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BASIC SCIENCES

ANATOMICAL RELATIONS OF THE OPTIC RADIATIONS AND THEIR NEUROOPHTHALMOLOGICAL SIGNIFICANCE

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Introduction. The trajectory of the optic radiations is intricated with tracts belonging to the language network and the visual-spatial network. Therefore, lesions that develop on their course can lead to a variety of cognitive deficits. Our study aims to describe the tridimensional anatomy of the optic radiations as a basis for a systematic approach to the neurological semiology of these lesions guided by the ophthalmologic findings.

Material and methods. Ten formalin fixed brains were prepared according to the Klingler method. The optic radiations were dissected in a stepwise manner using wooden instruments and a surgical microscope. Standard sections were performed in order to characterize the stratigraphy of the region.

Results. The optic radiations connect the lateral geniculate body with the occipital cortex. They are divided in three bundles (central, posterior and anterior) corresponding to the macular, upper and lower homolateral hemiretinas which see the central, lower and upper contralateral hemifields respectively. The central bundle has relations with the inferior fronto-occipital fasciculus which are involved in binocular vision and semantic language. The posterior bundle is medial to the superior longitudinal fasciculus, involved in phonological language and the anterior bundle has relations with the inferior longitudinal fasciculus which is responsible for semantic language and face recognition. Considering that neurological signs will correspond to the structures that have relations with the affected optic fibers, a list of possible associated cognitive deficits was proposed for each sector of the visual field.

Conclusion. Facing a patient with a visual field defect caused by a lesion of the optic radiations, associated signs should be expected according to the type of visual field defect and the dominant hemisphere.

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LEFT VENTRICULAR VOLUME ASSESSMENT BY GEOMETRICAL MODELS IN PATIENTS OPERATED ON FOR TETRALOGY OF FALLOT

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Introduction. MRI is proven to be an accurate method for noninvasive assessment of cardiac function in tetralogy of Fallot patients (TOF). Various geometrical models are used in healthy patients to quantify cardiac function. The purpose of this study is to assess the reproducibility and validity of these geometrical models in patients operated on for TOF by comparison with cMRI.

Methods. This is a retrospective study of 59 patients with TOF (mean age 22.46±6.67). Left ventricular (LV) volumes and ejection fraction (EF) were quantified based on a 1.5 Tesla MRI. The LV volumes and EF were either assessed with modified Simpson rule (SR), hemisphere cylinder model (HC), single plane ellipsoid model (EM) and 4 chamber Simpson rule (4cSR).

Results. Good correlations were found for all volumes and EF for SR mode compared with full volume data set (r2 ranged between 0.63 and 0.82 with a p value <0.001 for all correlations). The HC, EM and 4cSR models proved to be less useful for the EF assessment (r2 >0.53 for HC, r20.1 and r2>0.41 for 4cSR respectively).

Conclusion. Only SR model has proven to be a valuable method for the assessment of LV volumes, stroke volume and EF in TOF patients.

BURNOUT SYNDROME IN MEDICAL STUDENTS FROM THE UNIVERSITY CENTRE OF CLUJ-NAPOCA

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Introduction. By its multidimensional component, the burnout syndrome is already correlated with the level of professional performances and personal health alteration. Specific are coronary heart diseases and depressive syndrome with cognitive impairments, characterized by alteration of memory and attention. The purpose of this study was to investigate the level of the burnout syndrome among medical students as professionals in preparation period.

Material and methods. A cross sectional survey was conducted during 2015-2016 on medical students from all academic years by using an online questionnaire. The database and the descriptive statistics were developed in Microsoft Excel and Epi InfoTM.

Results. The self-sectioned students were 82.1% (CI95%: 76.3-86.8) females, with an average age of 21.6 (±2.36) years, originated heterogeneously from all academic years, but mainly (30,9%) from the second year. A form of burnout manifestation was present in 95.6% (CI95%: 92.1-97.6) of the students sample. The students main complaints were the emotional exhaustion (92.8%; CI95%: 88.8-95.6), working with people (71.2%; CI95%: 64.9-76.8) and the increased hard work (68.5%; CI95%: 62.1-74.3). A high-level burnout was found in 9.9% (CI95%: 6.3-14.6) of students and depersonalization was present in 4.1% (CI95%: 1.8-7.5) of students.

Conclusion. The burnout syndrome it's widely present among medical students and it is particularly caused by emotional exhaustion and hard work. The negative impact of burnout syndrome on their academic training and then professional performances could be significant.

