentiated (2.27%). Amyloidosis with glomerular lesions was present in 4.54% of cases.

Keywords: multiple myeloma, myelomatosis tubulopathy, Bence Jones proteinuria

IDENTIFICATION OF SALIVARY VIRAL MARKERS IN PATIENTS WITH ACUTE AND CHRONIC VIRAL HEPATITIS

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Methods: The study was conducted on 106 patients with positive serological diagnosis of viral hepatitis: 23 with hepatic infection with HAV, 21 with acute hepatitis with HBV, 28 patients with chronic B hepatitis, and 34 patients with chronic C hepatitis. 35 normal healthy subjects, with no serological markers of hepatitis infection formed the control group. Serological methods were adapted for saliva and the following markers were identified: anti-HAV antibodies (IgM), anti-HAV total antibodies (IgM+IgG), HBsAg, IgM anti-HBc, anti-VHC antibodies. **Results:** Salivary IgM anti-HAV identification test in patients with acute hepatitis A and positive serological test for anti-HAV IgM had 91.3% sensitivity, and was 100% specific. For total anti-HAV antibodies (IgM+IgG) the sensitivity was 95.65%, and the specificity 99.31%. Identification of the HBsAg in saliva of serological positive HBsAg patients had a specificity of 100%. If we consider all patients with positive serological HBsAg test (with acute and chronic B hepatitis), the test has a sensitivity of 89.59%. Considered separately, the sensitivity for acute B hepatitis was 95.24%, and 85.19% for chronic B hepatitis. For anti-HCV antibodies, the test has a 90.47% sensitivity, with a 100% specificity. In patients with chronic C hepatitis we found salivary anti-HAV antibodies with 100% specificity and a 88.2% sensitivity. **Conclusion:** Identification of viral markers in saliva has clinical relevance and may be use as an alternative of serological testing for the diagnosis of viral hepatitis, in epidemiological studies or to establish the prevalence of viral hepatic infections in population groups.

Keywords: salivary viral markers, hepatitis, specificity, sensitivity

CYTOTOXIC EFFECT OF DIFFERENT EXPERIMENTAL ENDODONTIC SELEARS, ON HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS CULTURES

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Background: When using a sealing material in endodontic treatment, the amount of residual monomer should be low, because the unreacted monomer is removed in time from the endodontic location in saliva, thus having a negative impact on the biocompatibility of the material. Endothelial cells are directly involved in all the inflammatory, allergic reactions and tumoral outgrowths. **Objective:** Evaluation of the effects for three experimental endodontic sealers, on human umbilical vein endothelial cells (HUVEC), both as solid samples and as artificial saliva and water extracts. We also determined the components of the endodontic selears dissolved in water and artificial saliva in order to assess the influence of the residual monomers on the cell viability in vitro. **Methods:** The experimental endodontic materials (E1, E4, E5) were prepared by dispersing in the organic phase the bioactive inorganic fillers. The chemical com-

position for glasses and the condition for synthesis in laboratory were: 45% SiO_2, 10% Al_2O_3, 17% B_2O_3, 20% BaO, 8% NaF–CaF_2; 40% SiO_2, 12% Al_2O_3, 7% B_2O_3, 25% SrO; 8% ZrO_2, 8% NaF–CaF_2 obtained through the conventional melting method at 1350° C. Residual monomer was measured using a HPLC chromatograph. The bioassays in vitro, on HUVEC cultures, were performed both on extracts in water and artificial saliva and solid specimens of the sealers. Cytotoxicity was measured using the MTS method. Annexin V-FITC staining was used to assess the induction of apoptosis. Inflammatory activation was measured through ICAM1 ELISA testing. **Results:** There were large amounts of residual monomer HEMA for the E4 material, while the HPLC results for the E1 and E5 showed a low residual monomer extracted both in saliva and water. Our data showed a consistent cell viability, apoptosis and inflammation similarity with that of the solvent when cells were treated with lower concentration of conditioned saliva, respective water, with biomaterials E1 and E5. When cells were exposed to the E4 biomaterial there were high cytotoxic effects obtained both with solid samples and extracted solutions in water and saliva. **Conclusion:** The data is consistent with our residual monomer findings, thus showing that in fact, the cytotoxicity, inflammation activation and apoptosis induction are directly linked with the unreacted monomer HEMA. This study showed that the E1, E5 composite may be used successfully for the endodontic therapy.

Keywords: endodontic materials, cytotoxicity, apoptosis

ENRICHMENT OF THE ENDOGENOUS NEUROGENESIS IMPROVED FUNCTIONAL RECOVERY AFTER STROKE IN AGED RATS

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Background: It is well known that the endogenous neurogenesis is maintained in the subventricular zone and the dentate gyrus of the hippocampus postpartum. Here we asked if stimulations of endogenous neurogenesis, before or after stroke, in aged rats, which are known to be more severly affected by cerebral ichemia than young rats, may improve recovery after stroke. **Methods:** In this study, stroke was induced by middle cerebral artery occlusion in aged rats and neurogenesis was stimulated at different time points, related to stroke moment, using pentylentetrazole or electrical stimulation. After surgery, rats were behaviorally tested for seven weeks and global gene expression and immunhistochemical analyses of the periinfacted region was done. **Results:** We observed that stimulation of neurogenesis before stroke does not improve post-stroke outcome, but stimulation of post-stroke neurogenesis is beneficial for behavioral recovery of aged rats. After global gene expression analysis we shown many new feature of gene expression associated with aging and led to identification of new genes involved in stroke pathophysiology. Immunohistochemistry has revealed many new features related to the neurovascular unit in the aged post-stroke animals. **Conclusion:** Stimulation of post-stroke neurogenesis is beneficial for behavioral recovery of aged rats.

Keywords: stroke, endogenous neurogenesis, behavioral recovery

HEART RATE VARIABILITY AND RESPIRATORY SYMPTOMS: PSYCHOPHYSIOLOGICAL REFLECTIONS OF ANXIETY

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Background: The activation of the limbic structures in psycho-emotional stress involves respiratory and cardiovascular responses. There are determined tight relations between the degree of activation of amygdala and the trait anxiety. **Objective:** The aim of the research is to see the effect of the individual anxiety on the heart rate variability (HRV) and respiratory distress in healthy subjects and patients with panic disorder. **Methods:** 24 healthy subjects and 25 patients with panic disorder (PD) were recorded during voluntary hyperventilation test, in lying position. The airflow was recorded by Biopac transducer (SS11LA) at rest – 5 min, hyperventilation (VH) – 3 min and posthyperventilatory period – 9 min, the ECG was recorded simultaneously. Before recording we determined: Trait Anxiety level (Spielberger), respiratory symptoms in VH and in daily life (Vegetative Profile Inventory of Moldovanu). The spectral and time domain analyses of RR intervals were performed to calculate normalised compounds of spectre: High (HFn), Low (LFn) and Respiratory Centred (RCFn) Frequencies, LF/HF index; average cardiac periods (CP) and variation coefficients (VCcp). **Results:** PD and 3 healthy subjects with increased levels of anxiety (more than 45) reported more respiratory complaints (dyspnoea) during VH and in daily life. The scores of dyspnoea in daily life correlate positively with the anxiety levels. The changes of HRV: decreased HFn, elevated LFn and LF/HF at rest and during VH; lower CVcp in all periods of tests; lower RCFn during VH and the last 3 min of posthyperventilation period were determined in PD and anxious healthy subjects. **Discussions:** The hyperactivity of anxiogenic structures and misinterpretation of body sensation increase anxiety in PD. Panic attack can be triggered by the increase of pCO_2,

hypocapnia has weaker panicogenic effect. The PD with remarkable respiratory symptoms are more responsible to VH. The decreased HRV in patients with higher anxiety is associated with more respiratory symptoms in daily life and during VH. **Conclusions:** PD patients with more respiratory symptoms can be treated like respiratory group, with higher activation of limbic anxiogenic structures that produces more autonomic changes and decreases the threshold for respiratory sensations. The appreciation of autonomic changes in anxious patients can be useful in treatment.

Keywords: heart rate variability, panic disorder

IN VITRO ADIPOGENIC DIFFERENTIATION PATHWAY

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Background: Solid tumors stroma contains several types of cells, such as adipocytes and fibroblasts, which interact and transform, thus contributing to tumor progression. **Objective:** This study investigated the molecular mechanisms involved in adipogenic potential of tumor-associated fibroblasts. **Methods:** Human tumor-associated fibroblasts (TAF) were isolated from 10 breast tumor surgical pieces using the enzymatic digestion method, and further cultivated in DMEM supplemented with 10% FCS and 2% Pen/Streptomycin solution. Nonhematopoietic stem cell medium for generation of adipocytes was used for differentiation of TAFs at passage 2. In days 3, 5, 7 and 21 of adipogenic induction, total RNA extraction was performed, and qRT-PCR method was used for quantification of gene expression for PPARγ, C/EBPα, LPL, Leptin, Leptin receptor, OB-R, huB219.1, huB219.2, huB219.3 and FABP4. Histochemical (Oil Red O) and immunocytochemical (FABP4) staining procedures revealed the differentiation rate. Mesenchymal stem cells (MSC) - derived adipocytes were submitted to similar procedures, while normal adipose and peri-tumoral adipose tissue total RNA was used for qRT-PCR gene expression control. **Results:** Both MSCs and TAFs can differentiate towards the adipocytic lineage in variable proportions (30–50%). The majority of molecular markers are present even in the early passages of both MSCs and TAFs, being downregulated with passage number and upregulated in mature adipocytes. C/EBPα and LPL are not present in undifferentiated MSCs and TAFs. Leptin is upregulated in TAFs along adipogenic induction. FABP4 and OB-R genes are upregulated in peri-tumoral adipose tissue. **Conclusion:** Present study could provide promising pathway for targeting specific molecules involved in adipogenesis.

Keywords: human tumor-associated fibroblasts, mesenchymal stem cells – derived adipocytes, adipogenesis

ASPECTS OF NEUROPSYCHIATRIC MANIFESTATIONS OF A GROUP OF CHILDREN WITH ENURESIS FROM DOLJ

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Background: Enuresis means involuntary pee of a child over 5 years. In patogeny of primary enuresis it was discover a delay of neurological maturation. **Objective:** We studied the neuropsychiatric manifestations in a group of children with enuresis. **Methods:** We studied a group of 115 children which were diagnosticated with enuresis at Neurophysiatric Child Hospital Craiova in 2008–2011 and compared with a control group of 200 children with no urinary symptoms. Age of children was between 5–12 years. We investigate: type of alimentation (natural, mixed or artificial) and also period of breast feeding. Electroencephalography was made with Micromed technology and electromyography with Nemus technology. **Results:** We noticed irritative aspects on electroencephalograms to 25% children from study group suggestive for spamophily; to 11% – focal bioelectric anomaly irregistrated spontaneous or after hyperventilated; rest of 64% had no disorders on electroencephalograms. Also 60% of study group of children were no breast feeding. From them, 24% presented lack of attention, delay of language 56%, psychic delay 18%, and encopresis 1.58%. In **conclusion**, majority of children from study group presented dysfunctions on electroencephalography and electromyography but also lack of attention, language delay, psychic delay, and encopresis. Most over half of study group wasn't breast fed, this aspect being important because maternal milk contain maturation factors for neuronal development.

Keywords: enuresis, electroencephalography, electromyography, nutrition

THE EFFECTS OF SLEEP DEPRIVATION ON PLATELETS REACTIVITY IN NORMAL SUBJECTS

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Background: Sleep deprivation has pathophysiological systhemic consequences. It was suggested that platlets may be a target of these processes. **Objective:** The aim of the study was to assess the changes in platelets reactivity after sleep deprivation in normal subjects. **Material and methods:** Patients including criteria consisted of absence of any system disease, no treatment or special diet, no excessive physical activity, nonsmoker and no other toxic environmental exposure. In the study were included 25 subjects. The patients were divided into two groups: control group without sleep deprivation, and a 30 hours sleep deprivation group. The platelets reactivity was assessed by evaluation of platelets circulating aggregates. **Results:** The platelets circulating aggregates were significantly increased in sleep deprivation subjects compared to the patients without sleep deprivation (were assumed to be due to the cathecolamine increase). **Conclusions:** Sleep deprivation compromises the cortical functions, especially a drastic decrease of alertness. The compromised cortical functions were associated with platelets hypereactivity and may lead consequently to the development of cardiovascular and cerebrovascular morbidities.

Keywords: sleep deprivation, platelets reactivity

EFFECTS OF ISCHEMIC PRECONDITIONING ON THE ELECTRICAL AND MECHANICAL FUNCTION OF RAT VENTRICULAR MYOCARDIUM FIBER

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Background: Myocardial preconditioning is an adaptative phenomena to the stress induced by short periods of ischemia and reperfusion. The protective effetcs consist of reducing the energetic consumption and the delay of the onset of celular lesions during reperfusion. The goal of the study is to present the electrical and mechanical changes induced by this phenomena. **Materials and methods:** We evaluated 3 groups of 20 rats each. The normal group was subjected to 40 minutes of stabilization in Tyrode solution. The control group underwent 20 minutes of stabilization in Tyrode solution and then 5 minutes of global ischemia induced by stoping the perfusion and replacing it with an unoxigenated and unglucosed Tyrode solution and 20 minutes of reperfusion. The preconditioned group was stabilized 20 minutes and then underwent 3 cycles of 2 minutes of ischemia each followed by 5 minutes of reperfusion before the global ischemia of 5 minutes followed by 20 minutes of reperfusion. The recordings were made using a Hugo-Sachs Plugsys system and classical glass microelectrodes. We measured the maximum amplitude of the contraction and the action potential duration at 30%, 50% and 90% from the maximum amplitude; also spontaneous action potentials and the incidence of arrhythmias were quantified. **Results:** Within the experiment we observed differences regarding the duration of the action potential, recovery of the contraction force and the incidence of arrhythmic phenomena. At the end of the global ischemia, the duration of the action potentials was longer in the control group as compared to the preconditioned group; this lengh disappeared with preconditioning. We obtained statisticaly significant differences in the shortening of APD90 in the preconditioned group ($p < 0.05$) and no differences for the APD50 and APD30. Also, preconditioning enhanced the recovery of the postischemic contraction force. Most of the arrhythmias were observed during the global ischemia and reperfusion in the control group. The spontaneous action potentials were more frequent in the preconditioned group as the control group. **Conclusion:** Ischemic preconditioning is definitively an adaptative way of the myocardium to the subsequent sustained ischemia, ensures a better recovery of the mechanical function and stability of the electrical membrane. The cardioprotective effects are probably multifactorial and may involve the reduction of both the metabolic demands and the celular ions shift which determines the shortening of the action potential duration, the reduction in the incidence of the arrythmias and recovery of the contraction force.

Keywords: myocardium, ischemic preconditioning, cardioprotection

EVALUATION OF PATIENTS WITH METABOLIC SYNDROME COMPONENTS NON-ALCOHOLIC HEPATIC STEATOSIS

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Background: Non-alcoholic fatty liver is a clinical-pathological change which is characterized by hepatic steatosis, inflammation and a variable degree of fibrosis. Non alcoholic fatty liver disease – hepatic manifestation of metabolic syndrome is an entity with the increasing incidence associated with diabetes, obesity, dyslipidemia, hypertension. **Objective:** To assess clinical and metabolic pa-

rameters in patients with non-alcoholic fatty liver disease associated metabolic syndrome. **Methods:** The study included a total of 87 patients with ultrasound diagnosed non-alcoholic fatty liver disease. Blood pressure, fasting glycemia, total cholesterol, triglycerides, fasting insulinemia, transaminases, glycated hemoglobin were measured. **Results:** Patients with fatty liver associated with metabolic syndrome had elevated liver enzymes. The fasting blood glucose and glycated hemoglobin were significantly higher in these. **Conclusions:** Metabolic syndrome can be considered an aggravating factor of fatty liver induced liver damage and a predictor of glucose metabolic disorder.

Keywords: metabolic syndrome, non-alcoholic fatty liver disease

MODERN TECHNIQUES FOR THE ASSESSMENT OF LOCAL SKIN BLOOD FLOW

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Objective: Local skin blood flow changes may occur in physiological circumstances, as well as in inflammatory dermatoses such as eczema, prurigo, psoriasis, lichen planus, lupus erythematosus, after trauma, surgery, in various skin cancers etc. Also, better understanding of cellular and molecular mechanisms regulating skin microcirculation is of real scientific interest. Thus, the assessment of local skin blood flow is a challenge for both clinical dermatology and fundamental scientific research. **Methods:** In this work we compare the Laser Doppler flowmeter, infrared thermography and reflectance confocal microscopy for the assessment of capsaicin-induced neurogenic inflammation in human subjects and experimental animals. **Conclusion:** Modern techniques for the assessment of local skin blood flow provides useful information about the mechanisms involved in skin inflammatory processes and may find an important place in investigating a wide range of dermatological conditions. Moreover, awareness of the advantages of each technique mentioned above allows us to choose the optimal method of evaluation.

Keywords: skin blood flow, neurogenic inflammation, capsaicin

A NEW APPROACH FOR EVALUATING MOVEMENTS DISORDERS IN MULTIPLE SCLEROSIS PACIENTS

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Objective: The objective of our study was to identify predictable parameters when monitoring gait disorders that will appear in the evolution of multiple sclerosis (MS) patients, by using visual evoked potentials (VEP) and tensiomyography (TMG). **Methods:** We assesses 86 parameters, 36 parameters in VEP evaluation, 50 in TMG, both on a group of patients suffering from certain Ms (20 patients) and a control group. The MS lot was grouped in two subgroups: subgroup A, with clinically detectable gait disorders and subgroup B, without clinically detectable gait disorders. All groups were tested by neurophysiologic evaluation methods such as VEP, using a pattern reversal full field stimulation and TMG on quadriceps components, femoral biceps, gastrocnemian muscles and tibialis anterior. **Results:** We recorded high values of wave N75 latencies in subgroup A. The delays of the P100 wave were presented in both subgroups. In our study, the contraction time as TMG parameter – recorded higher values in posterior muscular group of the thigh and anterior muscular group of the shank. **Conclusion:** After analyzing muscular displacement and relaxation time, we observed a higher muscle tonus in all muscular groups we tested, especially in gastrocnemian. The ratio direct/converse correlation is high in VEP/TMG correlations.