THE EFFECT OF BRASSICA OLERACEA ON ACUTE INFLAMMATION MODEL IN RATS

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Abstract

Aim. To investigate the effect of Brassica oleracea var. capitata (common cabbage) ethanolic extract (BOE) on acute inflammation and pain associated with inflammation in rats.

Methods. Carrageenan induced acute paw inflammation in rats was used as experimental model. Fifty Wistar rats were divided into five groups: 1) treated with saline solution (the control group), 2) and 3), as positive control groups, treated with diclofenac intraperitoneal (ip), 20 mg/kg, topical, respectively, 4) BOE orally (1 ml) and 5) BOE topical (0.1 ml) on the inflammated paw. The effects of the treatment were assessed by measuring paw inflammation with plethysmometer and mechanical induced pain with analgesy-meter at 90, 180, 270, 360 minutes.

Results. Data analysis showed significant differences between the means of paw volumes, relative to baseline for all 4 measurement moments. By comparing topical BOE and topical diclofenac, both had anti-inflammatory effects compared to control and there was no significant difference between the two groups. The highest anti-inflammatory effect has been observed for diclofenac ip at all moments. No significant difference was observed for oral BOE compared with control. Concerning pain, an analgesic effect was noticed at 90 min at the groups treated with diclofenac (ip and topical), and with topical BOE.). No significant differences were observed between the groups at rest of the analgesy-meter measurements (180, 270 and 360 min).

Conclusion. Brassica oleracea extract may exhibit a local anti-inflammatory effect.

STUDY OF THE ANTIALGIC EFFECT OF DOXYCYCLINE ON EXPERIMENTAL MODEL OF ACUTE INFLAMMATION.

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Introduction. Doxycycline is an antibacterial chemotherapic. Non-antimicrobial properties have been associated to doxycycline like anti-collagenolytic, anti-inflammatory, antiangiogenic, antiapoptotic, antioxidant and condroprotective. In the occurrence of nociceptive and neuropathic pain, inflammation plays a crucial role.

Objectives. The main objective was to study the antialgic effect of Doxycycline on experimental inflammatory pain. A secondary obective was to compare its analgesic effect with that of Ketoprofen, a known substance with anti-inflammatory and antialgic properties.

Material and method. Study sample included 40 Wistar Bratislava rats, randomly divided into 4 batches of 10 animals. Acute inflammation model was produced by injection of 0.1 ml Kaolin suspension into the rodents` posterior paw. It was followed by intraperitoneal injection of solutions corresponding to the 4 batches, as follows: saline solution(I), Ketoprofen 50 mg / kg (II), Doxycycline 50 mg / kg (III), Doxycycline 100 mg / kg. Statistical analysis: the Student T test (significance threshold $p = 0.05$). Analgesic effect was assessed at 1 hour, 3 hours and 24 hours by applying Randall-Selitto test, which measures sensitivity to a mechanically nociceptive stimulus. Machine used: Ugo Basile analgesy-meter.

Results. A statistically significant analgesic effect was recorded at 1, 3 and 24 hours for Doxycycline 100 mg / kg. The 50mg/kg dose of doxycycline showed a significant analgesic effect only at 24 hours. Ketoprofen had a significant analgesic effect at 1 and 3 hours. Ketoprofen demonstrated a more potent analgesic effect compared to high dose of doxycycline at 1 hour and statistically significant with low dose of doxycicline at 24 hours.

Conclusion. Doxycycline at a dose of 100 mg / kg had significant analgesic effect at 24 hours. Ketoprofen has a stronger antinociceptive action than doxycycline in the studied doses.

THE EFFECT OF MODERATE TRAINING IN ASSOCIATION WITH FLAVONOID ADMINISTRATION AGAINST EXPERIMENTAL DIABETIC PERIPHERAL NEUROPATHY

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Introduction. Diabetic peripheral neuropathy (DPN) is a frequent, serious and debilitating chronic complication of diabetes mellitus (DM) being characterized by an elevated nociceptive response with electrophysiological conduction abnormalities. Hyperglycemia and oxidative stress are involved in causing nerve damage in DM. The aim of this study was to provide a description of neurophysiological changes in the peripheral nerve of streptozotocin (STZ)-induced DPN rats and investigating the synergistic neuroprotective effect of moderate exercise training in association with quercetin administration.

Material and methods. DM was induced in Wistar rats by intraperitoneal administration of STZ (60 mg/kg). The diabetic rats received quercetin (30 mg/kg body weight/day) and performed exercise training program (30 minutes/day, 5 days/week) for 5 weeks. Sensory and motor DPN was evaluated by nerve conduction velocity measurements and electromyography.

Results. Diabetic rats showed significantly decreased sensory nerve conduction velocity (SNCV) and motor nerve conduction velocity (MNCV). Quercetin in association with moderate training restored sensory and motor peripheral neuronal activity from diabetic rats.

Conclusions. These findings suggest that moderate training in association with quercetin administration exert neuroprotective effects in DPN.

AWARENESS AND USE OF EVIDENCE-BASED MEDICINE INFORMATION AMONG ROMANIAN PHYSICIANS

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Introduction. Evidence-Based Medicine (EBM) is an approach designed to optimize the medical decision-making process by emphasizing the use of evidences sustained by systematic and valid medical research. The aim of this study was to assess the EBM awareness, information and daily practice among Romanian physicians.

Method. The instrument used in this study was design to explore awareness, knowledge, attitude in medical documentation, utility and the use of medical professional apps that support EBM [1]. The snowball sampling method using Facebook as the platform was used to collect data. The survey was available from January 1st to April 30th 2017.

Results. Four hundred and thirty-three physicians participated to this study. A significant higher percentage of responders were female (n=334, 77.13%, $p<0.0001$). The correct definition of EBM was correctly identified by most of the respondents (n=349, 80.60%). Affirmatively the majority of respondents declared that they are always looking level of evidences when reading scientific literature but less than 4% properly identified the uppermost evidences in the hierarchy. The name of the EBM resources used to support daily practice was shared by 32% of respondents. Fourteen (most of them being guidelines) out of 64 listed EBM resources accomplish the criteria to be classified as EBM.

Conclusion. Our results showed that Romanian physicians have limited information of the key aspects of EBM but a positive attitude towards the concept. Most have correctly identified the EBM definition, but failed to demonstrate the criteria that led to the concept. Romanian physicians use mobile online medical resources without understanding which are/not EBM.

BIOCOMPATIBILITY EVALUATION OF NEWLY DEVELOPED ANTIFUNGAL AGENTS IN VITRO

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Introduction. Fungal infections are a growing problem due to increased frequency and developing resistance to the existing antifungal products. Moreover, there is a high concern regarding the toxicity of long term treatments that are often necessary for nail or hair mycoses. Therefore, the current study aims to find new antifungal agents with increased efficiency and biocompatibility, based on an imidazole, namely Ketoconozole (KET). KET has a very poor water solubility, that greatly diminishes it's bioavailability. We investigated two new solid forms of this active pharmaceutical ingredient, ketoconazole-fumaric acid (KET-FUM) and ketoconazole- p-aminobenzoic acid (KET-PABA) in terms of solubility, antifungal efficiency and biocompatibility.

Material and methods. New solid co-crystal forms of Ketoconazole with fumaric acid and PABA were obtained by applying the solvent drop grinding method. Co-crystal formation was confirmed by powder X-ray diffraction, FT-IR and ss-NMR spectroscopy, and differential scanning calorimetry. Antifungal activity was evaluated against cultures of Candida species (ATCC). Biocompatibility evaluation was done in vitro on human dermal fibroblasts (HDFa, Gibco) and human umbilical cord endothelial cells (HUVEC, ECACC), by testing cell viability (MTS), cell death (FACS), DNA alterations-γH2AX (WB).

Results. Both co-crystals showed good stability in suspension and improved solubility and antifungal activity compared to KET. All compounds reduced cell viability and induced necrosis in HDFa. The most biocompatible was KET-FUM, followed by KET-PABA and KET.

Conclusion. These data show improved Ketoconazole properties by co-crystallization with fumaric acid and PABA, making these new antifungal formulations interesting candidates for developing antimycotic agents with enhanced bioavailability, biocompatibility and efficiency.

Acknowledgements: This research was funded through a national grant, project no. PN-III-P2-2.1-PED-2016-1521.

THE NEUROPROTECTIVE EFFECT OF THE COMBINED THERAPY WITH MELATONIN AND HYPOTHERMIA IN PREVENTING APOPTOSIS IN A NEONATAL RAT MODEL OF HYPOXIC-ISCHEMIC ENCEPHALOPATHY

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Introduction. Birth hypoxia is a leading cause of perinatal mortality and neurological morbidity resulting in central nervous system injury. Hypoxia and ischemia produce massive brain damage following a typical pattern which is defined by selective vulnerability of the brain regions. The neonates are most prone to hypoxic-ischemic injuries due to the lack of efficient antioxidant defense. The main objective of this study was to test the possible protective effect of melatonin and hypothermia in hypoxic-ischemic encephalopathy in newborn rats. The changes in terms of histology and apoptosis were determined in brain so as to assess the local damages induced by hypoxic ischemia.