Keywords: multiple sclerosis, movement disorders, visual evoked potentials, tensiomyography

CHANGES IN INFLAMMATORY AND OXIDATIVE STRESS MARKERS AFTER BARIATRIC SURGERY

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Background: Obesity has been recognized as a chronic inflammatory and prooxidant condition. It is associated with elevated inflammatory indicators including C-reactive protein (CRP), TNF-alpha (TNF-α) white blood cell count (WBC). Recent studies have shown elevated CRP and WBC as significant predictors of cardiovascular disease. Bariatric surgery is commonly performed as a treatment for morbid obesity offering significant reductions in premature myocardial infarction. **Objective:** The aim of this study is to assess the impact of silastic ring vertical gastroplasty (SRVG) on inflammatory and oxidative markers. **Method and patients:** We studied a group of 45 morbidly obese patients who underwent SRVG. Total oxidative status (TOS), total antioxidant capacity (TAC), nitric oxide (NO) metabolites (nitrite/nitrate), CRP, TNF-α and WBC were determined before and six months after surgery. The same parameters were also determined in a group of ten healthy, normal weight subjects. **Results:** BMI decreased significantly after SRVG ($p < 0.05$). TOS values were significantly higher in the morbidly obese vs. the healthy normal weight group ($p < 0.05$) while TAC values were significantly lower ($p < 0.05$). TNF-α values did not change significantly six after SRVG. However, nitrite/nitrate values increased from 57.57±31.62 micromol/l to 78.93±27.81 micromol/l ($p < 0.05$). PCR values decreased after surgery significantly ($p < 0.05$). **Conclusions:** Our study confirmed that morbid obesity is associated with chronic inflammation and oxidative stress. It seems that weight loss six months after surgery is not yet fully associated with a significant reduction of cardiovascular predictive factors.

Keywords: obesity, bariatric surgery, chronic inflammation markers

ATTENUATION OF PAIN AND INFLAMMATION IN A RAT MODEL OF ADJUVANT-INDUCED ARTHRITIS

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Background: Rheumatoid arthritis (RA), a chronic systemic autoimmune inflammatory disease, is characterized by a chronic inflammatory process which can lead to disabling lesions due to synovial inflammation and joint damage. It has recently been proved that RA is associated with a high cardiovascular risk and increased morbidity and mortality compared to the general population. In rheumatoid arthritis (RA), pain and joint destruction are initiated and maintained through the production of pro-inflammatory mediators. **Objective:** The present study explored the effects of chronic oral administration of Quercetin on inflammation and pain in a rat model of adjuvant-induced arthritis (AIA). **Methods:** Quercetin was administered orally (20 mg/kg body weight/day) to AIA male Wistar rats for 21 days after the onset of arthritis. The Quercetin-treated group was compared with 3 other groups: a group of healthy control rats, a group of non-treated arthritic rats and a group of arthritic rats treated with Indomethacin. For all the animals in this study the pain score was determined by measuring the change in the paw volume (as an indicator of edema) with a plethysmometer. **Results:** Quercetin effectively lowered the pain score of AIA rats from day 21 after the induction of arthritis, its efficiency being similar to that of Indomethacin. A large increase was observed in the hind paw volume of untreated arthritic rats compared with non-arthritic rats. In contrast, a gradual but significant decrease of the paw volumes was observed in arthritic rats treated with Quercetin and Indomethacin, until the end of the experiment. **Conclusions:** The study confirms the analgesic effect and the anti-inflammatory efficiency of Quercetin.

Keywords: rheumatoid arthritis, inflammation, pain, quercetin

THE STUDY OF SPECIFIC BIOLOGICAL PARAMETERS IN PATIENTS WITH PAROXYSMAL ATRIAL FIBRILLATION

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Objective: We studied the short-term evolution of biological parameters in 23 patients with paroxysmal atrial fibrillation admitted in the ER of the University Emergency Hospital Bucharest (first episode/reccurent paroxysmal atrial fibrillation – RPAF). **Material**

and method: NTpro-BNP, CK-MB, TGO, TGP, CRP, myoglobine, leucocytes count, were analised after 4/6 hrs, in treated patients. **Results:** NTpro-BNP increases after 4 hrs vs admission, initialy in both groups; in the next two hrs NTpro-BNP decreased in RPAF patients but continued to increase in patients with first episode of PAF. CK-MB, TGO, TGP did not significantly vary depending on age, gender, PAF/RPAF. CRP was higher in patients experiencing the first episode of PAF comparing to those with RPAF. Myoglobine and leucocyte count did not significantly vary depending on age, gender, PAF/RPAF. **Conclusions:** There are no myocardial lesions during episodes of PAF, since the specific/non-specific enzymes have no significant variations (TGO, TGP, CK-MB). The first episode of PAF is less tolerated than RPAF, since there is a higher and continuous increase of NTpro-BNP.

Keywords: paroxysmal atrial fibrillation, myocardial necrosis biomarkers

THE PRESSIONAL RESPONSES TO HANDGRIP TEST, AT ISOLATED ARTERIAL HYPERTENSION OF CONSULTATION SUBJECTS

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Hypertension is recognized as one of the major risk factors for vascular damage. The prevalence of uncontrolled hypertension is still apparently high. It is often forgotten that the blood pressure is a very labile hemodynamic parameter, which requires a correct methodology for its measurement, only rarely met, leading to misdiagnosis and wrong hypertensive monitoring. Isolated clinical hypertension or white coat arterial hypertension is defined by the clinical situation of arterial hypertension in the doctors office and normotension with the self-measurement of blood pressure and/or ambulatory blood pressure monitoring. The isolated arterial hypertension of consultation is not rare in general population (10%) and it can affect at least 20% of hypertensive patients. There have been communicated another alteration of cardiac structure in patients with isolated arterial hypertension of consultation. In context we have investigated the pressional responses at handgrip test. 93% of patients had pressional responses of hypertensive type suggesting the fact that isolated arterial hypertension of consultation and its clinical manifestations are harmful.

Keywords: arterial hypertension of consultation, handgrip test

BIOLOGICAL MECHANISMS UNDERLYING THE IN VIVO TOXICITY OF FUNCTIONALIZED MULTI-WALLED CARBON NANOTUBES

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Background: Carbon nanotubes (CNT) are repetitive structures made of carbon atoms. With a tubular shape, they can be single-walled (SWCNT) or multi-walled (MWCNT) structures. Various applications have been proposed for CNT, including medical field. However, their safety for human administration is a controversial subject. In vitro studies have pointed oxidative stress and inflammation as mechanisms involved in their cytotoxic effects, while there are only few in vivo studies, using especially pulmonary models. **Objective:** Based on our previous experience regarding SWCNT, we evaluated the capacity of functionalized MWCNT to generate oxidative stress after ip administration in rats. **Methods:** MWCNT were synthesized and purified by INCDTIM, Cluj-Napoca, and characterized by SEM, TEM and Raman spectroscopy. For in vivo administration, the dispersed MWCNT solutions were obtained after single strand DNA (ss-DNA) functionalization through sonication. The concentration of ss-DNA-MWCNTs solution was estimated by UV-Vis-NIR spectroscopy. The presence of MWCNT in blood and tissues was detected by Raman spectroscopy at seriate time points after their administration. The oxidative stress was evaluated in dynamics (1 h, 3 h, 6 h, 24 h, 48 h and 6 days) after the administration, both in blood and in different organs. **Results:** The most evident alterations were produced in blood of MWCNT treated animals comparatively with controls at 1 hour interval (malondialdehyde 3.01±0.22 vs 1.65±0.15 nmol/ml; protein carbonyls 1.67±0.12 vs 0.56 ±0.10 nmol/mg; reduced glutathione 16.55±1.15 vs 21.5±1.2 nmol/ml). We also assessed hepatic enzymes, markers of inflammation and angiogenesis. **Conclusion:** Our results demonstrate that ss-DNA-MWCNT produce oxidative stress both in blood and liver, with a transient pattern, and with a maximum at 1 hour after their in vivo administration.

Keywords: carbon nanotubes, oxidative stress

EVALUATION OF PROSTATIC PHYSIOLOGY IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Objective: The evaluation of prostatic physiology is less studied in obstructive sleep apnea syndrome (OSAS) patient. We evaluated the relation between the respiratory distress index and the quality of life of these patients. **Methods:** In the present study we have included 25 male subjects with different ages diagnosed with obstructive sleep apnea syndrome by a full night polysomnography (PSG) at Sleep Laboratory from Clinic of Pulmonary Disease from Iasi. All recordings were validated according to International Guidelines of Sleep Scoring. Also all patients fulfilled the International Prostate Symptom Score (IPSS) Questioners. We used Statistic tests, Mean of values, Standard deviation and Pearson Correlation. **Results:** The mean age of the patients was 50.32±9.29 years old and the mean of IPSS was 8,08 (included in the moderate symptoms group). According to IPSS, 60% of the study group presented mild urinary symptoms, 32% had moderate symptoms and 8% had severe urinary symptoms. After PSG, we recorded a mean AHI (apnea hypopnea index) of 35.54±28.12/hour, a minimum oxygen saturation (SpO2min) of 75.52±11.8% and mean of microarousals index of 32/hour. The BMI (body mass index) group was 35.7 kg/m2. We noticed a strong positive correlation between IPSS and AHI (r = 0.81), microarousals index (r = 0.45) and BMI (r = 0.60). Also we noticed a strong negative correlation between IPSS and SpO2min (r = -0.54). There was no correlation between IPSS and age (r = 0.09). Only 4 patients were diagnosed by clinical examination and by ultrasonography with benign prostatic hyperplasia. **Conclusions:** The prostatic physiology is affected in obstructive sleep apnea syndrome, especially with nocturnal decrease in SpO2min, increase of microarousals index and AHI; the age does not have any relevance in this correlation.

Keywords: obstructive sleep apnea syndrome, International Prostate Symptom Score

MEASURING THE INSTANTANEOUS ARTERIAL BLOOD PRESSURE FROM BIOIMPEDANCE WAVE

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Background: Bioelectric impedance plethysmography is a noninvasive technique by which small changes in volume can be readily detected. The hindrance to flow of an alternating current (AC) is known as impedance (Z) and is defined in terms of voltage (U) and current (I) by Z = U/I. In biologic tissues, (I) is carried by ions, the concentration of which is relatively fixed. The total number of ions in a given segment, such as the chest or the limbs, is related to the total amount of fluid present in both the intracellular and extracellular compartments. **Objective:** The objective of this study was to determine the instantaneous arterial blood pressure using the bioimpedance signal. **Methods:** Aortic and arterial pressures are classically determined by invasive methods, based on cardiac catheterization. The idea was to connect the variation of pressure to the variation of the bioimpedance. When the blood volume variation is maximum in the artery, the variation of the impedance is minimum, the blood pressure is at its maximum (the systolic pressure); when blood volume variation is minimum, variation of the impedance is maximum, the blood pressure is at its minimum (the diastolic pressure). Variation of the impedance waveform is similar to the aorta blood pressure curve. Our device has an injection module with a microcontroller which generates a sinusoidal pulse with adjustable frequency (10–200 kHz) and adjustable intensity. In output, the device delivers an analogic signal representing the variation of the impedance of the explored section. Disposable electrodes were used for the injection of the sinusoidal pulse and the collection of bioimpedance signal. The acquisition of the bioimpedance signal on PC was made easier by the use of a National Instrument data acquisition device, the NI USB 6009. The bioimpedance signal processing, the user interface and the display were managed by LabVIEW. A measurement was made on 20 volunteers, clinically normal. Because in the formula for calculating the pressure systolic and diastolic pressures are involved, they will be measured with an electronic sphygmomanometer and the values will be included in the calculation. **Conclusion:** The method allows with precision, in real time, in an inexpensive and noninvasive way, the determination of the continuous arterial pressure directly from bioimpedance signal including peripheral wave.

Keywords: instantaneous arterial blood pressure, bioimpedance, plethysmography

STUDY OF ALCOHOL CONSUMPTION ON COGNITIVE DECLINE IN A GROUP OF PATIENTS WITH METABOLIC SYNDROME

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Background: Moderate alcohol drinking has been proposed as a protective factor against mild cognitive impairment (MCI) and dementia in several studies, but contrasting findings also exist. In one hand, mild to moderate alcohol intake is associated possible protection against age-related cognitive decline. In the other hand, alcohol intake is a risk factor for cerebral hemorrhage and vascular dementia. **Objective:** The aim of this study is to find correlation between of the individual components of the metabolic syndrome, such as dyslipidemia and obesity, and alcohol consumption on cognitive decline assessed by The Montreal Cognitive Assessment (MoCA). **Methods:** We studied a group was composed of 35 subjects with MetS (mean age 69.3 years, 15 women and 20 men) with a history of cognitive impairment. Metabolic syndrome was defined as the presence of the following criteria: triglycerides > 150 mg/dl; HDL cholesterol < 40 mg/dl for men and < 50 mg/dl for women; waist circumference > 102 cm for men and > 88 cm for women. They received at least two MoCA examinations at to 6 months interval. The subjects were classified as non drinkers, moderate drinkers (< 3 glasses per days) and heavy drinkers (> 3 glasses per days). **Results:** 40% of the whole cohort were not drinkers, 37% moderate drin-kers and 23% heavy drinkers. MoCA at first visit was 22.3±2.8. MoCA decline adjusted for age, sex, education was 2.3±1.9. Greater consumption of alcohol significantly accelerated cognitive decline in patients with higher level of triglycerides ($r = 0.56$; $p < 0.0001$), whereas moderate consumption it did not influence significantly the progression of cognitive decline. The study also revealed that waist circumference and low HDL cholesterol were in particular linked to poorer scores at the MoCA test, while poorer results was obtained when the level of both markers is modified and consumption of alcohol is higher ($r = 0.49$; $p < 0.0001$). **Conclusion:** If metabolic syndrome is associated with increased alcohol consumption then there is a greater risk of cognitive deterioration and does not prove that a moderate consumption would be a protective factor.

Keywords: metabolic syndrome, alcohol consumption, cognitive deterioration

PARTICULARITIES OF CERTAIN CARDIOVASCULAR INDICATORS DURING THE PERIOD OF PSYCHOEMOTIONAL TENSION IN CORRELATION WITH THE BIORHYTHM OF THE BODY

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Background: Informational overloading during educational process affects pupils and is determined by the great amount of studying material, vegetative dysfunction, tiredness, way of life and biorhythms of human body. **Objective:** To evaluate the heart activity during psychoemotional stress induced in pupils by their teaching program. **Methods:** The evaluation of cardio-intervals during educational stress. **Results:** The educational stress determines the decrease of cardiointervals both of pupils with emotional and intellectual bio-rhythms in positive period (group I) and of pupils with biorhythms in negative period (group II). The indexes of cardio-intervals of group I in the conditions of educational stress are reduced with 25.69% in comparison with usual conditions of activity. The indexes of group II in usual conditions of activity were estimated as 71.97±2.97 ms, while during educational stress conditions the values were 49.56±4.18 ms ($p < 0.001$). The cardiac rhythm variability parameters reflect the correlation between sympathetic and parasym-pathetic activity. In educational stress conditions 12.03% of children from group I showed extrasystoles at the interval of 0.3–0.4s. Registered extrasystoles of pupils from group II showed that 48.75% from them had bigger decrease. 31.25% children from group II during educational stress presented ectopic, ventricular activities, arrhythmia, which is determined by psyhoemotional intense status and the period of biological rhythms. Pupils from group II were estimated as having more reduced values of chaos determined in bioelectrical activity of the brain. **Conclusions:** Educational stress and negative period of emotional and intellectual biorhythms determine intense phychoemotional modifications, associated with greater variability of cardiac rhythm and modification of the brain bioelectrical activity.

Keywords: emotional stress, cardiovascular system, educational process, biorhythm

THE INFLAMATORY CYTOKINE'S SECRETION BY THE CO-CULTURED KERATINOCYTES AND MELANOCYTES UNDER UVB IRRADIATION; THEIR POTENTIAL ROLE IN TRIGGERING PSORIASIS

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Background: The common embryological origin of melanocytes and neural cells, the capacity of melanocytes to produce cytokines in response of stress or UVB exposure and identification of keratinocytes as potential targets of the melanocytes secretion products, have outlined the hypothesis of the potential role of melanocytes as a local stress sensor. **Objective:** The purpose of our study was to establish in vitro models to induce oxidative stress in key skin cells, evaluate their implication in psoriasis patogenesis and establish the role of melanocytes as potential local stress sensors, providing communicatory link toward keratinocytes and stimulating the proinflammatory cytokine production (IL8). **Methods:** Blood was sampled from 19 patients with acute phase psoriasis vulgaris and 6 healthy volunteers. Normal keratinocyte cell line (HaCat) and melanocytes were cultivated alone and in co-cultures in specific media and supplements. The cultivated celles were irradiated in day three with UVB radiations (100 mJ/cm^2) in order to induce oxidative stress. Supernates from control and irradiated cells were collected in day 1, 2 and 5 after UVB exposure. Proinflammatory cytokine IL8 was determined with ELISA in both serum and supernatants. **Results:** We detected an increased IL-8 secretion in the serum of patients with psoriasis vulgaris as compared to the healthy volunteers, with a great interindividual variability. Significant difference in IL-8 production in vitro between control and irradiated cells, alone or in co-cultures, was observed only in keratinocytes, after 1 day from irradiation ($p < 0.05$). A manifold increase in this cytokine secretion was registered in co-cultures as compared to epidermic cells cultivated alone, both in control and irradiated cells ($p < 0.0001$). The amount of the secreted cytokine has increased gradually in every time point of evaluation, being the greatest after 5 days from irradiation. **Conclusions:** According to our results irradiation of the cells with UV-B caused an oxidative stress, comparable to psychical stress involved in the initiation of psoriasis in vivo. The significant increase in the secretion of IL-8 in co-cultures suggests that melanocytes and keratinocytes might cooperate in a paracrine–like manner and become an important source of proinflammatory cytokines, that in vivo can attract lymphocytes in dermis, contributing to the pathogenesis of psoriasis.

Keywords: oxidative stress, keratinocytes, melanocytes, psoriasis

MORPHOFUNCTIONAL AND CARDIOVASCULAR CORRELATION FOR A GROUP OF YOUNG ATHLETES

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Background: The judicious selection of future performance athletes and the training optimization brings sport performance. **Methods:** In this paper there have been studied the cardiac morphofunctional parameters on a group of 40 young athletes with ages between 10–18 years old (athletics tests) during training sessions and beyond. There have been measured: the height, the weight, the body mass index, the thoracic perimeter and the Erismann harmony index. There have been recorded the electrocardiograms for the 12 classic derivations using the HEART 112D device, and also the blood pressure and the heart rate values. The parameters obtained through echocardiography using the SIEMENS Acuson CV/70 device were: the cardiac cavity diameters, the cardiac volumes, the ejection fraction, the shortening fraction and the interventricular septum dimensions. These results were compared with the results obtained from a 40 subject control group, having the same age but not practicing any sports at a competitive level. **Results:** It has been observed that 32.5% were underweight, 62.5% had a normal weight, and the rest were overweight. The thoracic diameters were moderately statistically correlated ($r = 0.42$) with the slight increase of telesystolic and telediastolic volumes of the left ventricle. The cardiac volumes were within normal limits for age, being correlated with the presence of pulmonary regurgitation and with the ejection fraction for the athletes exposed to a sustained effort ($r = 0.78$). **Conclusions:** The aerobic athlete effort, for young athletes practicing athletics, has ameliorated the anthropometric and the cardiac morphofunctional parameters.