Material and methods. The experiment was conducted on 20 newborn Wistar rats that were given melatonin in a dose of 20 mg/kg/day for seven days as premedication. At the P7 the animals were exposed to hypobaric hypoxia (8% O2 for 90 minutes) and ischemia (by clamping the right carotid artery).

Results. In the hypoxic-ischemic encephalopathy, melatonin, in a dose of 20 mg/kg/day as premedication offers neuroprotection by reducing the number of cells expressing apoptosis in CA1, CA2, CA3 and dentate gyrus of the hippocampus under the conditions of conjugation with post-injury hypothermia. In the cerebral cortex the melatonin protective effects were not hypothermia dependent.

Conclusion. The results of this study prove that melatonin offers neuroprotection in ischemic-hypoxic brain injuries, but the protection is conditioned in most of the brain regions (excepting cerebral cortex) by conjugation with post-injury hypothermia treatment.

INCREASED GLYCEMIC VARIABILITY IN TYPE 2 DIABETES PATIENTS TREATED WITH INSULIN – A CONTINUOUS GLUCOSE MONITORING (CGM) STUDY

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Introduction. Chronic hyperglycemia is an important cause for the development of chronic complications of diabetes, but glycemic variability emerged in the recent years as an independent contributor to diabetes-related complications. Our objective was to evaluate glycemic variability in patients with T2DM treated with insulin compared with other antidiabetic drugs.

Material and methods. In this retrospective study we collected 24-hours continuous glucose monitoring (CGM) recording data from 95 patients with T2DM, of which 27 treated with insulin and 68 with non-insulin treatment. We calculated and compared among insulin-treated and non-insulin treated groups 16 glucose variability parameters. Results. Insulin treated patients had significantly higher values of parameters describing the amplitude of glucose values fluctuations (standard deviation of the glucose values, percentage coefficient of variation [%CV], and mean amplitude of glycemic excursion [MAGE], $p < 0.05$) and time-dependent glucose variability (percentage of time with glycemic values below 70 mg/dl and continuous overall net glycemic action [CONGA] at 2, 4 and 6 hours, $p < 0.05$).

In conclusion, insulin therapy in T2DM is correlated with significant higher glycemic variability.

NEUROPROTECTIVE, NEUROCHEMICAL AND BEHAVIORAL EFFECTS OF SOME NATURAL COMPOUNDS IN A RAT MODEL OF EXPERIMENTAL-INDUCED ANXIETY

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Introduction. Anxiety disorder can associate with oxidative stress and behavioral changes. We aimed to evaluate the effects of some natural compounds, Quercetin (Q), Hypericum maculatum (HM) and Hypericum perforatum (HP) on brain oxidative stress biomarkers and ambulatory activity in rats with experimental-induced anxiety.

Materials and methods. 42 Wistar rats were used in the study. Partial inverse agonist at the benzodiazepine allosteric site of the GABAA receptor (FG- 7142) has been chosen to induce neurochemical and behavioral anxiety-like effects in rats. The animals were divided into 7 groups (n=6/group): Control, Carboxymethylcellulose (CMC), FG, Alprazolam + FG (APZ+FG), Q+ FG, HM+ FG, HP+ FG. APZ (0.08 mg/kgc), Q (30 mg/Kgc), HM and HP (350 mg/kg-1) were orally administered for 21 days. FG (7.5 mg/kgc) was intraperitoneally administered 1 hour before the behavioral tests, Open Field Test (OFT) and Elevated Plus Maze (EPM). Oxidative stress biomarkers in hippocampus and frontal lobe homogenates (malondialdehyde-MDA and catalase - CAT), brain GABA levels, plasma corticosteron and serotonin levels were assessed. NF-kB activation (western blot) and the histopathological changes in rats`brain were also analyzed.

Results. The natural compounds improved the ambulatory activity, decreased the oxidative stress levels, both in hippocampus and frontal lobe, decreased plasma corticosteron levels and increased brain GABA levels. Histopathologically, no microscopic changes were found.

Conclusions. Our findings may support the anxiolythic and brain protective effect, provided by natural compounds (i.e. Q, HM and HP) administration.

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CYTOKINE PROFILE IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS (NASH)

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Introduction. Cytokines play a critical role as mediators of injury, inflammation, fibrosis and cirrhosis in NASH. The study aimed to investigate the cytokines profile (TNF-α, IL-6 and IL-10) in patients with NASH and to correlate their level with respective genotypes.