Keywords: cardiac morphofunctional parameters, young athletes

THE STUDY UPON DIFFERENCES IN REACTION TIMES IN LEXICAL AND JUDGEMENT TASKS USING A PATENTED PSYCHO-VERBAL STIMULATION INTERFACE

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Objective: The study aims to assess the differences between the means psychometric reaction times (RTs) depending by gender and types of lexical and judgment tasks, using a patented psycho-verbal stimulation interface. **Methods:** The experiment used two groups of 25 males and 25 females, between 19–23 year old, students, which performed three types of lexical tasks: word recognition, letter recognition and judgment tasks on 500 words with high frequency in common language. **Results:** The results are estimated as means reaction times by female and male groups. Visual recognition and motor reaction times was superior (shorter) on male groups, letter recognition times were superior on female group and judgment times were equal on each group. **Conclusions:** Sensitive-motor times shows that manual dexterity was superior in male group, but female groups shows a higher skills in lexical-letter decoding. The equivalence in judgment reaction times shows a thinking compensation time in female group or lexical judgment implies a different strategy of lexical decoding that deny the apparently conclusion that "women it looks to be smarter than men" ?

Keywords: psychometric reaction time, psycho-verbal stimulation

THE VALIDITY OF LINGUISTIC SPECIFICITY FOR N400 COMPONENT IN COGNITIVE VISUAL EVOKED POTENTIALS TECHNIQUE

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Objective: The experiment want to demonstrate the validity of linguistic specificity for N400 component in cognitive visual evoked potentials technique whatever is the level and the strategy of decoding. **Methods:** The acquisition of visual evoked potentials was performed in Cz, Pz, Fz, Oz leads, using a group of 50 adult persons between 19–21 year old, students who made two recognition tasks using decoded of 500 strings of symbols and decoding 500 strings of letters (words and non-word) with an average number of 7 characters. EPs was analyzed in a 1000 ms interval, after it used Grand AVG function for 50 person's recordings at each task, on 17 of 100 ms interspersed intervals, looking through SPSS software using ANOVA method which assess the highest difference in amplitude for each interval. **Results:** Averaged EPs was poor in component after 300 ms for non-linguistic strings of symbols, but for linguistic stimuli it appeared a pronounced negative wave between 350–450 ms ($t = 6.25$, $p < 0.001$) and others negative and positive reverberation was present after this latency ($t = 1.10$, $p > 0.05$), especially in Fz and Pz. P300 was present on both tasks. **Conclusion:** The N400 component is related with linguistic stimuli, regardless of semantic or non-semantic types (pseudo-words) which confirm the findings of other studies.

Keywords: cognitive visual evoked potentials, N400, lexical recognition, neurosciences and biomedical engineering

SENESCENCE-ASSOCIATED CHANGES IN MITOCHONDRIAL RESPIRATION: A HIGH-RESOLUTION RESPIROMETRY STUDY

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Objective: Although it is well established that mitochondrial respiratory function gradually declines with age, age-related differences of oxidative phosphorylation mentioned the influence of different substrates. The present study was purported to compare the mitochondrial respiration rates energized with glutamate + malate (G+M) and rotenone + succinate (Rot+S), respectively, in old vs. adult rat hearts. **Methods:** To this aim, rats were randomized in two groups (n = 6/group): the senescent group and the adult group. Mitochondria were isolated by differential centrifugation and a final concentration of 0.1 mg/ml mitochondrial proteins was added in the closed chamber (37°) of the Oxygraph-2k (Oroboros Instr. Ltd.). The Substrate-Uncoupler-Inhibitor Titration (SUIT) Protocol used was as follows: complex I and complex II-dependent respiration was stimulated by G+M and Rot+S, respectively (LEAK state) and subsequent ADP (OXPHOS state) addition; cytochrome c addition evaluated the intactness of the outer mitochondrial membrane; ATP synthase was inhibited by oligomycin; non-coupled respiration was obtained by FCCP titration in steps of 0.1 μM optimal concentration (ETS capacity); respiration was inhibited with antimycin A. Oxygen concentration was maintained by intermittent H_2O_2 additions into the chamber. **Results:** The following mean values were obtained for CI dependent respiration: Leak 41.6±4.9 pmol/(s*ml) vs. 48.3±1.9 pmol/(s*ml), OXPHOS 480.17±85.2 pmol/(s*ml) vs. 673.38±32.54 pmol/(s*ml), ETS 470.43 ±63.77 pmol/(s*ml) vs. 547.95±24.02 pmol/(s*ml) and RCR 11.58±1.89 vs. 13,62±1.1. For CII dependent mitochondria the obtained data are as follows:

Leak 138.14±16.67 pmol/(s*ml) vs. 159.03±9.64 pmol/(s*ml), OXPHOS 536.71±101.8 pmol/(s*ml) vs. 630.60±25.53 pmol/(s*ml), ETS 588.08±100.78 pmol/(s*ml) vs. 667.7±28.63 pmol/(s*ml) and RCR 3.85±0.33 vs. 3.97±0.19. **Conclusion:** Our results showed an important decline for the leak state, OXPHOS capacity, ETS and RCR (as the ratio between OXPHOS and LEAK states) in the senescent group as compared to the adult group, for mitochondria energized with both complex I and complex II substrates.

Keywords: mitochondrial respiratory function, senescence, high-resolution respirometry

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CHARACTERISTICS OF SOMATOSENSORY EVOKED POTENTIALS PARAMETERS AT PROFESSIONAL HANDBALL PLAYERS

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Background: Somatosensory evoked potentials SSEPs represent a cerebral bioelectrical response of the nervous system, obtained by electrical stimulation of peripheral sensory or mixed nerve, so, being an electro-physiological method for nervous system investigation. **Objective:** Our study objective was to determine the parameters (latencies) of SSEPs waves, produced by the cortical non-specific areas, cortex of association (P30, N35, P40) at professional handball players and to compare the obtained results with the ones of sportsmen from different sport categories: volleyball, fence, in order to emphasize specific cortical plastic functional modifications induced by performance training and to outline a characteristic neurophysiologic profile for each studied sportive category. **Methods:** The studied group was formed of 21 athletes, males, homogenous regarding age (average age was 19 years), height, weight and training regime, active for between 5 and 12 years exclusively in one of the mentioned sports. SSEP responses obtained by stimulating (electric stimuli of an intensity superior by 3-4 mA to the motor threshold, a duration of 0,2 ms and a frequency of 3 Hz) the median nerve in the fist articulation (radial- carpal) bilaterally and successively, were recorded with surface electrodes placed on the scalp according to the electroencephalography 10-20 system and processed using the Nihon Kohden Neuropack MEB-9100 device. For statistical analyse was used the Student test (p values). **Results:** Obtained latencies values of the cortical non-specific areas waves at handball players, statistically compared with the ones of the entire athletes group revealed significant differences for P30 ($p = 0.037$), N35 ($p = 0.039$), P40 ($p = 0.005$) waves obtained by stimulating left hand and a statistic significant difference for P40 ($p = 0.035$) wave by stimulating both hands. For volleyball and fence subgroups, the differences reported to the entire studied lot were not statistically significant. **Conclusions:** By comparing handball subgroup with the entire group, were emphasized statistic significant differences for the wave latencies originated in the cortical non-specific areas, so the association cortex proved to be a location more functionally and plastically changed by specific sports training.

Keywords: somatosensory evoked potentials, professional handball players

THE PHOTOPROTECTIVE EFFECTS OF GRAPE SEEDS POLYPHENOLS ON SKIN EXPOSED TO MULTIPLE DOSES UVB IN SKH-1 HAIRLESS MICE

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Objective: Photochemoprevention with natural products represents a simple but very effective strategy in the management of cutaneous neoplasia. The study investigated the protective activity of red grape seeds (Vitis vinifera L, Burgund Mare variety) (BM) extracts in vivo on multiple doses of UVB-induced deleterious effects in SKH-1 mice skin. **Methods:** Sixty 8-weeks-old SKH-1 mice were divided into 6 groups: control, vehicle, UVB irradiated, vehicle + UVB irradiated, BM 2.5 mg polyphenols (PF)/cm^2 +UVB irradiated, BM 4 mg PF/cm^2 + UVB irradiated. The extract was applied topically in a dose of 2.5 mg and 4 mg polyphenols (PF)/cm^2 before each UVB exposure (240 mJ/cm^2) for 10 days consecutively. Superoxid dismutase (MnSOD), catalase (CAT) and glutathione peroxidase (GPx) activities, reduced glutathione (GSH, malondialdehyde (MDA) and Il-1β levels were determined in skin at 24 hrs after the last irradiation. Also, the generation of cyclobutane pyrimidine dimers (CPDs) and sunburn cells in skin were evaluated. **Results:** The antioxidant activity of BM extract is higher than gallic acid (kBM = 0.017, kgallic acid = 0.013). Multiple doses of UVB generated the formation of CPDs ($p < 0.0001$) and sunburn cells ($p < 0.01$), increased GPx and CAT activities respectively GSH and Il-1β levels in

skin. Twenty-four hours following the last UVB irradiation BM extract 2.5 mg PF/cm^2 inhibited UVB-induced sunburn cells (41% inhibition), restored the MnSOD activity near the control group and increased insignificantly CAT and GPx activities. The BM 4.0 mg PF/cm^2 treatment decreased GSH level ($p < 0.02$) and reduced the percentage of CPDs positive cells in skin (33% inhibition; $p < 0.01$). **Conclusions:** Our results suggest that BM extract might be a potential chemo-preventive candidate in reducing the damage induced by multiple doses of UVB in skin.

Keywords: photochemoprevention, red grape seeds

A COMPARATIVE STUDY OF LIVER MITOCHONDRIAL RESPIRATION IN ADULT VS. SENESCENT RATS

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Objective: Ageing is associated with a progressive decline in of cellular functions including the mitochondrial ones. **Methods:** To characterize the effects of ageing on mitochondrial respiration we thought to measure the respiratory rates of liver mitochondria isolated from adult (4–6 months) vs. senescent (18–20 months) Wistar rats. Liver mitochondria were isolated by differential centrifugation technique. Mitochondrial respiration was measured using a Clark-type oxygen electrode (Strathkelvin Ltd.) at 37° C in the presence of the following sequence of additions: glutamate/malate (Complex I dependent substrates) or succinate (Complex II dependent substrate in the presence of rotenone) to measure basal respiration (State 2), ADP-stimulated respiration (State 3), cytocrome c (used to assess the intactness of outer mitochondrial membrane), olygomicin (used to inhibit the ATP synthesis – State 4). Respiratory rates were expressed as natomO_2/min/mg protein and the respiratory control ratio (RCR) was calculated as the ratio of State 3 and State 4 respiratory rates. Rat liver mitochondria isolated from old animals (n = 5) showed a clear decline in the State 3 rate of respiration compared with mitochondria from mature animals (n = 7) when using either complex I (100.7±2.1 vs. 124.8±5.6, p = 0.0013) or complex II (124.3±1.9 vs. 144.0±5.9, p = 0.0085) linked substrates. The State 4 rate of respiration, which is a sensitive indicator of damage to the inner mitochondrial membrane, remained unchanged. Consequently, RCR declined in the presence of complex I (6.08±0.42 vs. 7.68±0.35, p = 0.0098) and complex II (3.27±0.12 vs. 3.85±0.19, p = 0.0298) linked substrates. Our results indicate a decline in energy production in old animals and will be further used as reference values in order to assess hepatoprotective interventions at mitochondrial level.

Keywords: liver mitochondrial respiration, energy production, hepatoprotection

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DIABETES MELLITUS AND THEIR TYPE COMPLICATIONS PREVALENCE AT PATIENTS WITH TYPE 1 DIABETES AND THYROID DISEASES

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Background: Diabetes mellitus (DM) complications are usually related to the age of diabetes and glycemic imbalance degree. Also, in diabetes mellitus type 1 are predominant microangiopathic complications, represented by retinopathy and diabetic nephropathy. **Objective:** To study the prevalence of diabetes complications and their type in patients with type 1 diabetes and thyroid disease. **Methods:** In 60 patients with type 1 diabetes and thyroid disease, 32 (31 women and 1 man) ($p < 0.001$, $X2 = 42$) had complications of diabetes. In all cases were evaluated: lipid profile: total cholesterol (TC), triglycerides (TG), HDL-cholesterol (HDL-C), LDL-cholesterol (LDL-C); glycemic balance: fasting blood glucose, glycosylated hemoglobin; investigation of the thyroid gland: TSH, FT4, FT3, thyroid antibodies, thyroid ultrasound, the eye fundus for diagnosis of diabetic retinopathy, proteinuria/ albuminuria for the diagnosis of diabetic nephropathy, systolic and diastolic blood pressure, EKG for coronary heart disease, oscillometric for diabetic arteriopathy. All investigated subjects had type 1 diabetes. **Results:** The main complications encountered in patients with type 1 diabetes and thyroid disease were diabetic polyneuropathy in 40% cases (100% F vs. 0% M, $p < 0.001$, $X2 = 48$), diabetic retinopathy in 35% cases (100% F vs. 0% M, $p < 0.001$, $X2 = 42$), coronary heart disease in 28.33% cases (100% F vs. 0% M, $p < 0.001$, $X2 = 34$), diabetic arteriopathy in 1.66% cases (0% F vs. 100% M, $p = 0.15$, $X2 = 2$), hypertension in 1.66% cases (100% F vs. 0% M, $p = 0.15$, $X2 = 2$) and diabetic nephropathy in 1.66% cases (100% F vs. 0% M, $p = 0.15$, $X2 = 2$). The presence of complications was associated with age and diabetes glycemic imbalance degree. **Conclusions:** In patients with type 1 diabetes and thyroid disease, diabetes complications were more common in women. There was an increased prevalence of coronary heart disease due to type 1 diabetes association of thyroid disease. They, especially those accompanied by hypothyroidism, is an additional risk for developing atherosclerotic cardiovascular disease. It is necessary early detection of the association between type 1 diabetes and thyroid disorders and their correct treatment for the prevention of atherosclerotic cardiovascular disease

Keywords: diabetes mellitus, thyroid diseases, cardiovascular morbidity

PREVALENCE OF METABOLIC SYNDROME AND ITS IDENTIFICATION CRITERIA BY SEX AT PATIENTS WITH IMPAIRED GLUCOSE TOLERANCE AND EUTHYROID DIFFUSE GOITER

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Background: Metabolic syndrome contains a group of disorders which determinate a higher incidence of cardiovascular diseases. **Objective:** study of metabolic syndrome prevalence at patients with impaired glucose tolerance (IGT) and euthyroid difuse goiter. **Methods:** 81 patients with IGT and euthyroid difuse goiter (76 female and 5 male), 55 (67.9%) (51 female and 4 male) had metabolic syndrome. The criteria used for identification of metabolic syndrome were: abdominal circumference (above 80 cm at girls and above 94 cm at boys), glucose concentration above 100 mg%, HDLc concentration under 40 mg% at boys and under 50 mg% at girls, blood pressure above 130/85 mmHg, triglyceride concentration above 150 mg%. We evaluated: lipid profile (total cholesterol, triglyceride, HDL cholesterol, LDL cholesterol); systolic and diastolic blood pressure; fasting glycemia; abdominal circumference and body mass index (BMI); investigation of thyroid gland: determination of TSH, FT4, FT3, antithyroid antibodies, thyroid ecography. **Results:** We noticed no significance difference between prevalence of metabolic syndrome at female and male (62.96% vs. 80%, p = 0.44, X2 = 0.59). Besides presence of IGT, the criteria used for definition of metabolic syndrome, more frequent were abdominal circumference (100%) (100%F vs. 100%M, p < 0.001), blood pressure levels (56.36%) (49.09% F vs. 100% M, p = 0.06, X2 = 3.34), HDLc concentration (72.72%) (72.54% F vs. 75% M, p = 0.74, X2 = 0.10) and triglyceride concentration (29.09%) (29.41% F vs. 25% M, p = 0.85, X2 = 0.03). **Conclusions:** Metabolic syndrome shows a higher risk of cardiovascular mortality-morbidity, especially for cardiovascular arteriosclerosis disease. The association of thyroid disease, which in time can evolves with hypothyroidism, represents a supplementary risk factor for cardiovascular arteriosclerosis disease.

Keywords: metabolic syndrome, cardiovascular morbidity

METABOLIC SYNDROME AND THE RISK OF CARDIOVASCULAR DISEASES

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Background: Metabolic syndrome is a cluster of risk factors of metabolic origin that directly promote the development of cardiovascular diseases and their complications. The common pathogenic factor to all these disorders is insulin resistance. **Objective:** Highlighting the impact of metabolic syndrome components concerning the human body, individually, especially by summing effects. **Methods:** A retrospective study concerned 159 patients hospitalized in departments such as Medical I and Diabetes Care – Nutritional Diseases (Târgu Mures County Emergency Hospital, 2007–2010, that met the diagnostic criteria established by the World Health Organization for the metabolic syndrome. Patients were divided into two groups: Group I – the main diagnostic criterion for impaired fasting glucose or impaired glucose tolerance – 77 pacients, Group II, the main diagnostic criterion – diabetes mellitus type 2 – 82 patients. Laboratory parameters followed: fasting glycemia, oral glucose tolerance test, triglyceride levels, high density lipoprotein cholesterol, total cholesterol, uric acid, body mass index (BMI), microalbuminuria, blood creatinine.Levels of fibrinogen and C-reactive protein, blood mats, electrocardiogram, echocardiography, abdominal echography, Doppler echography, retinal examination. **Results:** Of the total number the number of men was higher than that of women (60% in group I and 44% in II), 59% of patients of both sexes fell in the age group 50–59 years; to the main criterion for diagnosis is being associated in 89% of the cases to other three secondary endpoints and in 11% of cases the other two secondary endpoints; obesity was present in 96% of all patients studied; 100% of women were obese, and 13 of the second group of patients had morbid obesity (BMI > 40 kg/m^2); 68% of patients already had heart disease, more common in women and patients from group II. Instead vascular pathology is more common in males and in patients inside group II. **Conclusions:** One or two of the criteria in this syndrome is associated with increased risk of mortality from ischemic heart disease. Hypertensive women, obese and diabetic patients with age > 50 years requires careful monitoring since 100% of the patients studied suffered from ischemic heart disease; For patients in group II, type 2 diabetes specific late complications are additional factors to increase morbidity and mortality. Treatment should be initiated and maintained primarily by intensive measures of lifestyle change which is crucial for long-term therapeutic success, also by imposing regular health checks and good interdisciplinary collaboration.

Keywords: metabolic syndrome, cardiovascular risk

EFFECT OF SELENIUM ON PROINFLAMMATORY CYTOKINES AND OXIDATIVE STRESS IN HYPERTHYROIDISM-EXPERIMENTAL STUDY

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Background: Much of the reactive oxygen species production occurs in mitochondria, via oxidative phosphorylation. It is well known that mitochondria is the favorite target for the thyroid hormones. For this reason, oxidative stress is regarded as a pathogenic factor in hyperthyroidism. Selenium (Se) in the form of selenocysteine is an essential component of the family of the detoxifying enzymes glutathione peroxidase (Gpx) and of the iodothyronine selenodeiodinases that catalyze the extrathyroidal production of tri-iodothyronine (T3). Thus, Se deficiency may seriously influence the generation of free radicals, the conversion of thyroxin (T4) to T3 and a thyroidal autoimmune process. **Objective:** Our purpose was to determine the relationship between the oxidative stress and the inflammatory cytokines and to investigate how selenium influences oxidative damage and cytokine response in hyperthyroidism. **Methods:** Experiments were performed on white, male Wistar rats, divided into three experimental groups: first group-control, second group: rats intraperitoneally injected with L- thyroxin and the third group: rats rendered hyperthyroid, treated with selenium. Serummalondialdehyde (MDA), protein carbonyl groups, Selenium-glutathione peroxidase (SeGPx), thyol groups, plasma IL-6 and TNF-alpha were measured. MDA, protein carbonyl groups, IL-6 and TNF-alpha levels increased after L-thyroxin induction. SeGPx and thyol groups, representing the antioxidant defense, were found in low levels. Selenium administration led to opposite results. **Conclusions:** Our study highlighted that oxidative stress is related to cytokine response in the hyperthyroid rats. Selenium treatment suppresses the hyperthyroidism-induced oxidative damage as well as proinflammatory response. Selenium association to hyperthyroidism treatment is recommended.

Keywords: oxidative stress, selenium, hyperthyroidism

GRAPE SEEDS POLYPHENOLS EXTRACT IMPROVES COGNITIVE FUNCTION IN RATS EXPOSED TO HYPOXIA

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Background: Hypoxia can unbalance the oxidant/antioxidant equilibrium in the brain tissue, which might lead to severe psychological changes. The oxidative stress plays and important role in the pathogenic mechanism of these changes. Therefore, antioxidant supplements usually reduce the negative effects of the oxidative stress. **Methods:** Forty male Wistar rats (weight 210±15 gr), divided into four equal groups, had been used. Two groups (1, 2), have been exposed to chronic hypoxia for two weeks (simulated altitude 5500 m), in the hypobaric chamber, while the other two (3, 4), were the control groups and had been kept at normal atmospheric pressure. The animals from groups 2 and 4 received a supplement of polyphenols (c. 50 mg/kg, through gavage), daily. The oxidative stress and the antioxidant defense markers (malondialdehyde, carbonyl proteins, reduced glutathione, and hydrogen donors' capacity) have been assessed from both blood serum and brain tissue. The learning ability has been tested using a shuttle-box. **Results and conclusions:** Our study showed that the exposure to hypoxia induces a significant increase of the oxidative stress markers and decreases the learning capacity. The polyphenols supplement had no effects on the rats maintained at normal atmospheric pressure, but significantly increased the antioxidant defense and improved the learning capacity in rats exposed to hypobaric hypoxia.

Keywords: Grape seeds, polyphenols, cognitive function, rat, hypoxia

PECULIARITY OF METABOLISM IN MONOZIGOTA CONCORDANT PATIENTS WITH DENTAL FLUOROSIS

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Background: Dental fluorosis caused by long-term intake of high levels of fluoride is characterized by clinical manifestations in teeth and metabolic disturbances. Fluor is the most active halogen, which is widespread and leads to chronic oxidative stress with numerous pathological consequences. **Objective:** Comparative examination of the 4 salivary parameters in the monozigota concordant petients-sisters with severe dental fluorosis. **Material and methods:** The monozigota concordant 10 patients (20–28 years) with dental fluorosis and 16 healthy subjects were examined. In the saliva determined the contents of protein, urea, proline, and calcium (Ca^{2+}) using spectrophotometric methods (Humalyzer 2000, DE). **Results:** Examination of the monozigote concordant patients-sisters with

dental fluorosis shown the sufficient metabolic disturbances. The following difference between indices (components) were determined in the saliva of two homozigota pairs of sisters-twins: protein – 1.5 g/L and 1.60 g/L, urea – 0.672 mmol/L and 0.248 mmol/L, proline – 0.818 mmol/L and 1.203 mmol/L, calcium – 1.583 mmol/L and 1.181 mmol/L. **Conclusion:** An imbalance of salivary components of the monozigota concordant patients has been determined. In all fluoride-endemic regions it is necessary to carry out the prophylactic actions especially in the small-schools, pregnant women and feeding mothers. This prophylaxy action will decrease the risk of chronic intoxication by fluorides and correct the metabolic imbalance in the patients with fluorosis.

Keywords: dental fluorosis, monozigota concordant petients-sisters, salivary components

GLUTATHIONE REDUCTASE AND GLUTATHIONE-S-TRANSFERASE IN PATIENTS WITH MAMMARY TUMORS

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Background: In patients with mammary tumors the processes of peroxide oxidation of lipids (POL) are increased and metabolism disturbed. The enzymatic redox-system of glutathione is one of the main pathway of antioxidant defense system in the human organism. **Objective:** Comparative investigation of the glutathione reductase (GR) and glutathione-S-transferase (GST) activities in the blood plasma and leucocytes in the patients with dishormonal hyperplaziae (DH) and mammary cancer (MC). **Material and methods:** Leucocytes were separated from blood using Boyum A. method (2001). Activity of enzymes determined in 25 patients (15-DH; 10-MC) with SP methods (Humalyzer 2000) as was described (Gavriliuc L., 2008). The control group included 20 healthy adults. **Results:** Specific activity of GR in the blood plasma of DH patients was 14.83 U/g protein and in leucocytes – 30.83 U/g protein. Activity of GR in MC patients was 4.23 U/g and 18.45 U/g. Specific activity of GST in blood plasma of DH patients was 20.54 U/g and in leucocytes – 43.44 U/g; in MC patients in blood plasma – 10.20 U/g, in leucocytes – 36.49 U/g. **Conclusion:** The activities of GR and GST were significantly decreased in the blood of the BC patients in comparison with the DH patients.

Keywords: glutathione reductase activity, glutathione-S-transferase activity, dishormonal hyperplaziae, mammary cancer

CLINICAL AND PARACLINICAL STUDY AT A LOT OF HYPERTENSIVE PATIENTS IN KOSOVO AREA

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Background: High blood pressure is a major public health problem, being the most common cause of cardiovascular morbidity and mortality. **Methods:** The authors studied clinical and paraclinical at a group of 50 patients of high blood pressure (HBP) aged between 20–80 years, hospitalized in the Department of Cardiology, Hospital District "Prim Dr. Daut Mustafa"-Prizren in Kosovo for a period of four years. There have been exploring current laboratory to detect the metabolic syndrome, electrocardiogram (ECG), echocardiography with appliances NIHON KOHDEN 9020K and ALOKA 4000 determining the presence of left ventricular hypertrophy (LVH). It was monitored for systolic and diastolic arterial tension (SAT and DAT) diurnal and nocturnal, with a Holter equipment using the appliance MESA Medizintechnik GmbH. **Results:** The results of the investigation suggest that the concentric type of LVH showed 42% of studied patients, predominantly men. MAPA monitoring showed that for 32% of patients the values of daytime Systolic arterial tension (SAT) where between 170–190 mmHg. During the night we note that for the 2% of patients, SAT and DAT did not decrease; they were considered "non dipperr" and this drawing attention to the increased risk of cardiovascular morning events in these patients. **Conclusion:** This study opens perspectives for cardiovascular disease prevention project in general and for hypertension, especially in the Kosovo area.

Keywords: hypertension, blood pressure Holter monitoring, "non dipper"

EVALUATING MYOCARDIAL ISCHAEMIC PRECONDITIONING MEASURING SPONTANEOUS MECHANICAL AND ELECTRICAL ACTIVITY IN A MURINIC EX-VIVO MODEL

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Background: It has been suggested that the protective action of myocardial ischaemic preconditioning could be evaluated measuring the period of time from the beginning of a prolonged ischaemic event until the electric activity of the heart stops completely in conjunction with the period of mechanical activity (efficient contractions) **Objectives:** Our goal was to determine if the two parameters can be used to evaluate myocardial preconditioning in our laboratory setting. **Materials and methods:** The experiment was conducted in the Cardiovascular Physiology Dept. Targu-Mures between March 2010 and June 2010 using 30 Wistar rats randomised in two groups: with IPC (n = 15) and without IPC (control) (n = 15). The animals were anesthetized, iv anticoagulant was given and the hearts were carefully excised. The aorta was cannulated and Krebs-Hanseleit solution was perfused in a retrograde fashion using the Langendorff apparatus. All hearts in the IPC group were subjected to a preconditioning protocol consisting of 5 min. of ischaemia followed by 5 min. of reperfusion before a sustained period of ischaemia (30 min). The control group only received a 30 min. period of ischaemic injury. **Results:** Regarding the mechanical activity of the heart we did not find a significant difference between the two groups (p = 0.08). The period in which the hearts maintained a measurable electric activity after the prolonged ischaemic insult differed significantly (p = 0.01). **Conclusion:** We concluded that the mechanical activity of rat hearts is not useful for evaluating ischaemic preconditioning. On the other hand, electric activity can be used for the purpose of quantifying preconditioning effect of ischaemia.

Keywords: myocardial ischaemia, preconditioning, mechanical activity, electric activity

MODIFICATIONS OF SPIROGRAPHIC PARAMETERS IN PATIENTS WITH PARKINSON'S DISEASE

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Background: Respiratory dysfunction in patients with Parkinson's disease (PD) is a result of abnormalities in ventilatory control and due to treatment effects. **Objective:** The aim of this study is to evaluate the relationship between PD and the pulmonary function. **Method:** 20 patients diagnosed with PD and 20 patients without respiratory problems (C) of the same age and height as those with PD were included in this study. The symptoms of the disease and disability were evaluated by means of the Unified Parkinson's Disease Rating Scale (UPDRS). Pulmonary functions were determined by computerized spirometry: forced vital capacity (FVC), forced expiratory volume in 1s (FEV_1), peak expiratory flow (PEF), maximal expiratory flow at 50% from vital capacity (MEF_{50}). Respiratory muscle force was measured by the maximal inspiratory (MIP) and expiratory pressure (MEP). **Results:** The study has shown a statistically significant decrease of spirographic parameters FVC% in PD was 87.72±7.1 vs C – 95.7±7.7 ($p < 0.0001$), FEV_1% PD – 88.6±7.5 vs C – 92.13±6.7 ($p < 0.01$); PEF PD – 6.74±1.47 l/s vs C – 8.1±2.07 l/s ($p < 0.001$); MEF_{50} PD – 4.11±1.1 l/s vs C – .97±0.8 l/s ($p < 0.01$) in patients with over 5 years of evolution of PD, by comparison with the control group. Decrease of FEV_1 but with normal Tiffeneau index proved an restrictive pulmonary dysfunction in PD patients. Mean MIP and MEP was below normal in 32% of PD patients. MIP and MEP values correlated negatively with bradykinesia and UPDRS scores. **Conclusions:** PD patients have pulmonary dysfunction determined by the disturbances in respiratory muscle force. This should be taken into consideration in the rehabilitation of PD patients.

Keywords: Parkinson's disease, maximal inspiratory pressure, maximal expiratory pressure

RENAL DYSFUNCTION PROLONGS THE QT INTERVAL IN HYPERTENSIVE PATIENTS

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Background: The QT interval, measured on the surface electrocardiogram, partially indicates the duration of ventricular depolarization and repolarization. Recent studies have confirmed the value of QT interval as mortality predictor in hypertensive patients. **Objective:** The aim of the study was to explore the QT interval in hypertensive patients with renal dysfunction. **Method:** 50 patients with hypertension were included in our study. In all patients there were measured the following biochemical parameters: glycemia, cholesterol, HDL cholesterol, triglycerides, glomerular filtration rate (GFR), blood urea nitrogen, serum creatinine, serum uric acid,

and 12-lead resting ECG were recorded. QT interval was calculated by Atria 3100 interpretive electrocardiograph. The QTc was determined with Bazett's formula, and a value exceeding 440 msec. was considered prolonged. QT dispersion, defined as the longest QT interval minus the shortest QT interval and a value exceeding 50 msec. was considered abnormal. We compared biochemical parameters in hypertension with (31 patients) and without (19 patients) prolonged QTc. **Results:** QTc prolongation (451.9±32.31 ms) was observed in 62% hypertension patients by comparison with 38% hypertension with normal QTc 425.2±24.6 ms ($p < 0.01$). We found higher values for glycemia 126.8±31.6 mg/dl vs 96.2±15.2 mg/dl, ($p < 0.01$), triglycerides 177.5±51.2 mg/dl vs 132±11.5 mg/dl ($p < 0.05$), creatinine 1.28±0.21 mg/dl vs 0.82±0,25 mg/dl, ($p < 0.01$), urea 64.5 ±11.6 mg/dl vs 32±6.8 mg/dl, ($p < 0.001$), QTd 52.6±5.65 ms vs 49.32±10.21 ms, ($p < 0.05$) in hypertensive patients with a prolonged QTc, compared to the patients with QTc in normal limit. GRF values was lower 72±12 ml/min vs 111±25 ml/min $p < 0.001$ in hypertensive patients with a prolonged QTc, compared to the patients with QTc in normal limit. **Conclusion:** Hypertensive patients with impaired renal function have increased QTc. This finding suggests that such patients have a greater inhomogeneity of repolarization and QT interval can become a mortality predictor in hypertensive patients with renal dysfunction.

Keywords: QTc prolongation, impaired renal function, hypertension

DEVELOPMENT OF A SIMPLIFIED COMPUTATIONAL MODEL OF HIPPOCAMPAL CA1 PYRAMIDAL NEURONS

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Background: The hippocampus is involved in memory formation for facts and events. Because of its low seizure threshold and its possible role in Alzheimer disease and schizophrenia, the hippocampal region is of particular interest for researchers and clinicians as well. The main output of the hippocampus is through area CA1 pyramidal cells, thus understanding the integrative properties of this neuron type is particularly important. Besides the experimental techniques in neuroscience, a large number of computational studies have been published involving CA1 pyramidal neurons. **Objective:** The aim of our study was to develop a model of CA1 pyramidal neurons that reproduces the experimentally observed main firing properties, with relatively low computational effort. **Material and methods:** We constructed a compartmental model of a pyramidal neuron with simplified geometry, composed of 15 compartments using the NEURON program. Active conductances were implemented in the soma, axon and dendrites (Na^+ current, K^+ current of DR, A, M and AHP type, h current, T type Ca^{2+} current and an intracellular Ca^{2+} buffer shell). **Results:** We compared our model with other computational models and experimental data, and demonstrated that it could reproduce the main firing properties of the CA1 pyramidal neurons (maximal firing frequency, spike frequency adaptation, characteristics of the action potentials and action potential back-propagation in the dendrites), with lower computational cost then the models published so far. In **conclusion**, our model is suitable to be incorporated in large neural network simulations.

Keywords: hippocampus, pyramidal neuron, compartmental model

COMPARABLE CARDIOPROTECTIVE EFFECTS OF MAGNESIUM OROTATE AND OROTIC ACID AT REPERFUSION IN ISOLATED RAT HEARTS

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Background: Acute administration of magnesium orotate (Mg-Or) at reperfusion has been previously shown to elicit significant protection in isolated rat hearts. It has been also reported that magnesium has a cardioprotective effect in experimental ischemia-reperfusion models. **Objective:** The aim of the present study performed in Langendorff perfused rat hearts was to compare the effects of 1 mM magnesium orotate (Mg-Or), orotic acid (OA) and magnesium chloride ($MgCl_2$), respectively when given throughout the postischaemic reperfusion on cardiac functional parameters and infarct size. **Methods:** Recovery of post-ischaemic ventricular function was assessed by the left ventricular developed pressure (LVDP) and the maximal and minimal first derivatives of left ventricular pressure and (dLVP/dtmax and LVP/dtmin) as indices of contractility and relaxation. Infarct size was quantified by the 2,3,5-triphenyltetrazolium chloride staining. All contractile parameters were expressed as percentage of their pre-ischaemic values. **Results:** Mg-Or induced a substantial improvement in functional recovery comparable to the one elicited by OA for all functional parameters: LVDP: Mg-Or 67.83±2.75%, OA 67±1.52%, vs. Control 39.2±3.21%, $p < 0.001$; dPdtmax: 61.5±2.79% vs. Control 38.8±4.63%, $p < 0.01$; dPdtmin (OA 75±7%, $p < 0.05$, Mg-Or 72±4.45%, $p < 0.01$, vs. Control 47.6±4.61%). When considering the infarct size, the most important antinecrotic effect was obtained for 1 mM Mg-Or comparing to Control (Mg-O 32.07±1.8% vs. Control 70.4±3.7%, $p < 0.001$) suggesting an augmentation of beneficial effects of orotic acid by magnesium. In contrast, magnesium chloride administrated at reperfusion did not show a significant recovery of any functional parameter or anti-infarct protection. **Conclusion:**

Both magnesium orotate and orotic acid (1 mM) administrated at reperfusion elicited beneficial effects on contractile parameters and infarct size that could not be recapitulated for the same concentration of magnesium chloride.

Keywords: isolated rat heart, cardioprotection, magnesium orotate

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OXIDATIVE STRESS AND DNA DAMAGE IN THE PERILESIONAL AREA OF YOUNG VS AGED POST-STROKE RATS. A GENOMIC APPROACH.