Material and method. Sixty-six patients with NASH were included in the study. The plasmatic level of IL-6, IL-10 and TNF-α were determined by ELISA. The levels of investigated cytokines were correlated with anthropometric and laboratory parameters. The genotypes for IL-10 -1082 G/A, IL-6 -174 G/C and TNF-α –308 G/A polymorphisms were determined using PCR-RFLP technique. The obtained results were analyzed using MedCalc Statistical Software version 17.5.5, with a level of statistical significance of $p<0.05$.

Results. IL-6, TNF-α and CRP levels were significantly higher in patients with NASH. There was a positive correlation between proinflammatory cytokines ($p<0.015$) and a negative correlation between IL-10 and proinflammatory markers ($p<0.001$). There was a positive correlation between anthropometric parameters and IL-6 and TNF-α ($p<0.01$). Regarding IL-10 -1082 G/A polymorphism, AA genotype was correlated with a low plasmatic level of IL-10. A allele in position 308 of TNF-α gene was associated with high plasmatic level of it.

Conclusion. A ssystemic inflammation is present in patients with NASH. There was an imbalance of pro- and anti-inflammatory cytokines in patients with NASH. IL-10 -1082 G/A and TNF-α -308 G/A genotypes were correlated with the plasmatic levels of cytokines.

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HOW UNDERGRADUATE STUDENTS USE SOCIAL MEDIA IN MEDICAL EDUCATION

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Introduction. Social media is used for a variety of purposes to engage and educate students. We aimed to assess medical student preferences associated with the value of online learning methods such as social media.

Methods. A questionnaire has been developed and applied to medical undergraduate students on two sites: at the Iuliu Haţieganu University of Medicine and Pharmacy Cluj-Napoca (Romania) and at the University of Foggia (Italy). The anonymous survey ran from 12.12.2016 to 09.01.2017 (Italy) and from 27.02.2017 to 8.05.2017 (Romania) and data were collected by a Google form.

Results. One thousand one hundred ninety-six answers were collected, 326 (18.0% [16.3 - 19.9]) from the Italian university, and 870 (20.63% [19.41 - 21.88]) from the Romanian university. Most of the respondents (92.64% Italy, 98.62% Romania) used Facebook, mostly from home (96.32% Italy, 98.39% Romania). The average time spent on social media is 1-3 hours on both sites, with higher frequency among Romanian as compared with Italian students (98.39% vs. 57.36%, $p<0.0001$). The Smartphones are most used tool to access social media platforms (95.09% Italy, 94.14% Romania). Over 90% of the responders (95.40% Italy, 93.10% Romania) use social media for learning purposes, but this is not exclusively, as they use other information sources in their learning process (such as school bibliography and the general Internet). Majority of the responders (77.91% Italy, 88.97% Romania) would like that teacher to communicate with them on Facebook. The most frequent searched information is a specific medical topic, management of daily student activity (e.g. planning of the exams, lectures, etc.), or topics related to courses taught at school (just Romanian students). In addition, Romanians also frequently share information with other colleagues (40.11% [36.78 - 43.45]).

Conclusion. The medical students use social media in learning process in similar way in Italy and Romania.

OPINIONS OF THE ROMANIAN MEDICAL DOCTORS ABOUT THE USE OF COCOA IN STRESS

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Introduction. Cocoa (C) is known for its beneficial effects on health and stress. More and more phytotherapeutic (PT) and food (FD) products are based on C and C extracts (CE).

Objectives. The objective was to assess the opinion of Romanian medical doctors (MD), about C and CE use in stress.

Material and methods. MD of different medical specialties (42), without a C and CE training, voluntarily responded to a complex questionnaire having the topics: 1) importance of medical education for C and CE use in stress modulation; 2) C and CE mechanism of action and effects on stress; 3) C and CE use in oxidative stress; 4) how many publications about C and CE MD have consulted; 5) C and CE recommended for stress prevention; 6) PT and FD products containing C and CE.

Results. Majority of MD participants responded as follows: 1) medical education about C and CE is important to know more and correctly about their use in stress modulation; 2) MD have incomplete information about C and CE mechanism and effects on stress; 3) MD know little about C and CE use for oxidative stress; 4) most of MD have consulted under 4 publications about C and CE; T5) MD know little about C and CE usefulness in stress prevention, but they agree to apply them after a proper knowledge; 6) MD know some FD products containing C and little about PT products containing C.

Conclusions. 1) MD believes that information about the correct use of C and CE in stress is important for their use in therapy and prevention. 2) Although the mechanisms of action and effects of C and CE in stress are many known, MD are scientifically little informed about them. 3) MD should know the PT and FD products on the market, containing C and CE, in order to use them in an adequate way. 4) Evaluate MD proved interest in using C and CE for stress modulation.