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Background: Aging is a high risk factor for stroke wherein oxidative stress triggers brain cell death. **Method:** We employed microarray and real time qPCR to evaluate several gene sets encoding oxidative stress, antioxidant and DNA damage response proteins in the perilesional area of post-stroke young and aged rat brains. By using GeneChip Rat Genome 230 2.0 Arrays (Affymetrix) expression profiling we found that generally, the old rats had more up- but also down-regulated genes related to the genomic response to DNA damage and oxidative stress and the difference increased by day 14. **Results:** Oxidative stress will initiate DNA damage and repair process supported by many genes. Of these we mention new genes implicated in telomere maintenance like Tpp1 and Rtel1 or genes that are involved in DNA repair and cellular response to DNA damage like Bhlhb3 and Immt1. Among genes involved in DNA damage and repair we noted the up-regulation of new genes like P4hb, Tpp1 and Rtel1. Finally, we mention a new gene activated in response to DNA damage in eukaryotic cells that activates cell cycle checkpoints, Mapkapk2. The oxidative stress in stroke is closely related to inflammatory response. Txnip (thioredoxin interacting protein) is, along with Interleukin-1beta (IL-1beta), reactive oxygen species (ROS), and thioredoxin-interacting protein (TXNIP), part of the NLRP3 inflammasome are all implicated in the pathogenesis of type 2 diabetes mellitus. The levels of Txnip increased from 2- to 4-fold from day 3 to day 14 after stroke in both age groups. New genes tightly associated with the anti-oxidant response are Brca1, Maff and Mt1a. Brca1 (breast cancer 1) is a breast cancer susceptibility gene recently involved in antioxidant-response gene expression and protects cells against oxidative stress. Small Maff play critical roles in the Nrf2-mediated activation of antioxidant response element (ARE)-dependent genes. Accordingly, the expression of Maff (v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)) was highly up-regulated (10- to 11-fold) during the acute phase of stroke in both age groups. Thereafter the expression of Maff was kept significantly up-regulated (5.3-fold) in the infarcted area of aged rats only. **Conclusion:** Old rats have to cope with a persistent oxidative stress milieu on a background of a strong inflammatory reaction to stroke.

Keywords: oxidative stress, DNA damage, stroke, rats

ANGIOTENSIN-CONVERTING ENZYME GENE I/D POLYMORPHISM IN MOLDAVIAN PATIENTS WITH ISCHEMIC STROKE

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Objective: The aim of the study was to assess whether the carrying of I/D polymorphism angiotensin-converting enzyme ACE gene is changed may influence depend of age and sex in the development of ischemic stroke (IS) in the population from Republic of Moldova. **Material and methods:** The ACE I/D polymorphism was examined by PCR in 156 subjects with IS and in 90 control subjects. The frequency of ACE genotypes (II, ID and DD) in the patient group was assessed in subgroups divided on the basis of blood pressure, age and sex. **Results:** The frequency of D allele was 63.8% in patients and 43.3% in controls (x2 = 1.76, p = 0.19). The frequencies of the genotypes of the ACE gene were II: 20.8%, ID: 49.4% and DD: 29.9% in patients, and II: 23.6%, ID: 56.2% and DD: 2.2% in controls (x2 = 2.70, p = 0.26). A statistically significant increase in the frequency of ACE DD genotypes has been found only in male patients at age 32–56 years (OR = 3.53; range 1.05–11.86, x2 = 4.90, p = 0.03) when compared to the remaining ACE genotypes (ID and II) and the control. No increase in ACE DD genotype frequency was seen in females and male with age 57–72 years, when compared with the respective control group. Moreover we have found decreasing in total of the D allele frequency in the group with age 57–72 years (x2 = 4.96, p = 0.02) till 43.7% compared with IS at age 32–56 years, which carried in 60.6%. Also we have reported positive association of ACE D allele and hypertension between male carriers. The frequency of D allele (60%) in hypertensive group of male carriers is more prevalent compared with female patients (50%) and male carriers of control group (48.4%) (x2 = 3.62, p =

0.04). Moreover there are positive correlations between D allele carrying with total cholesterol (r = 0.24, p = 0.03), triglycerides (r = 0.26, p = 0.02) and VLDL (r = 0.25, p = 0.02). **Conclusions:** The determination of D allele carrying in clinical practice could be helpful for prevention of the hypertension and ischemic stroke between young and middle age men.

Keywords: angiotensin-converting enzyme gene I/D polymorphism, stroke

SINGLE WALLED CARBON NANOTUBES FUNCTIONALIZED WITH SINGLE STRAND DNA EFFECTS OVER REDOX BALANCE. AN IN VITRO AND IN VIVO STUDY.

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Background: Single wall carbon nanotubes (SWCNT) represent a material of high medical interest. Recent in vitro studies showed increased oxygen free radical production after cells exposure to SWCNT. However, reports regarding in vivo effects of SWCNT over redox balance as well as concentration effect over in vitro and in vitro SWCNT toxicity are still scarce. **Objective:** Our aim was to evaluate the in vitro and in vivo induced by various concentrations of SWCNT functionalized with single strand DNA (ssDNA- SWCNT) solutions. **Material and methods:** ss-DNA-SWCNT water solution was obtained through sonication. In vitro experiments were carried out on Hep G2 cell line. 5, 10 and 20 mg/L concentrated solutions were prepared. MTT assay and 5-(and-6)-carboxy-2-',7'-dichlorofluorescein diacetate (DCFDA) assay were performed. In vivo experiments were carried out on male Wistar rats (170±10 g), i.p. injected with 1.5 ml single walled ss-DNA-SWCNT solutions of different concentrations (70 g/l, 250 g/l, 390 g/l). Controls were similarly i.p injected with 1.5 ml serum. Malondialdehyde (MDA), carbonylated proteins (PC), hydrogen donor ability (HD), sulfhydryl groups (SH) were assessed at 3, 6, 24 and respectively 48 hours after the SWCNT administration. **Results:** We obtained a significant in vitro and in vivo alterations of oxidative balance peaking at 24 hours from administration. ($p < 0.05$). Results show significant dependence of observed effects on concentration. At 48 hours from exposure, levels of the analyzed markers remained altered. **Conclusion:** Our results support the ability of ss-DNA-SWCNT to generate oxidative stress, the pattern of alterations depending on the concentration of SWCNT solutions.

Keywords: single wall carbon nanotubes, oxidative stress

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TPEAK-TEND INTERVAL, ISOINTEGRAL MULTIPOLAR QRST MAPS AND QT INTERVALS IN POSTINFARCTION HEART FAILURE PATIENTS

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Background: Tpeak-Tend interval (Tpe), a measure of transmural dispersion of repolarization, is considered the best predictor of life-threatening ventricular arrhythmias. **Hypothesis:** It was hypothesized that Tpe correlates with other noninvasive predictors of ventricular arrhythmia. **Methods:** A total of 35 postinfarction heart failure patients were included in the study. They underwent standard 12-lead ECG and 64-lead body surface mapping. Isointegral QRST maps were obtained for each patient. QTmax (maximal QT interval duration in all 12 ECG leads), QTc (heart rate corrected QT interval), QTm (mean QT interval duration in all measurable leads), QTd (QT dispersion: the difference between maximal and minimal QT interval duration), Tpe (Tpeak–Tend interval), T0e (T wave duration) and Ta (T wave amplitude) were manually assessed. **Results:** QTmax and QTc were prolonged in 86% and 71% of the patients, respectively. Tpe significantly correlated ($p < 0.01$) with: mulipolar maps (Bravais Pearson correlation coefficient r = 0.65), QTmax (r = 0.45) and QTm (r = 0.34). Multiple regression analysis revealed a significant association of Tpe ($F < 0.01$, Multiple R = 0.99) with multipolar isointegral maps, QTmax, QTc, QTm, QTd and heart rate. **Conclusion:** Tpe can be predicted using multipolar isointegral QRST maps, QT intervals and QTd in postinfarction heart failure patients.

Keywords: Tpeak-Tend interval, Tpeak-Tend interval, postinfarction heart failure

IN VITRO MODEL OF SUSTAINED REENTRY INDUCED IN PATTERNED CULTURES OF VENTRICULAR NEONATAL RAT MYOCYTES

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Background: Altered conduction of the action potential in the heart may result in sustained reentry that leads to tachyarrhythmias. Thus, a better understanding of how a reentrant excitation could be initiated and stopped is of critical importance for the diagnosis and therapy of these life threatening disorders. We present here an in vitro model of reentry induced in anatomical circuits of myocytes. **Method:** Ventricular myocytes isolated from neonatal rats were cultured in the shape of a ring (length = 3.3 cm, width = 0.6 cm) on mycoelectrode arrays (MEAs) equipped with both stimulating and recording electrodes. After 3–5 days of incubation, reentry was induced following asynchronous electrical stimulation at two sites in a manner that generated unidirectional conduction. The head and the tail of the reentrant wave were critically close due to the chosen length of the circuit. **Results:** In 11 out of 14 preparations, reentry was induced and persisted for many hours with a very stable conduction velocity. Elevated potassium in the culture medium and the sodium channel blocker lidocaine reduced the conduction velocity with about 70% but failed in terminating reentry. The increase of AP duration with BayK or barium caused a moderate increase in cycle length without stopping reentry. **Conclusions:** Our model allows the monitoring of reentry for long periods of time under various conditions (pacing, antiarrhythmic drugs, diverse patterns of the reentrant circuit).

Keywords: in vitro model of sustained reentry

THE STUDY OF FOOT STABILITY ON THE BASIS OF GAIT BIOMECHANICAL ANALYSIS AND EVALUATION IN MULTIPLE SCLEROSIS

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Background: Stability and motor disorders are clinical manifestations prevalent in multiple sclerosis (MS). Foot stability refers to the general position of the foot, especially during the propulsive phase, on which the foot striking during the next gait cycle entirely depends. **Methods:** There were studied 20 subjects with MS, who were previuosly evaluated clinically, functionally and paraclinically from neurological point of view and were divided into two subgroups: subgroup A – with clinically detectable gait disorders (13 patients) and subgroup B – without clinically detectable gait disorders (7 patients). To complete clinical and paraclinical data we proposed the study of foot stability through biomechanical gait analysis and evaluation using RSScan system. **Results:** We noticed a disturbance of foot stability at all patients from subgroup A as well as their lack of tendency to reach a neutral position. We also observed a billateral and complementary disturbance of foot stability at subgroup A, meaning the presence of supination at one foot and pronation at the counterlateral foot. As far as the patients belonging to subgroup B are concerned, we determined the presence of a supination with values within -59° and -10°, as a significant functional element, in each of the three gait phases studied. **Conclusion:** Objective analysis of biomechanical parameters led us to the conclusion that, despite the fact that the patients were clinically divided into two subgroups: with or without gait disorders, there were yet determined subclinical disturbances, detectable only through Kinetic analysis.

Keywords: multiple sclerosis, motor disorders

CORRELATION NO – TOTAL ANTIOXIDANT CAPACITY, LABORATORY TESTS WITH MARKERS POTENTIAL IN EVOLUTION OF POST-COMBUSTION WOUNDS

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Background: The accumulation of free radicals (O_2 and nitrogen) strongly decreases the total antioxidant capacity of plasma (TAOP), which together activates the intracellular contraction force that breaks the cytoplasm and cellular membranes. **Methods:** We realized our study upon healthy, young-volunteers subjects (group A), comparatively with surgical patients with burned body surface (group

B) from Plastic and Reconstructive Surgery Department of the Emergency County Hospital of Craiova. Patients from all groups received: crystalloidal solutions, colloidal solutions and the patients from group B received only a restrictive transfusion to restore the hematological values of hemoglobin. For each group we determined the values of leukocytes, thrombocytes, coagulability index, TAOP and nitric oxide after each of the three transfusions made. We used Oczan Erel technique to obtain all the values for oxidative stress evaluation: TAOP, free radicals, oxidative stress index. **Results:** After the first transfusion, 70% of cases belonging to group B, developed a hypercoagulability. We also observed great fluctuations of thrombocytes count in group B, independently associated with TAOP values. The total antioxidant capacity and free radical reactions of group B increased. In group B, the values of ROS increased progressively from the first to the third transfusion, inducing an excessive consumption of endogenous antioxidants. The production of NO decreased, which explained the appearance of vasoconstriction and intravascular coagulation, associated with oxidative stress, especially in patients with bad evolution from group B. **Conclusions:** NO has a good effect in normotensive and normoperfused patients, assuring the red cells to enter into peripheral tissues, because of peripheral vasodilatation. NO overproduction installs at the same time with oxidative stress, strongly decreasing TAOP values, which are predictive. That is why it is considered one of the golden standard test.

Keywords: total antioxidant capacity of plasma, combustion wounds

STUDY OF LEUKOCYTE ROLLING AND ADHESION AFTER INCUBATION WITH INFLAMMATORY MEDIATORS OF ENDOTHELIAL CELLS DIFFERENTIATED FROM HUMAN HEMATOPOIETIC STEM CELLS

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Objectives: 1. Isolation of hematopoietic stem cells (HSC) from human bone marrow and differentiation toward endothelial lineage. 2. Behavior study of endothelial cells (EC) obtained in culture using expression analysis of adhesion molecules (ECAM) inducible on EC surface after incubation with inflammatory mediators. **Materials and methods:** HSC were isolated from human bone marrow using MACS–direct AC133 progenitor cell isolation kit and cells were cultured on specific media. HSC differentiation toward endothelial lineage was induced by VEGF. In order to validate the endothelial morphological characteristics was used contrast phase microscopy and immunohistochemical analysis of CD31 and von Willebrand factor. We analyzed the expression of ECAM by flow-cytometry, when EC were incubated with inflammatory mediators, administered in similar concentrations to those generated in vivo. **Results:** Utilization of VEGF supplemented media can induce transformation of HSC in EC. Our study reveals that, in basal conditions, EC expressed only CD54 and expression of other adhesion molecules (VCAM-1, E-selectin, P-selectin) are considered insignificant. The incubation of EC with TNFα, LPS or H_2O_2 was found that the expression of ECAM did not change compared with basal conditions. In case of cells pretreatment with TNFα or LPS, before incubation with H_2O_2, the expression of ECAM were not statistically significant change compared with basal conditions. This observation suggests that these cells present an impairment of leukocyte rolling and adhesion after a previous action of inflammatory mediators. These results suggest that EC does not behave as mature functional cells (EC-like). **Conclusions:** Positive selection using MACS-direct CD133 progenitor isolation kit is a very good method for HSC isolation. Cell culture and expansion of HSC in VEGF medium lead to occurrence of EC-like within 4 weeks. The resulting EC-like are functionally immature.

Keywords: hematopoietic stem cells, differentiation, endothelial lineage, adhesion molecules, inflammatory mediators

A POSIBLE MECHANISM INVOLVED IN THE GENERATION OF LIVER FIBROSIS AFTER BILE DUCT LIGATION IN WISTAR RATS

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Background: Bile duct ligation (BDL) is a viable model for the evaluation of the dynamic process of liver fibrosis from incipient lesions to cirrhosis. **Objective:** The aim of our study was to evaluate different parameters in the liver at an early stage of cholestasis and a late stage of cirrhosis in order to decipher the mechanisms involved in different stages of fibrosis. **Materials and methods:** We divided 30 female Wistar rats in three groups: 1 Control group, 2 (BDL – 7 days) the animals were sacrificed after 7 days after bile duct ligation was performed, and 3 (BDL – 100 days) respectively after 100 days. The following parameters were measured in the liver and plasma: malondialdehyde (MDA), carbonylated protein (CP), glutathione (GLUT), total SH groupings, nitric oxide (NO), γ-glutamyltransferase (GGT), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) and TGF-beta. A descriptive histopathological examination and 2D and Doppler ultrasound evaluation were also performed. **Results:** BDL induced an increase in the levels of MDA, PC, NO after 100 days ($p < 0.001$). After 7 days MDA and NO were increased but not significantly. GGT was

very high after 7 days; after 100 days it returned to baseline. TGF-beta had an ascendant trend being significantly higher after 7 days ($p < 0.05$) and even more so after 100 days ($p < 0.001$). We confirmed the hepatic lesions specific to cirrhosis both by histopathogical exam and ultrasound. **Conclusion:** BDL induces significant oxidative stress and nitrosative stress; their levels escalate in time confirming their implication in the pathological mechanism of fibrosis.

Keywords: bile duct ligation, oxidative stress, nitrosative stress, liver fibrosis

KERNICTERUS OCCURRENCE FREQUENCY IN HEMOLYTIC NEWBORN DISEASE THROUGH ALLOIMMUNIZATION IN ABO AND RH SYSTEM

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Objective: The aim of this study is to establish the frequency of kernicterus in hemolytic newborn disease through alloimmunization in ABO and Rh system. **Methods:** We conducted a retrospective study for a six months time span in The Neonatology Clinic of Constanta County Hospital. The study was performed on 1800 children. Fifteen of these children had the diagnosis of hemolytic disease of newborn through alloimmunization in ABO and Rh system. Kernicterus has developed in two of the children, both having the indication for exchange transfusion. Only one of the children benefited from the transfusion. For all 15 diagnosed cases, the following tests were performed: red blood cells count, hemoglobin determination, hematocrit, total, direct and indirect bilirubin, direct Coombs test, blood smear. **Results:** The results revealed a quick evolution toward normal levels for bilirubin and hemoglobin after exchange transfusion, with a rapid decrease of the neurotoxicity risk represented by high bilirubin level. In **conclusion**, in hemolytic disease of newborn through alloimmunization in the ABO and Rh system, the frequency of kernicterus occurrence requires a quick therapeutic approach. We have to take in consideration the fact that the exchange transfusion is an invasive method that can involve many possible complications. Nowadays, the use of i.v. immunoglobulins has decreased the frequency of exchange transfusion, thus reducing the associated risks.

Keywords: hemolytic newborn disease, kernicterus

THROMBELASTOGRAPHIC STUDIES ON PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Objective and Methods: Our study was performed in The Cardiology Clinic of Constanta County Hospital, with the purpose of monitoring and enhancing the changes in the mechanisms of hemostasis recorded using thrombelastography on two groups of patients diagnosed with acute myocardial infarction receiving streptokinase and heparin. **Results:** The results obtained revealed a superior effectiveness in thrombolytic treatment compared to the heparin treatment for obtaining the status of sudden yet so necessary hypocoagulation in order to prevent the thrombotic complications associated with myocardial infarction. Thrombelastography allowed a much more accurate and fast assessment of changes in the hemostasis mechanisms compared to the normal hemostasis tests. Also, the thrombelastographic studies evaluated the existing hemorrhagic risk in these patients, with the best therapeutic management indication. **Conclusion:** In conclusion, monitoring patients with the help of thrombelastography decreases the risk of thrombotic events and prevents hemorrhagic complications. The thrombelastography is a non-invasive and very fast method that allows the accurate observation of changes in the hemostasis mechanisms.