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THE EFFECTS OF SERTRALINE IN EXPERIMENTAL GASTRIC ULCER

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Introduction. With the increase rate of diagnosis of depressive disorders, there is also an increase number of patients treated with antidepressants. The most commonly used are selective serotonin reuptake inhibitors (SSRIs). Higher digestive bleeding are documented as adverse reactions, but their frequency among SSRI users is uncertain. This study attempts to test the hypothesis that sertraline, one of the most commonly prescribed SSRIs, aggravates the progression of gastric ulcers.

Material and methods. The experiments were performed on a total of 40 Rattus norvegicus rats, weighing between 140 g and 180 g. The animals were obtained from Biobase University of Medicine and Pharmacy „Iuliu Haţieganu" Cluj Napoca. Ulcerogenesis was induced in all lots of animals by intraperitoneal administration of ketoprofen solution. Sertraline (Zoloft) was administered intraperitonealy into 3 doses aleatory.

Results. The results were statistically processed using the Microsoft Excel 2016 and GraphPad Prism 7.00 programs. Statistical significance was established at $p \leq 0.05$. Some of the rats died before being sacrificed. Ulcers were counted with the magnifying glass, noting their location and size. The total number of ulcers correlated with the weight of the stomach and the dry weight of the stomach. There is a significant difference between the number of ulcers in the control group and increased number of ulcers, suggesting that there is a link between the number of body ulcers and the administration of sertraline. Lots receiving higher sertraline doses had on average a high number of large ulcers compared to the lowest-dose group, the effect is dose-dependent.

Conclusion. Intraperitoneal injection of ketoprofen induces gastric and duodenal ulcers. Sertraline in high doses aggravates the induced ulcers with ketoprofen.

PRESSURE MANAGEMENT SCORES IN IRRITABLE BOWEL SYNDROME PATIENTS

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Introduction. Irritable bowel syndrome (IBS) is a functional disorder which affects up to 20% of the population and is the result of interaction between genetic and environmental factors. The aim of this study is to look for the possible correlation between IBS and Pressure Management (PM), assessed by a specific questionnaire: Pressure Managment Indicator (PMI).

Materials and methods. A total of 39 patients with IBS, according to the Rome III criteria and 37 gender and age-matched healthy controls were investigated using a self-administered questionnaire: PMI. Patients were classified into groups of IBS with diarrhea (IBS-D): 22, IBS with constipation (IBS-C): 14 and IBS with mixed symptoms (IBS-M): 3.

Results. Significant correlation between IBS and PM evidenced by organizational satisfaction, mental wellbeing, physical wellbeing, sources of pressure, type A behavior, coping was found ($p<0.001$), but there was no correlation between occupational classification, workout program, norm, health status, major disease, negative pressure in the last 3 months, smoking, alcohol consumption, work hours, number of years in the organization and IBS.

Conclusions. This is the first assessment of PM in IBS, by a validated specific questionnaire. PMI scores are higher in IBS than in controls, emphasizing the role of professional stress in this condition.

PATTERN OF SERUM COTININE ON PATIENTS WITH CRITICAL LIMB ISCHEMIA

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Introduction. Critical limb ischemia (CLI) is the final stage of peripheral arterial occlusive disease. Smoking has a negative impact on vascular changes and aggravates comorbidities, resulting in a poor prognosis of the disease. Plasma cotinine, the primary metabolite of nicotine, was measured on a cohort of CLI patients to identify its pattern and its association with the disease complications.

Material and methods. A cohort study was conducted between November 2015 and December 2016 on subjects hospitalized at the Second Surgery Clinic, Emergency County Hospital in Cluj-Napoca, Romania. Serum cotinine higher than 15 ng/mL was considered abnormal.

Results. Forty three patients with the mean age of 60.74±10.46 years were included in the study. Most of the participants were as expected men. Most subjects included in the study had serum cotinine values ≤15 ng/mL (29 patients). Majority of subjects with serum cotinine >15ng/mL had urban origin (p=0.0016). The median cigarettes declared by those with serum cotinine ≤15 ng/mL was 5 cigarettes while the value for those with serum cotinine >15 ng/mL was 22.5 cigarettes. No differences regarding symptoms and comorbidities were observed between those with serum cotinine ≤15 ng/mL and those with values >15 ng/mL. A cut-off of serum cotinine equal with 9.765 proved a sensibility of 80% and a specificity of 75% as a biomarker for necrectomy among smokers with CLI (AUC=0.7232 [0.5307-0.9157]).