Keywords: thrombelastography, acute myocardial infarction

HIPPOCAMPAL EPILEPTOGENESIS ASSESSED BY IN VIVO ELECTROPHYSIOLOGY, MOLECULAR CELL BIOLOGY AND COMPUTER MODELING

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Background: Epilepsy causes both suffering and stigmatization of patients and relatives representing in the same time an important socio-economic burden for the society. The number of people affected indirectly by this disease (i.e. family members, etc) is actually

much higher. Almost indifferently of the type of epilepsy the disease will lead to psychopathological complications (hiposexuality, memory loss, depression) as well as the stigmatization of the patients. Thus epilepsy causes an important socio-economic burden as well as affecting the quality of life for both patients and relatives. Therefore revealing the mechanisms of epileptogenesis and creating new drug targets is essential and it is worth the intellectual and financial effort. Seizure activity reflects the hypersynchrony of a local neuronal network that ultimately recruits adjacent networks until the activity generalizes. Epileptogenesis produces permanent changes in excitatory and inhibitory transmission, which can be reproduced by kindling. **Objective:** Our goal was to develop a complex epileptic model, which is relevant for the epileptic process and also allows us to study the functional and morphological changes associated with epileptogenesis. **Methods:** In this regard we used Wistar rats with recording electrodes implanted into the hippocampus and premotor cortex (bilateral) as well as a bipolar stimulating electrode into the lateral nucleus of the amygdala. After postsurgical healing we used a modified kindling model to gradually elicit epilepsy while recording the electrical activity and behavior (video) of freely moving animals. **Results:** By repeating daily the stimulation protocol, we gradually achieved 5th grade seizures (according to Racine scale, corresponding to secondary generalized seizures in humans). Next, we proceeded with stimulation (overkindling) until spontaneous seizures occurred. Animals were than sacrificed and brain slices were prepared for immunohistochemistry. Double immunofluorescent imaging was used in order to differentiate between changes regarding perisomatic and dendritic inhibition. **Conclusion:** The implemented model proved to be a valuable tool for correlated morphological and electrophysiological analysis of changes induced during epileptogenesis.

Keywords: epilepsy, epileptogenesis, hippocampus, in vivo, electrophysiology

DENDRITIC CELLS RESPONSE TO IN VITRO ALLERGEN CHALLENGE

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Background: The physiologic role of DCs is to perform a continuous survey of the antigen-exposed sites of the body, and to orientate the response to an antigen towards an immunogenic or a tolerogenic pathway. They play an important role in the pathogenesis of allergic disorders through their ability to initiatiate the Th2 immune response. The aim of study was to evaluate the in vitro effect of Der p 1, the major allergen of Dermatophagoides pteronyssinus, on IL-4, IL-13 and IFN-γ production by monocyte-derived dendritic cells (DCs) and by naive CD4+ T cells co-cultured with DCs from house dust mites (HDM) allergic patients and their influence in total IgE synthesis, in comparison with the healthy donors. **Method:** CD14+ monocytes were isolated from the venous peripheral blood of HDM allergic patients and differentiated to immature DCs using GM-CSF and IL-4. Generated DCs were pulsed for 24 hours with Der p 1. Pulsed DCs were then co-cultured with the autologous naive CD4+ T cells for 24 hours. Supernatants removed after each phase were assayed for IL-4, IL-13 and IFN-γ levels, as well as for the induction of IL-10 and IL-12 synthesis. Total serum IgE was measured by electrochemiluminescence. **Results:** Der p 1 up-regulates CD86 and CD83 expression on DCs from allergic patients and is associated with a higher production of IL-10 (58.81±14.48 pg/ml), a promoter of Th2 response. IL-13 production (10.18±12.208 pg/ml) by Der p 1 pulsed DCs significantly correlates with total serum IgE (R-square = 0.704, p = 0.026), while IL-4 production (14.12±12.546 pg/ml) does not. Naive T cells stimulated by autologous Der p1 pulsed DCs produced IL-4 (5.576±8.061 pg/ml), showing a stronger correlation than that between IL-13 (8.177±7.795 pg/ml) and total serum IgE (R-square = 0.886, p = 0.039). In contrast, T cells from healthy donors secreted significant higher levels of IFN-γ (32.71±10.73 pg/ml) ($p < 0.001$). **Conclusions:** The up-regulation of total IgE synthesis is highly related to both IL-4 and IL-13 in HDM allergic patients. Der p 1 up-regulates different surface markers expression on DCs in allergic patients, and in healthy donors. Autologous naive T cells from allergic patients in coculture with Der p 1-pulsed DCs induced higher IL-4 production than in healthy donors. The modulation of immune response and the establishment of the balance between allergy and tolerance against an allergen are close dependent on the immune status of the individual.

Keywords: dendritic cells response, house dust mites, allergic patients

EVALUATION OF THE HEPATIC OXIDATIVE STRESS IN METABOLIC SYNDROME

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Background: Today, non alchoholic fatty liver disease is considered the impact of the metabolic syndrome on liver. Non alcoholic fatty liver disease represents a spectrum of liver injuries beginning to simple steatosis – nonalcoholic fatty liver, NAFL –, going through nonalcoholic steatohepatitis – NASH – and finishing to cirrhosis. The trigger of disease seems to be the lipid overload of the hepa-

tocytes, which creates an imbalance between the antioxidative capacity of the liver and oxidative aggression. Thus, reactive oxygen species in excess lead to lipid peroxidation, inflammation and fibrogenesis. **Objective and Methods:** In order to elucidate the early metabolic syndrom impact on liver, we evaluated the level of oxidative stress in NAFLD patients. Oxidative stress was expressed as plasma carbonyls, malondialdehyde, total glutahion, superoxiddismutase and catalase antioxidant activity determination. **Results:** The parameters of oxidative stress (plasma carbonyls, and malondialdehyde) were significantly increases in NAFLD subjects compared to healthy subjects. Instead, the antioxidant enzyme activity and total glutahion were significantly reduced ($p < 0.05$). Extended data will be necessary to give consistency and to integrate these results in clinical approach of the metabolic syndrome.

Keywords: oxidative stress, non alchoholic fatty liver disease

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OXIDATIVE STRESS AND NITRIC OXIDE IN CHRONIC PERIODONTITIS

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Background and Objective: The majority of tissue destruction in periodontitis is considered to be the result of an aberrant inflammatory/immune response to microbial plaque adjacent to the gingival margin and to involve prolonged release of neutrophil enzymes, reactive oxygen species (ROS) and reactive nitrogen species (RNI). Based on the pathogenetic mechanisms, the novel therapeutic approaches have changed the trend towards pharmacologic modulation of exaggerated host response, namely host modulatory therapy (HMT), in addition to microbial elimination. Therefore, in the present study we aimed to evaluate oxidative stress in patients with chronic marginal periodontitis before and after the treatment. **Methods:** Blood samples were harvested from 76 patients with chronic marginal periodontitis and 20 healthy volunteers. Oxidative stress evaluation was done by total oxidative status (TOS), total antioxidative reactivity, malondialdehyde (MDA), protein carbonyl, total sulfhydryl (SH) groups and glutathione (GSH). Nitric oxide synthesis was evaluated systemically through its serum metabolites nitrites/nitrates (Griess). Tests were performed before the treatment, after root scaling and after surgical treatment. **Results:** Systemic nitrite/nitrate and total oxidative status increased significantly and correlated with disease severity compared to the control group. TOS was reduced by both treatments, TAR increased only after the root scaling, but oxidative index decreased after both treatments. MDA and GSH were not significantly influenced, PC and SH decreased only after the surgical treatment. NO synthesis was lowered by the surgical treatment. **Conclusions:** 1. In chronic marginal periodontitis ROS and NO synthesis increase in correlation with disease severity. 2. Oxidative stress and NO synthesis were reduced mostly after the surgical treatment. 3. TAR was improved by the root scaling.

Keywords: oxidative stress, chronic periodontitis

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CHARACTERIZATION OF STEM CELLS OF DIFFERENT ORIGINS

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Background: Bone marrow-derived mesenchymal stem cells (MSCs) have long been considered as prototype of stem cells with marked proliferative potential, increased plastic ability, and presence of certain surface molecules. **Objective:** We isolated and cultured stem cells from different sources – bone marrow, dental pulp, skeletal muscle and umbilical cord – and comparatively analyzed their characteristics. **Materials and methods:** Tissue samples were processed using enzymatic digestion (Collagenase IA) or explant method, and adherent, fibroblastic-like cells were cultured in DMEM/F12 medium supplemented with 10% FCS. Starting with passage 2, using appropriate differentiation media, cells were induced towards the mesodermal lineages – adipocytes, osteoblasts and chondrocytes. Subsequently, differentiated cells were analyzed for presence of characteristic immunocytochemical markers: FABP4 and PPARγ, Osteocalcin and Collagen type I, Aggrecan and Collagen type II, respectively. Phenotypical profile of undifferentiated cells was assessed by flowcitometry using characteristic surface markers, and we determined the ratio of positive cells between different populations: CD29, CD34, CD44, CD45, CD73, CD106, CD117, VEGF-RI/RII, TGF-β RII/RIII, HLA-DR, and CXCR4. Immunocytochemical staining was also used to confirm presence of stem cells characteristics. **Results:** Although cells of each type

were obtained from 10 different subjects, we could not confirm the differentiation of dental stem cells towards adipocytes, compared with stem cells from the other sources, which presented differentiation ratios ranging from 20% (UC stem cells) to 85% (muscle stem cells). CD29, CD90 and CXCR4 were significantly higher expressed in dental stem cells compared with the other cellular types, while HLA-DR and CD106 was also significantly lower in muscle stem cells. Expression of CD117 was increased in all cellular types when compared with MSC. **Conclusion:** Stem cells from other sources are endowed with different differentiation potential and express in various proportions characteristic surface markers, which make them more suitable for diverse clinical applications.

Keywords: stem cells, differentiation, cell culture, comparative analysis.

CORTICAL CONNECTIVITY CHANGES FOLLOWING NOCICEPTION STIMULATION IN RAT

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Background: Cortical connectivity is considered to be one of the most sensitive parameters for estimating nervous function. In this study we aimed to evaluate changes in cortical connectivity induced by nociceptive stimulation in rats, during anesthesia. **Material and methods:** In this experiment, we used Wistar rats (in number of 5), of about 250–300 grams. each. Anesthesia was induced and maintained with chloral hydrate, at an anesthetic depth, estimated by the median-frequency of 2 Hz. During the experiment, the brain electrical activity was recorded using electrodes chronically implanted on the dura mater. Signal acquisition was made using BIOPAC MP 150 system. Two leads were used, frontal and parietal on each hemisphere. After a 5-min control path, a painful stimulus which consisted of mechanical clamp, using a clip, was applied for 1 minute, to the left hind paw. Electroencephalographic signal was then analyzed in the right hemisphere. Cortical connectivity was assessed using the median frequency variation in the two leads (fronto-parietal index). **Results:** During painful stimulation, median frequency increases (MEF pain = 3 * MEF control) in both leads, fronto-parietal index does not change compare with control, and frontal cortex activation time is double (2 minutes) compared with the time of painful stimulation (1 minute) and greater than in the parietal cortex. **Conclusions:** Cortical connectivity is one of the most sensitive parameters of the nervous function estimate, and our results support cortical connectivity analysis to estimate the anesthetic depth and quality of analgesia during anesthesia.

Keywords: nociception, cortical connectivity, electroencephalography, anesthesia

CARDIOPROTECTIVE EFFECTS OF ANESTHETIC PRECONDITIONING WITH SEVOFLURANE IN ISCHEMIA/REPERFUSION INJURY

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Background: Human heart is efficiently protected against ischemia-reperfusion (I/R) by volatile anesthetics through a pharmacologic preconditioning effect. Bone marrow stem cells (BMSCs) are an important endogenous pool of regenerative cells responsible for vascular and myocardial integrity and homeostasis. Current experimental and clinical evidence suggests a possible mechanistic link between APC cardioprotection and tissue regeneration by stem cell-like progenitor cells. **Objective:** Our research project aims at demonstrating that cardioprotective effects of sevoflurane late preconditioning also involves enhanced bone marrow stem cells (BMSCs) mobilisation and recruitment into the I/R injured heart. **Methods:** We used an in vivo model of APC (anesthetic preconditioning) and I/R (ischemia/ reperfusion) injury designed on inbred male Wistar rats. Heart I/R injury was induced by occluding the left anterior descending artery for 30 min immediately (early phase) or 24 h (late phase) after APC. Rats were randomly assigned to experimental groups (n = 10), as follows: control group, EAPC (early anesthetic preconditioning) group and LAPC (late anesthetic preconditioning) group. EAPC and LAPC groups were exposed to sevoflurane 2.5% immediately before or 24 h previous to the I/R injury, respectively. **Results:** Serum vascular endothelial growth factor (VEGF) levels were observed at several timelines after APC, and also CD34+ and CD34+/flk-1+ stem cells in the peripheral blood were estimated through flow citometry. Compared with the control treatment, both the early and late phases of APC protected the heart against I/R injury, as observed through apoptosis assays, immunoflurescence and histological preparations.

Keywords: ischemia / reperfusion injury, cardioprotection, anesthetic preconditioning, sevoflurane

CONTRIBUTION OF OBESITY TO DEVELOPMENT OF THE METABOLIC SYNDROME

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Objective: The aim of this study was to investigate the relationship between BMI, waist circumference and components of the metabolic syndrome in overweight and obese women. **Design and methods:** 19 overweight women (BMI 27.32±1.36 kg/m^2) and 17 obese women (34.28±4.46 kg/m^2) were compared to 19 women with normal weight (22.06±1.48 kg/m^2) matched for age. In all participants we determined lipid and lipoprotein concentrations, fasting glucose and insulin levels, homeostasis model assessment of insulin resistance (HOMA-IR), we measured waist circumference, systolic and diastolic blood pressure. **Results:** No significant differences in the lipid indices were found between the overweight persons and the control group. In the obese subjects triglyceride levels, LDL-cholesterol levels and triglyceride to HDL-cholesterol ratio were significantly elevated compared with the healthy subjects ($p < 0.05$, $p < 0.05$ and $p < 0.01$, respectively). Fasting insulin and insulin sensitivity assessment parameter HOMA were higher in the overweight women ($p < 0.01$ for insulin and $p < 0.001$ for HOMA) and in the obese women ($p < 0.05$ for insulin and $p < 0.01$ for HOMA) than in the control group. Also systolic and diastolic blood pressure were significantly higher in the overweight women ($p < 0.01$ and $p < 0.001$,respectively) and in the obese women ($p < 0.05$ and $p < 0.001$, respectively). In the overweight and obese subjects BMI positively correlated with triglyceride levels ($r = 0.52$, $p < 0.001$), triglyceride to HDL-cholesterol ratio ($r = 0.38$, $p < 0.05$), fasting glucose levels ($r = 0.33$, $p < 0.05$), HOMA ($r = 0.42$, $p < 0.01$), systolic blood pressure ($r = 0.56$, $p < 0.001$) and diastolic blood pressure ($r = 0.53$, $p < 0.001$). The same type of associations were found between waist circumference and triglyceride levels ($r = 0.54$, $p < 0.001$), triglyceride to HDL-cholesterol ratio ($r = 0.41$, $p < 0.01$), HOMA ($r = 0.43$, $p < 0.01$), systolic blood pressure ($r = 0.6$, $p < 0.001$) and diastolic blood pressure ($r = 0.63$, $p < 0.001$). **Conclusion:** We have demonstrated an association between BMI, waist circumference, the better marker of abdominal obesity, and components of the metabolic syndrome in overweight and obese women. These findings are consistent with hypothesis that obesity, especially abdominal obesity, decreases insulin sensitivity and contributes to development of the metabolic syndrome.

Keywords: abdominal obesity, metabolic syndrome

COLLECTION, ISOLATION AND CHARACTERISATION OF STEM CELLS FROM UMBILICAL CORD BLOOD

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Background: Recently umbilical cord blood has represented another rich source for hematopoetic and mesenchymal stem cells, and they can be used in cell therapy. **Objective:** The aim of our studiy was to optimise the method for isolation and characterisation of stem cells from umbilical cord blood (UCB). **Methods:** Collections (n = 50) were obtained from normal full term deliveries and the processing of umbilical cord blood was made withen 24–48 hours from collection. The mean UCB volume was 71.84±25.29 ml (range 42.0–147.0). The mean total nucleoted cell count was 11.2±9.85 × 10^6/ml (range 1.0–52.6). The stem cells were isolated from umbilical cord blood using dextran for isolation progenitor cells; determinated CD34, CD45 and CD90 by flow cytometry, and finally cultivation cells in nutrient medium DMEM with ulterior biochemical and cytogenetic investigation. **Results and Conclusion:** We found that gestational age ($r = 0.33$, $p = 0.003$), newborn weight ($r = 0.45$, $p = 0.001$), placental weight ($r = 0.47$, $p = 0.0005$) influence the total volume collection, but not quality of cellular grafts. The separation of cells by using dextran is an effective and less costly, the amount of mononuclear cells obtained constituted 85% of the total. In result, it was found using biochemical, morphological and karyotype methods any pathological changes during 5-days cultivations of isolated cells from umbilical cord blood.

Keywords: stem cells, umbilical cord

RELATIONSHIP BETWEEN CIGARETTES CONSUMPTION AND CHANGES IN BRACHIAL FLOW-MEDIATED VASODILATATION

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Background: Brachial flow-mediated vasodilatation (brachial FMD), the ability of vascular bed to adapt to increasing blood flow increasing is a process dependent on endothelial release of nitric oxide. **Objective:** The purpose of this study was to determine the relationship between brachial FMD and cigarettes consumption in patients with different cardiovascular pathologies.**Material and**

methods: 32 patients with angiographically confirmed coronary artery disease (BCV group), 12 patients with arterial hypertension (HTN group) and 12 patients with atherogenic dyslipidemia (DYS group) were compared with 12 control patients, age and sex matched. We recorded in every patient the cigarettes consumption that was estimated in pack-years. High-resolution brachial artery ultrasonographic studies were performed to assess endothelium-dependent [expressed as% flow-mediated dilatation (FMD)] responses. **Results:** Cigarette consumption was found significantly higher in BCV group compared with HTN group ($p < 0.001$), DYS group ($p < 0.001$) and CON group ($p < 0.001$). Brachial artery FMD was significantly reduced in BCV group compared with HTN group ($p < 0.001$), DYS group ($p < 0.001$) and CON group ($p < 0.001$). The correlation between the cigarettes consumption and brachial FMD was negative, strong and significant for BCV group ($r = -0.72$, $p < 0.001$), HTN group ($r = -0.76$, $p < 0.001$) and DYS group ($r = -0.82$, $p < 0.001$). In CON group the correlation between cigarettes consumption and brachial FMD was negative, weak but significant ($r = -0.29$, $p < 0.001$). **Conclusion:** These findings demonstrate that smoking is a significant risk factor involved in endothelial-dependent vasodilator response modification.

Keywords: cigarettes consumption, brachial flow-mediated vasodilatation, angiography

CAROTID INTIMA-MEDIA THICKNESS IN SMOKING SUBJECTS WITH DIFFERENT CARDIOVASCULAR PATHOLOGIES

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Background: Smoking-induced damage to the cardiovascular system has been shown in many studies but the degree of damage varies in different cardiovascular pathologies. **Objective:** The aim of this study was to evaluate the values of carotid IMT in different cardiovascular pathologies and the link between carotid IMT and cigarettes consumption. **Material and methods:** The study was performed on 32 patients with angiographically confirmed coronary artery disease (BCV group), 12 patients with arterial hypertension (HTN group) and 12 patients with atherogenic dyslipidemia (DYS group), that were compared in terms of cigarettes consumption and carotid IMT values with 12 control patients, age and sex matched. In every patient we recorded the cigarettes consumption that was estimated in pack-years. **Results:** Carotid IMT was significantly increased in BCV group compared with HTN group ($p < 0.001$), DYS group ($p < 0.001$) and CON group ($p < 0.001$). The cigarette consumption was significantly higher in BCV group compared with HTN group ($p < 0.001$), DYS group ($p < 0.001$) and CON group ($p < 0.001$). The correlation between the cigarettes consumption and carotid IMT was negative, moderate and significant for BCV group ($r = 0.30$, $p < 0.001$). We did not found any significantly correlation between carotid IMT and cigarettes consumption in HTN group, DYS group and CON group. **Conclusion:** Our study proved that coronary artery disease interacts with smoking in determining the most advanced value of carotid IMT. Carotid IMT may provide distinct and independent information about the complex atherosclerotic process present in patients with coronary artery disease.

Keywords: carotid intima-media thickness, smoking subjects, cardiovascular disease

THE WAY THE IMPORTANCE OF EDHF IN ENDOTHELIUM–DEPENDENT RELAXATION INCREASES DISTALLY IN MESENTERIC ARTERIES, DEPENDING UPON THE CONTRACTING AGENT

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Background: The importance of endothelium-derived hyperpolarizing factor (EDHF) in endothelium-dependent relaxation (EDR) is influenced by multiple factors, including vascular territory and caliber, pre-existing tone and it's determining factors. **Method:** Using isometric myography we noticed that in rat mesenteric resistance arteries (RMA2; 2nd order branches) EDHF-mediated relaxation is increased when precontraction is induced by prostaglandin F2 (PGF) compared to phenylephrine (PHE) and we investigated the participation of certain K channels (Serban IL & Serban DN (2006) J Muscle Res Cell Motil 26(1):71). Here we extend the study on more proximal vascular fragments; from mesenteric arcade and from 1st order branches. **Results:** The EDHF component of EDR is stronger distally only when precontraction is induced by PHE. Moreover, morphometric analysis shows a strong inverse correlation between the magnitude of EDHF response and arterial caliber. **Conclusions:** Other authors have shown that EDHF increases in relative importance distally, but we show that this change in EDR profile depends upon the contracting agent used, with implications regarding the physiological relevance of accumulated data refering to EDHF and nitric oxide as mediators of EDR in resistance arteries.

Keywords: endothelium-derived hyperpolarizing factor, endothelium-dependent relaxation

CORRELATIONS BETWEEN THE BREAKAGE RESISTANCE OF THE FIBRIN CLOT AND THE HISTORY OF THROMBOTIC EVENTS IN A GROUP OF PATIENTS WITH DYSLIPOPROTEINEMIA

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Background: Growing compelling evidence demonstrates that quantitative and qualitative alterations in plasma lipids have a highly proatherogenic and prothrombogenic potential. This potential is clinically expressed by the increase in the incidence of thrombotic vascular events, cerebral or coronary. **Objective:** In this study, we aimed to highlight the haemostatic abnormalities in a group of patients with dyslipoproteinemia who have a history of thrombotic vascular events. For this purpose, we chose fibrinrezistometry as main method to assess haemostatic abnormalities, a method which measures the breakage resistance of the fibrin clot. Material and methods. We conducted a retrospective study in which we determined the breakage resistance of the fibrin clot in a lot of 86 patients with dyslipoproteinemia, 43 men and 43 women, who presented for consult. In parallel, we investigated haemostasis by already acknowledged **Methods:** PT, INR, APTT, platelet count and plasma fibrinogen concentration. In this study group, a subgroup of 44 patients had a history of one or more ischemic strokes or myocardial infarction. **Results:** Mean breakage resistance of the fibrin clot was significantly decreased (p = 0.002) in the no thrombotic event subgroup (285.76±33.60 UF), by comparison with subgroup with a record of thrombotic events (307.27±30.93). We found a high degree of correlation between high values of breakage resistance and positive history for one thrombotic event (OR = 4.21, CI = 1.66 to 10.64; chi square = 9.70, p = 0.002). All standard coagulation tests were within normal range. **Conclusions:** The increased fibrinresistometric values indicate the presence of an increased potential for thrombosis. These correlated with the incidence of thrombotic events such as stroke or myocardial infarction in the evaluated patients. We believe that the breakage resistance of the fibrin clot may prove to be a valuable marker in evaluating the prothrombogenic status.

Keywords: dyslipoproteinemia, thrombotic vascular events, haemostatic abnormalities

CORRELATIONS BETWEEN THE BREAKAGE RESISTANCE OF THE FIBRIN CLOT AND WAIST CIRCUMFERENCE IN A GROUP OF PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Background: It is currently accepted that body mass index, and especially waist circumference, as measure of the abdominal fat, are independent risk factors for cardiovascular events, or ischemic stroke. **Objective:** In this research, we intend to study the relationship between the breakage resistance of the fibrin clot and anthropometric characteristics in patients with type 2 Diabetes mellitus, by comparing a lot of obese with a control of non-obese patients. We chose fibrinrezistometry as main method to assess haemostatic abnormalities. This method measures the breakage resistance of the fibrin clot. **Material and methods:** We conducted a prospective study on a group of 54 patients with diabetes, 25 men and 29 women, mean age 63.5±9.00 years. We determined the breakage resistance of the fibrin clot, anthropometric parameters, plasma fibrinogen, plasma lipids, platelet count and other parameters of haemostasis. **Results:** Average values of the breakage resistance were increased in both studied groups. The greatest increase was found in patients with a waist circumference > 100 cm (345.5±17.3 FU). There is a strong positive correlation between the increased values of the breakage resistance of the fibrin clot and abdominal circumference (r = 0.621, p = 0.003) and a weaker correlation between BRFC and body mass index (r = 0.453, p = 0.025). Plasma fibrinogen, plasma lipids, platelet count were significantly higher in the obese group compared with the non-obese. We found high correlations between triglycerides and breakage resistance for the obese (r = 0.551, p = 0.004) and non-obese (r = 0.498, p = 0.003) groups. **Conclusions:** The breakage resistance of the fibrin clot is significantly greater in obese by comparison with non-obese diabetic patients, indicating a tendency towards hypercoagulability. The investigated parameter can prove to be a predictor of the prothrombotic status present in diabetic patients, obese or not.

Keywords: breakage resistance of the fibrin clot, diabetes mellitus, obesity

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INHIBITION OF VASCULAR MONOAMINE OXIDASE-A: EXPERIMENTAL STUDIES OF VASCULAR REACTIVITY IN ISOLATED RAT AORTIC RINGS

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Background: Recent data have incriminated monoaminooxidases (MAO) with two isoforms, A and B, as important source of deleterious hydrogen peroxide production in cardiovascular pathology, especially in the presence of an additional oxidative stress. **Objective:** The present study was purported to determine whether MAO-A (the predominant isoform in the cardiovascular system) inhibition could improve the vascular relaxation in normal rat vessels. **Methods:** To this aim segments of thoracic aortas were harvested from female Wistar rats and vascular rings (2–3 mm) were placed in two individual jacketed organ baths. After equilibration at 37°C under 2.00 cN passive tension the tissues were pre-contracted with 10^{-5} M phenylephrine (PE). Cumulative concentration-response curves (10^{-9} to 10^{-4} M) for: acetylcholine (ACh), and sodium-nitroprusside (SNP) were recorded in presence vs absence of MAO-A inhibitor (Clorgyline 10^{-5} and 10^{-4} M). Indometacine (10^{-5} M), as inhibitor of cyclooxygenase, was present in organ baths, throughout the experiments in order to eliminate the influence of prostaglandine synthesis on vasodilator response. **Results:** No significant differences in the vasodilator effect was observed in the presence vs. the absence of incubation with Clorgyline as demonstrated by the values of maximal relaxation (70.57±6% ivs. 70.45±4.5%, respectively, $p = 0.45$). **Conclusions:** In normal rat aortas, inhibition of MAO-A had no effects on either the PE-induced contraction nor on the vasodilator response to ACh. Further experiments are required to elucidate if the same results will be obtained in the presence of exogenously applied hydrogen peroxide.

Keywords: monoaminooxidase A isoform, vascular reactivity.

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STUDY ON THE EFFECTS OF ULTRASOUND THERAPY ON CLINICAL AND OXIDATIVE STRESS PARAMETERS IN KNEE OSTEOARTHRITIS PATIENTS

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Background: Oxidative damage has been associated to pathogenesis of osteoarthritis (OA), a disabling degenerative disease of the joint cartilage. Nowadays, the ultrasound therapy is successfully used to treat OA, but its precise mechanism of action and its effects on oxidant/antioxidant balance are a matter of debate. **Objective:** The present study monitored the effects of the ultrasound therapy over the clinical, functional and oxidative stress parameters in OA patients. Study design: A group of 20 patients diagnosed with knee OA were treated with ultrasound therapy (US) (0.5 W/cm^2, for 5 minutes/session, 10 sessions). Before, immediately and 14 days after therapy clinical and biochemical parameters were measured. As clinical parameters we used the Womac score (WS), estimating pain, stiffness and physical function, and the Lequesne index (LI), pertaining to pain, discomfort, and activities of daily living. Oxidative/antioxidant balance was explored by measuring total antioxidant capacity, hydrogen donating ability, nitric oxide and malonaldehyde concentrations in plasma. The results obtained after therapy were compared to those before therapy and also to those of a control group ($n = 20$), consisted of OA patients which received no treatment. **Results:** A statistically significant improvement ($p < 0.05$) was observed regarding clinical and functional parameters (WS and LI) and also the antioxidant capacity (total antixidant capacity $p = 0.05$, hydrogen donating ability $p = 0.005$) in US treated patients. OA patients in control group had higher values of oxidative stress indices (malonaldehyde $p = 0.02$) as compared to patients treated with US. **Conclusions:** Ultrasound therapy improved joint function, increased the total antioxidant capacity and decreased the oxidative stress parameters in knee OA. The two latter findings might explain, in part, the favorable effects of ultrasound in OA.

Keywords: osteoarthritis, ultrasound therapy, oxidative stress

PHYSIOPATHOLOGICAL MECHANISMS INVOLVED IN SYSTEMIC REACTIVE INFLAMMATION SYNDROME (SIRS) AND SEPSIS

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Background: Pathophysiological mechanisms, the adaptive role of defense, triggered by the appearance in the blood of the fragments of bacterial cell wall and endotoxin, are the cascades activation: coagulation-fibrinolysis, kinine, complement, followed by the release

of leukotrienes, prostaglandins, cytokines, and pro-inflammatory mediators and cellular metabolism in anaerobic transposition. Altered ratio oxidant / antioxidant such events is a way to quantify the degree or intensity of infection, the transition from stage to SIRS and sepsis survival to non-survival. **Objective:** Study objectives were the strict definition of the parameters that reflected the involvement of oxidative stress (Sox.) in the adaptive response, the ability to highlight the failure of the O_2 after the attack and associated endotoxins and oxidative effect of the administration of packed red cells or whole blood O_2 dissociation curve of Hb. Activation of tissue factor, secondary aggression exerted on vascular-tissue unit, induces coagulation in the microcirculation, an epiphenomenon, whose magnitude depends on the further development of the wound. Empirical antibiotic therapy, or monotherapy with a cephalosporin antibiotic selected by antibiotics, are some effective ways, which blocks the passage of SIRS for sepsis, if lesions found in the initial stages. Oxidative stress triggered by respiratory burst of leukocytes and endothelial cells is favorable for the destruction of microorganisms, in an early stage, in which leukocytosis and intensity of peroxidase reaction reflects an increased defensive potential. Excessive uncontrolled ROS production after a period of time, causes the production of necrosis and apoptosis of endothelial cells and tissue depth and general condition worsened, forcing the multiple surgical reinterventions.

Keywords: systemic reactive inflammation syndrome, sepsis

EVALUATION OF FUNCTIONALITY OF EPITHELIAL-LIKE CELLS INDUCED IN VITRO FROM HUMAN MESENCHYMAL STEM CELLS. IN VITRO AND IN VIVO ASSAYS.

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Background: There are lots of data reporting the plastic potential of mesenchymal stem cells (MSCs) to the mesodermal cell lines: bone, cartilage, adipocytes. The epithelial cells obtained in vitro from the human adult MSCs opening interesting perspectives because ex vivo manipulation of the cells can lead to obtaining a high cell quantity for using in the tissue restoration processes. **Objective:** In this study, the in vitro and in vivo functionality of epithelial-like cells (EpLCs) induced from MSCs was assayed. **Material and methods:** MSCs were isolated from 4 bone marrow samples, harvested (after obtaining writing informed consent) from patients undergo surgical hip replacement. MSCs at third passage were grown in medium supplemented with EGF, KGF, FGF, and IGF-2 for 3 weeks. The obtained cells were assayed for characteristic epithelial markers (immune-citochemistry, immune fluorescence, PCR) and functional in vitro tests were performed: evaluation of membrane markers (flow-citometry), secreted cytokines (ELISA), and cell adhesion to fibronectin (flow-chamber). For in vivo assay, 10 B6D2F1 male mice were used. Animals were supplementary immunosuppressed with i.p. Dexamethasone for 3 weeks, when the skin lesion was induced. Human EpLCs and MSCs were superficially injected at the site of the lesion. After 14 days, we assessed the human EpLCs and MSCs presence at the injury site. **Results:** In vitro, after 21 days in epithelial-induction cytokine cocktail, MSCs acquired a rounded or polygonal shape and expressed epithelial markers (pancitokeratin, citokeratin 10, 14, 19, E-Cadherin, integrin beta1). Functional in vitro study revealed increased expression of receptors for TGF beta 1 (RII and RIII), increased levels of IL4, IL10, VEGF and TGF beta1 in culture supernatant and increased adherence of EpLCs to fibronectin in comparison with undifferentiated MSCs. In animal model, lesions treated with MSCs stained positive for Vimentin and beta1-integrin, while treated with EpLCs stained positive for E-Cadherin. **Conclusion:** EpLCs expressed epithelial markers and in vitro seems to have immune properties. In vivo, EpLCs induced a faster healing of skin lesions, while undifferentiated MSCs had a minor immediate contribution to epithelization process, when injected at the site of the injury.

Keywords: epithelial-like cells, human mesenchymal stem cells

OPTIMIZATION OF CHEMOTHERAPY ANTI-INFECTIVE IN SEVERE FORMS OF ACUTE PANCREATITIS

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Background: Acute pancreatitis is still associated with an extremely high mortality even if the treatment is more complex, medical-surgical, in the Intensive therapy sectors. Infections of pancreatic tissue with necrosis cause a mortality of about 40%. Hence the necessity to initiate the chemotherapy very quickly. **Methods:** This study is a retrospective study and analyzes the relative effectiveness of chemotherapeutic associations used in acute pancreatitis of 450 patients hospitalized in the Emergency County Hospital Oradea in the period 01.01.2000–31.12.2009. **Results:** The average period of hospital stay was reduced significantly for the patients treated with chinolone (8.2/12.0, M / F) compared with patients treated with beta-lactamic antibiotics (23.7/11.5) and even cephalosporins (18.0/21.0) in case of severe forms of pancreatitis. In case of edematous forms the best results were obtained with beta-lactamic antibiotics and cefalosporine. Regarding the frequency of use of certain classes of antibiotics and chemotherapy in the first place is beta-lactamic antibiotics + carbapenems (294), cephalosporins (145), metronidazole (16), quinolones (7) and macrolides (2). Associa-

tions of antibiotics and chemotherapy must address to a big antimicrobial spectrum, the infections are caused by multiple bacteria, usually gram-negative bacilli and flora anaerobe. A special problem of chemotherapy in acute pancreatitis is represented by fungal superinfection, which also requires a complex approach and multidisciplinary. **Conclusion:** In conclusion, the treatment of infection in severe acute pancreatitis is a key component in decreasing of the mortality but also a desideratum regarding the best combinations of chemotherapy.

Keywords: acute pancreatitis, anti-infective chemotherapy

INFLUENCE OF DIAZOXIDE AND CYCLOSPORINE A COADMINISTRATION ON MITOCHONDRIA ISOLATED FROM RAT HEARTS SUBJECTED TO GLOBAL ISCHEMIA/REPERFUSION INJURY

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Background: Modulation of mitochondrial function during ischemia and/or early reperfusion represents an emerging cardioprotective therapeutic approach. **Objective:** The present study investigated the effects of diazoxide (Dx, 100 microM/L)), an opener of the mitochondrial ATP-dependent potassium channels, cyclosporine A (CsA, 0.2 microM/L), a desensitizer of the mitochondrial permeability transition pore and their association at reperfusion on mitochondria isolated from Langendorff perfused rat hearts subjected to 40 min global ischemia and 15 min of reperfusion). **Methods:** Mitochondria were isolated by means of differential centrifugations technique. Mitochondrial calcium retention capacity was evaluated by luminescence spectroscopy using the calcium-sensitive probe Calcium Green 5N. Mitochondrial swelling was monitored by measuring the decrease in light scattering in the presence of complex I substrates (glutamate/malate) and complex II substrates (succinate/amytal). **Results:** In the presence of CsA (but not of Dx) at reperfusion, mitochondria respiring on CII (but not of CI) dependent substrates were particularly resistant to calcium overload ($p < 0.001$ vs. the non-treated control). Surprisingly, their association at the very onset of reperfusion reversed this cardioprotective effect ($p < 0.001$ in CsA & Dx group vs. CsA alone) in the presence of both CII and CI supported respiration. Dx and CsA given independently significantly decreased the swelling of mitochondria energized with glutamate/malate ($p < 0.001$ vs. the ischaemic control), an effect that was again reversed by their association. In conclusion, in isolated rat heats subjected to 40 min of global ischaemia and 15 min of reperfusion, association of the two cardioprotective agents at mitochondrial level, diazoxide and cyclosporine A, elicited a deleterious effect on mitochondrial function that clearly warrants further investigation.

Keywords: diazoxide, cyclosporine A, mitocondrial function, ischemia/ reperfusion injury.