Conclusions. This study showed that values of serum cotinine higher than 15ng/mL are observed among subjects who smoke on median 22.5 cigarettes per day. Among smokers with critical limb ischemia, serum cotinine at a cut-off equal with 9.765 ng/mL could be a biomarker for necrectomy.

ANALGESIC AND ANTIINFLAMMATORY EFFECT OF NIGELLA SATIVA OIL ON ACUTE EXPERIMENTAL INFLAMMATION IN RATS

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Introduction. The use of Nigella sativa (NS) oil within traditional medicine has pointed the wide spectrum of its pharmacological effects such as diuretic, antihypertensive, antidiabetic, anticancer and immunomodulatory, analgesic or antiinflammatory effects. The purpose of the present study was to evaluate the analgesic and antiinflammatory activity of NS seed oil in carrageenan induced inflammation model in rats.

Materials and methods. The study was carried out using fifty Albino Wistar rats of either sex with weight between 180 and 200 g. The antiinflammatory and analgesic effect of NS oil was evaluated by carrageenan-induced paw hyperalgesia and carrageenan-induced paw edema in rats. Analgesiometer and plethysmometer were used to evaluate the analgesic and antiinflammatory effects, respectively of NS oil oral administration. Paw inflammation and the mechanical induced pain were measured at 90, 180, 270, 360 minutes. The rats were divided in five groups as following: group (A) the control group which received normal saline solution; groups (B), (C) and (D) which received NS oil in a dose of 1, 2 and 4 mL/kg, respectively; and group (E) which received intraperitoneal diclofenac sodium, as positive control group, 20 mg/kg.

Results. In the model of acute inflammation, all concentrations of administrated NS oil showed statistically significant antiinflammatory activity as compared to control (A) group. When compared to positive control group (E), no significant difference was observed between group E and C, D, respectively at 90, 180 and 270 min. Moreover, at 360 min, all three administrated NS oil concentrations had antiinflammatory effect with comparable results as the positive control group. Regarding the analgesic effect, no significant differences were observed among groups.

Conclusion. The results of this study suggest that NS oil possesses significant antiinflammatory activity but no analgesic effect.

PERFORMANCES ON WALKING TESTS OF PATIENTS WITH LOWER EXTREMITY PERIPHERAL ARTERY DISEASE

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Introduction. Peripheral artery disease (PAD) is a circulatory condition in which obstructed arteries as a consequence of atherosclerotic plaques decrease blood flow to the extremities. Muscles do not receive sufficient blood to have a normal function resulting in claudication and pain. Our study aimed to evaluate how walking tests can objectively asses the functional disturbances that PAD produces in the lower limbs.

Material and methods. We conducted a non-randomized cohort study on adult subjects admitted with the diagnosis of PAD grades Rutherford from I to IV at the Second Surgery Department, County Clinical Emergency Hospital from Cluj-Napoca since March 2016 to October 2017. Every patient who agreed to participate was invited to perform three walking tests, namely 6 minute walking test, climbing stairs test and treadmill test.

Results. The mean age of investigated cohort was 67.18±10.37 years, with a higher frequency in men (68.98%, $p<0.0001$). The frequency of smoking among investigated cohort was 41.27% (95%CI [36.29−46.54]). Most of the investigated women were with normal weight (41.96%, 95%CI [33.04−51.78]) while most of the men were overweight (56.63%, 95%CI [50.20−63.05]). Among co-morbidities, arterial hypertension was most frequent (78.95%) followed by type II diabetes (58.73%) and ischemic cardiac disease (49.31%). The medians and inter-quartile ranges (IQR provided in square brackets) for the applied tests were as follows: 300 [200−340] meters on 6 minute walking test, 88 [63−90] stairs on climbing stairs test, and 210 [110−240] meters on 11 minutes on treadmill test. As expected, the results of the walking test significantly correlate positively with each other, with values between $\rho=0.8263$ ($p<0.0001$, 6 minute walking test vs. treadmill test) and $\rho=0.9122$ ($p<0.001$, 6 minute walking test vs. climbing stairs).

Conclusion. All of the investigated tests turned out to be reliable instruments to identify patients with most severe PAD.

EVALUATION OF TACROLIMUS WHOLE BLOOD CONCENTRATIONS IN TRANSPLANT PATIENTS

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Introduction. Assay accuracy, full automation, and laboratory cost are the key of future technologies for the therapeutic drug monitoring of immunosuppressive drugs. This study aimed to evaluate the agreement between two quantitative methods (ELISA and chemiluminescent imuno-assay) for the measurement of Tacrolimus blood concentrations in transplant patients.