BREAST TUMORS AND THE LOCAL OXIDATIVE STRESS

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Background: Breast cancer has become a major health problem, being the most common malignant cancer and the second cause of death in women. Some experimental studies indicate the involvement of free radicals in carcinogenesis. SRO appearance (in small quantities) and lipoperoxidation are triggers and at the same time key mediators of apoptosis, which removes precancerous or cancerous cells. Highlighting the involvement of oxidative stress in the development of breast tumors, in order to select the type of therapy and timing of implementation to achieve the minimization of aggressive development, metastasis and the worsening of tumor genesis. **Objective:** Selection of variables, with marker role, for evaluating clinical laboratory changes that allow prediction of the development of breast tumors **Material and methods:** We followed a group of 96 patients: 54 women with breast neoplasm confirmed intraoperatory operated, compared to a witness lot of 42 women with benign breast tumor processes, from the sections of surgery with the permission of their chiefs and the permission of the patients to respond and allow us to take tumor fragments of the tumor excision. Patients were observed during the early period of pre, intra and post surgery. **Results and** d**iscussions:** We noticed a normal duration of hospitalization or even reduced for patients whose TAOP value was unchanged against the witness. ($p = 0.003$). The reduction of the number of days for drain retention ($p = 0.001$) and suture applied, after the extraction of the drain ($p = 0.03$) was observed in patients and witness, whose the ISO and TAOP values were maintained between normal limits. Our study confirms the hypothesis that cancer survivors require the changing of lifestyle, starting with the reduction of the intensity of oxidative stress and the increase of TAOP. Even if the diet with vitamin C did not convince us of its ability to change the TAOP value, however, is remarkable for its role as vascular tonic. Selenium and vitamin E reduce the major effects of plasma oxidative stress. **Conclusions:** Evolution of the oxidative stress / TAOP observed in the oxidative stress index; show that antioxidant therapy, applied as antitumor effects are not immediate in

the case of tumors with metastatic potential, the plasma antioxidant status is dependent on exogenous and endogenous factors which do not reflect the tumor oxidative stress.

Keywords: breast tumors, oxidative stress

CLINICAL-PARACLINICAL SPECIFIC FEATURES ON A GROUP OF HYPERTENSIVE PATIENTS

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Methods: The authors examined a number of 220 hypertensive patients, from those: 128 male and 92 female (41.82%), aged between 24–65 years old. A number of 56 (25.45%) were hypertensive patients under 40 years old, 75% (42 patients) from urban milieu and 12 patients from rural milieu, from those: 40 men and 16 women. Among the factors with atherogenous potential, on all patients have been determined: cardiovascular hereditary background, excess of sugars, lipides, alcohol and smoking (tobacco), presence of stress and overtime work. As atherogenous blood stigma have been determined HDL, LDL, total lipides, glycemia, coagulation factors: fibrinogen, hematocrit value, uric acid. **Results:** Making a comparison between the group of young hypertensive patients and the rest of hypertensives, have been established both similitudes and differences in relation with the atherogenous factors. For example, on the young patients traced out more often the hereditary background (18% to 11% on the rest of hypertensives) and the alcohol consumption (21% to 14%). The stress generated by the missing or change of work place and by the disagreement between resposibility work and insufficient professional training was more often on young patients also (24% to 16%). On the other hand, for the over 40 years old patients prevailed excess of lipides (36% to 21% at young patients) and tobacco (60% to 41%) and work overtime (37% to 23%). **Conclusions:** Blood humoral modifications have been characterized on all hypertensive patients by the increase cholesterol, total lipides and glycemia, and less of the uric acid and fibrinogen, and the humoral modifications poignancy depended on the high blood pressure duration and gradation (1st and 2nd stages).

Keywords: arterial hypertension, atherogenous factors

MAPKS MEDIATE THE NUR77-INDUCED APOPTOSIS OF PRO-B CELL TYPE BA/F3

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Leukemias are the most common malignancy in children, and acute lymphoblastic leukemia (ALL) accounts for 85% of all childhood leukemias. The rate of apoptosis in B-ALL is deeply altered and in a total imbalance with cell proliferation. Recently, we demonstrated that cyclosporine A, a well known inhibitor of mitochondrial permeability transition, is facilitating Nur77 activation-induced apoptosis of pro-B cell type Ba/F3. Nur77 (NR4A1, nuclear receptor subfamily 4, group A, member 1) associates with Bcl-2 in the mitochondria, resulting in a conformation change that exposes the Bcl-2 BH3 domain, a presumed pro-apoptotic molecule of Bcl-2. Cellular clone Ba/F3 was derived from murine bone marrow and expresses B-cell-specific surface glycoprotein B220 but has unrearranged immunoglobulin genes. It lacks T-cell, myeloid and mature B-cell antigens and strictly requires IL-3 for growth in vitro. Ba/F3 cells are thus immortalized pro-B lymphocytes presenting anti-apoptotic phenotype. We further explored the mechanisms underlying the facilitating effects of cyclosporine A on pro-apoptotic behavior of Nur77 in Ba/F3 cells. We used JC-1 [5,5',6,6'-tetrachloro-1-,1',3,3'-tetraethylbenzimidazolyl-carbocyanine iodide or CBIC2(3)], a very sensitive marker for mitochondrial membrane potential, calcein-AM as a marker for the mitochondrial permeability transition pore opening and annexin V and propidium iodide to discriminate between apoptosis and necrosis. Cyclosporine A is an inhibitor of calcineurin and might be related to the alteration of MAPKs functioning. The use of PD98059, an inhibitor of MAPKs and ERK 1/2; pathways, showed that Nur77-induced apoptosis in Ba/F3 cells is involving these ones. This study could represent the first one to show the relationships between the Nur77 protein export from nucleus and ERK 1/2; activation in Ba/F3 cells.

Keywords: acute lymphoblastic leukemia, apoptosis, Nur77 protein

MAGNESIUM OROTATE AND CARDIOPROTECTION AT REPERFUSION: NEW VISTAS FOR AN OLD DRUG

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Myocardial ischaemia/reperfusion (I/R) injury, associated with acute coronary syndromes and cardiac/non-cardiac surgery, represents a leading cause of death due to myocardial infarction and disability due to heart failure worldwide. Orotic acid, a key intermediate in the biosynthetic pathway of pyrimidines, and its salts have been previously shown to exert protective effects in chronic administration in both experimental and clinical studies, yet the mechanisms of protection are far from being elucidated. The present report summarizes our experience with magnesium orotate in acute administration during the postischaemic reperfusion in two experimental models, isolated perfused rat hearts subjected to global ischaemia and in situ regional ischaemia in anaesthetized rat hearts, respectively. New insights into novel, putative mechanisms underlying the cardioprotective effect of the drug in this setting are presented.

Keywords: ischaemia/reperfusion, magnesium orotate, cardioprotection.

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VASOACTIVE PEPTIDES, CALCIUM CHANNELS AND VASCULAR REACTIVITY: RECENT FINDINGS AND EMERGING CONCEPTS

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Plasmalemmal calcium channels in the vascular smooth muscle and endothelium have been intensely investigated for decades. Here we review the very recent progress made in elucidating the operation mechanisms of these channels and their functional implications for vascular reactivity in health and disease, with a focus on voltage-independent pathways, such as store-operated calcium entry (SOCE). On one side SOCE in vascular smooth muscle cells appears to be a key mechanism for the calcium influx required during their sustained response to contracting agents. On the other side SOCE in endothelial cells is involved in the release of vasoactive agents from the endothelium. The involved plasmalemmal channel may belong to the TRP family (transient receptor potential), but another pore-forming protein has also been proposed (ORAI), while the detailed biochemical link between reticular calcium release and SOCE activation is under investigation. In correlation we also highlight the successful efforts made to understand vascular smooth muscle and endothelium as an integrated signaling network acting for the local regulation of blood flow. Here we focus on new findings regarding the role of endothelial calcium-dependent potassium channels and the mechanisms of conducted vasodilation. In context of all the above we examine the case of some vasoactive peptides, such as angiotensins, endothelin, natriuretic peptide C, calcitonin gene related peptide, adrenomedullin. The relevance for human disease of both local and general perturbations in vascular reactivity is simply overwhelming. We therefore believe that such new findings and concepts regarding the molecular mechanisms of vascular reactivity will have a strong impact on clinical progress in the near future.

Keywords: vasoactive peptides, calcium channels, vascular reactivity.

DIAGNOSIS AND GENETIC ABNORMALITIES IN PRIMARY EOSINOPHILIA

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The importance of eosinophilia in the last decade is due to the progresses recorded in the study of normal and pathological genome and to the therapeutical progresses able to interfere with the pathogenical chain of malignant transformation. The differential diagnosis of an eosinophilia needs in the first step the exclusion of a proliferation with a reactive characteristic (exposure to toxins, allergic diseases, immune diseases, neoplastic hematological and non-hematological diseases). Next follows the determining of the clonality through identifying a chromosomal or sub-chromosomal marker or/and obtaining the criteria of diagnosis for a mieloproliferation or myelodysplasia. This step implies the histological, cytogenetical and molecular biology of bone marrow examination. The evaluation of the rearrangement of antigen receptor of T lymphocyte, of imunophenotype of the same lymphoid population, of serical concentration for the tryptasys and IL-5, allows clinical orientation in eosinophilia. The final step of the diagnosis is the impact evaluation of the disease on the human organs and tissues: lung, heart, digestive tract and nervous system. Identifying a genetical abnormality is meant

to underline the clonal characteristic of mieloproliferation and also the possibility of a therapeutical answer favorable to imatinib. The cytogenetical lesions often met in primary eosinophilia refer to: PDGFRA rearrangement (including FIP1L1-PDGFRA), PDGFRB, Kit, 8p11. There is no classification completely accepted of primary eosinophilia because the main criterion can be balanced on the phenotype (clinical-pathological aspect) or on genotype (cytogenetical/molecular lesions). The clinical-pathological promiscuity offered by the same molecular lesions must not discourage, as long as it assures the prediction of the therapeutical answer (on the model SMP Ph1(+). The cytogenetical and molecular biology discoveries (BRC/ABL, c-kit, 8p11, PDGFRA/B, JAK2 mutations, etc) allow semi-molecular views of primary eosinophilia, and also of SMPC.

Keywords: primary eosinophilia, genetic abnormalities.

CONSIDERATIONS ON THE ROLE OF CARDIAC MARKERS IN DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION

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Myocardial infarction can be defined based on several criteria: clinical, electrocardiographic, biochemical and morphological. Because the term implications for social behavior, psychological and epidemiological importance – as an indicator of a major health problem – it needed a universally accepted definition of this entity. Unlike the old name of myocardial infarction, in which the role of primary diagnosis was for electrocardiogram in the presence of a suggestive clinical picture (even dictating this exploration indications thrombolysis), brings to the fore the current definition of biomarkers of myocardial necrosis, with nearly absolute myocardial specificity and sensitivity far superior. In this context, the indications for thrombolysis review, taking into account markers of myocardial necrosis. Cardiac biochemical markers must be determined in all patients presenting with chest pain suggestive of acute coronary syndrome. They allow the diagnosis of myocardial necrosis and prognosis estimation, there is a direct quantitative relationship between blood levels of the marker and the risk of complications evolution.

Keywords: biomarkers of myocardial necrosis, myocardial necrosis.

STRESS- INDUCED INFLAMMATION IN ATOPIC DERMATITIS

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Atopic dermatitis (AD) is an inflammatory, pruritic, chronically relapsing skin disorder associated with skin barrier dysfunction. Psychosocial stress is considered to have an important effect on both the onset and exacerbation of symptomatology in AD through dysregulation of neural, endocrine, immunologic and behavioral pathways. Furthermore, various types of psychological stress induce alteration in the barrier function of the epidermis and delays skin barrier recovery after disruption in AD and also wound healing in generally. At the same time, AD implies an immense psychological burden and a negative effect upon the mental health of the patient, thus generating a vicious cycle of psychological distress-atopic dermatitis. Considerable evidence suggests that psychological stress aggravates inflammation through modified neuroendocrine and immnune responses, increased release of neurogenic components as neurotrophic factors and neuropeptides and also through local metabolic events. Current paper reviews the connections between stress-induced immune mediated and neurogenic inflammatory processes and atopic dermatitis pathogenesis. In conclusion, though the underlying mechanisms of stress-related inflammation need further clarification, psychological factors must be taken into consideration in the integrated therapeutic model of AD.

Keywords: atopic dermatitis, stress, skin barrier dysfunction.

NEWS IN THE THERAPY OF ATRIAL FIBRILLATION

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The atrial fibrillation is characterized by electrical cardiac activity disorganized and progressive deterioration of atrial electromechanical function. The study data of the case shows that the rhythm disorder is associated with an increased risk of death, enhanced by other thromboembolic disease, which requires the establishment of therapy with most patients. The sotalol determine a significant reduction of clinically ventricular frequency of atrial fibrillation with tachycardial type leadership, but also during the new crises of atrial fibrillation. After performing heart surgery, the patients may present persistent atrial fibrillation or paroxysmal with fast leadership, not well tolerated hemodynamically and therefore frequently require treatment or establishment of prophylactic measures. It was demonstrated

that the administration of sotalol may have reduced the frequency of rhythm disturbances and is obtained a reduction in the frequency of ventricular fibrillation in case event, in this case betablocantii sotalol being more effective than conventional.

Keywords: atrial fibrillation, sotalol, ventricular fibrillation.

EFFECTS OF GLUCOCORTICOIDS AND ANNEXIN V

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Glucocorticoids have anti-inflammatory actions, released shortly after tissue injury in order to offer some protection against a runaway inflammatory response. They can induce apoptosis in eosinophils and promote phagocytosis of apoptotic cells. Glucocorticoids also, modulate the expression of proteins that have anti-inflammatory properties, most notably annexin-1. Short peptides derived from the amino terminus of annexin-1 retain biological activity, but there is more interest in finding small molecule drugs that interact with the receptor or receptors through which annexin exerts its activity. Annexin-1 and leucotriene A2 bind to a common receptor which appears to have been conserved as a multi-function receptor with a role in the control of inflammation. Indeed, several in vivo models of inflammation have illustrated that annexin-1 plays a central role in promoting resolution and have thereby highlighted the therapeutic potential of annexin-1 mimetics, particularly now that its receptor has been identified. Annexin V is a calcium-dependent glycoprotein with a potent anticoagulant capacity in vitro by reducing plaque adhesion and aggregation. Circulating ANV can be released from the cells of vascular wall (endothelial cells, smooth muscle cells) or from secretor cells of spleen and the liver. In the plasma, it binds to blood cells (platelets and erythrocytes) or to endothelial cells. Annexin V possesses a high apoptotic cell affinity as these cells produce a large amount of phospholipids, particularly phosphatydilserine. ANV appears to form an antitrombotic shield around the phospholipids, displacing their coagulation factors. ANV binds to the phosphatidylserine inhibiting the pro-coagulant and pro-inflammatory activities of the dying cells. It is considered as an unspecific apoptosis mark

Keywords: glucocorticoids, annexin-v, apoptosis.

BETA-BLOCKERS EFFECTS ON CARDIOVASCULAR SYSTEM, BENEFITS AND UNEXPECTED EVENTS IN ARTERIAL HYPERTENSION

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Beta-blockers comprise a relatively heterogeneous class of antihypertensive drugs with differing effects on resistance vessels and on cardiac conduction and contractility. Beta-blockers are negatively inotropic and chronotropic, the total peripheral resistance will rise compensatory and the blood pressure will not be immediately changed. In time, as the blood pressure becomes lower, the peripheral vascular resistance will be reduced. Exercise endurance in a healthy person depends, in part, on a properly functioning sympathetic nervous system and beta-blockers, by antagonizing this effect, may hamper exercise capacity. During effort, the cardiac output and the maximal effort capacity are reduced; in case of long beta-blocker treatment the patients develop tolerance to these effects. Long period treatment is reducing the muscular blood flow, but this effect is compensated by the higher oxygen extraction by tissues. The beta-blocker effect on muscular metabolism during effort can be hardly differentiating from the effects on the oxygen consumption and blood flow. Clinical trials have shown that beta-blockers should not be the first line agent for the treatment of uncomplicated arterial hypertension, irrespective of the heart rate. Beta-blockers reduce blood pressure compared with placebo, but when compared with other antihypertensive agents, the blood pressure-lowering efficacy is suboptimal. Beta-blockers have a lesser effect on the more important central aortic pressure when compared with renin-angiotensin system blockers, diuretics, and calcium antagonists. A number of large studies and meta-analyses have suggested that patients with uncomplicated hypertension may be at greater risk of stroke with no benefit for endpoints of all-cause mortality and cardiovascular morbidity and mortality.

Keywords: beta-blockers, cardiovascular system, arterial hypertension.

THE INHIBITION OF PLATELET FUNCTION BY ALPHA-TOCOPHEROL

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In addition to its protective effects on LDL from oxidation, alpha-tocopherol is also know to reduce platelet activation, adhesion and aggregation. Abnormal platelet function is widely accepted to play an important role in thrombosis and cardiovascular events. It has been suggested that the inhibition of platelet function, especially adhesion, by vitamin E, plays a crucial role in the prevention of cardiovascular disease. Platelet incorporation of alpha-tocopherol was associated which a significant reduction in platelet sensitivity to aggregation by adenosine-5'-diphosphate, arahidonic acid. Alpha-tocopherol inhibited aggregation of platelets by a protein kinase C dependent mechanism. Vitamin E inhibited collagen-induced platelet aggregation and tromboxan A2 formation in a dose dependent manner. Ca 2+ mobilization and formation of inositol 1,4,5-triphosphate were too inhibited by vitamin E. Alpha-tocopherol inhibits collagen-induced platelet activation by blunting hydrogen peroxide formation. Vitamin E inhibited trombin-induced platelet aggregation in a concentration dependent manner. This inhibitory effect of alpha-tocopherol on platelets was widely reversible upon dilution of vitamin E with autologous platelet poor plasma

Keywords: platelet, alpha-tocopherol

ACTIONS OF LIPOXINS IN INFLAMMATION

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Lipoxins are arahidonic acid metabolites which directly modulate the activity of leucocytes. They inhibit migration of polymorphonuclear neutrophyl (PMN), inhibit PMN adhesion to and migration through the blood endothelial wall and inhibit PMN-induced increases in vascular permeability. In contrast to these negative effects upon PMN activity, lipoxins are also stimulatory towards peripheral blood monocytes, acting as potent stimulators of monocyte migration and adherence. In this way, lipoxins both slow the migration of PMN into sites of inflammation and accelerate removal of PMN that have already migrated into those sites by stimulating the localized generation of phagocytic macrophages. In vivo, lipoxins have been shown to be therapeutically active in several models of inflammatory diseases: gastritis, immune-mediated glomerulonephritis. Cicloxigenase (COX) expressing blood vessel endothelial cells convert EPA (eicosapentaenoic acid) into lipid intermediates which are then metabolized by PMN into tri-hydroxy derivatives that inhibit transendothelial migration. Similar COX-2 catalyses the metabolism of DHA (decosahexaenoic acid) into di-and tri-hydroxy derivatives shown to resolve inflammation. COX-2 mediated conversion of both EPA and DHA is stimulated by aspirin, still one of the most widely used and readily available anti-inflammatory drugs. Lipoxins have anti-inflammatory and pro-resolution actions that include: inhibition of leucocyte-mediated injury, stimulation of macrophages clearance of apoptotic neutrophils, repression of pro-inflammatory cytokine production, inhibition of cell proliferation and migration.

Keywords: lipoxins, inflammation, leucocytes

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