Material and methods. The longitudinal retrospective study contained nine children with organ transplant recruited from one single medical center between 2012 and 2015. Data collected included Tacrolimus whole blood concentration measured at three time points: 1-3 months, 3-6 months and 6-9 months. The objectives of study were: i) to assess the concordance between Tacrolimus measurements; ii) to compare inter-assay variability and iii) to compare the changes over time of Tacrolimus blood concentrations.

Results. The Bland-Altman method revealed concordance between Tacrolimus blood concentrations determined by ELISA and chemiluminescence but the inter-assay coefficient of variance for the ELISA method was on average equal to 31.01% ± 24.4% (95% CI: [12.24; 49.76]) while the inter-assay coefficient of variance for chemiluminescent method was 13.8% ± 10.3% (95% CI: [5.9;21.7]).

Conclusion. An accurate value of Tacrolimus concentration is important in monitoring the evolution of children with organ transplant. As such, we recommend the chemiluminescence method for the determination of Tacrolimus whole blood concentration.

MANAGEMENT IN PATHOLOGICAL GAMBLING

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Introduction. Pathological gambling has been recently classified as an addictive disorder. There is scientific evidence that pathological gamblers have a family history of psychiatric conditions, different psychiatric comorbidities, as well as personality traits such as impulsivity.

Objectives. The description, of a clinical case part of a large number of young patients with gambling problems, from which only a few seek help and treatment.

Methods. A 20 year-old male, diagnosed with pathological gambling and impulsive personality disorder (according to ICD-10 and DSM-V), known with a pattern of alcohol abuse when gambling, presented to hospital admission because of his suicidal thoughts. The onset of the first gambling episode was at the age of 17 when his father, known with gambling problems, gave him money and forced him to play. The patient began gambling after each negative life event, or in the context of peer pressure, loosing great sums of money and was forced to steal or beg.

Results. Considering the clinical picture, a number of risk factors for treatment resistance were identified and also multiple psychiatric comorbidities. Early age of first gambling experience is correlated with gambling severity. The presence of the same psychiatric problem in a first degree relative has an important impact over the case management.

Conclusion. Our findings support that in pathological gambling, family factors and family structure have a significant influence on this behavioral addiction that needs more clinical research for prevention and treatment.

THE IMPORTANCE OF EVALUATING AMIODARONE PLASMA CONCENTRATION IN PATIENTS WITH ATRIAL FIBRILLATION

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Introduction. Atrial fibrillation (AF) is one of the most common sustained cardiac arrhythmia. This is associated with significant morbidity, mortality and poor quality of life. Amiodarone is one of the most frequently used antiarrhythmic drugs in patients with atrial fibrillation both in prophylaxis and treatment. The objective of this study was to assess the plasmatic concentration of amiodarone in patients with AF and also to identify possible factors that could influence it. The results were correlated with used doses, with concomitantly administered drugs, renal and liver function.

Material and methods. A prospective observational study was conducted in 27 consecutive patients treated with amiodarone from May to July 2017 in a Clinical University Hospital. The patients included met our inclusion criteria. HPLC-MS was the device used to determine the plasma concentration of amiodarone.

Results. The mean age of those 27 included patients were 65.6±11 years, 44.4% women. The used doses were 200 mg or 400 mg/day. In our patients, plasmatic concentration was in therapeutically interval (500-2500 ng/ml) only to 51.8%. In the patients with lower plasmatic concentrations of amiodarone the drugs associated in therapeutic plan belonged to: diuretics, beta blockers, statins, antiplatelets, non-steroidal anti-inflammatory drugs. It was observed a statistically significant difference between the plasmatic concentrations of amiodarone in patients treated with furosemide vs patients treated concomitantly with other drugs. It was observed that an increasing of transaminases or creatinine is correlated with increasing of amiodarone's plasmatic concentration.

Conclusion. 48.2% from the patients with AF under the chronic treatment with amiodarone had the plasmatic concentration of amiodarone out the therapeutic range. It was found a significant interaction between furosemide and amiodarone. In order to confirm this interaction, we need to continue the research on a larger sample.

ANTIBACTERIAL EFFECT OF SOME CALCIUM PHOSPHATE SYNTHETIC MATERIALS FOR MEDICAL PURPOSE

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Introduction. The research in the field of reconstructive medicine is in a continuous search of synthetic biomaterials, but also of new solutions for prosthetic or regeneration of living tissues. The chemical composition of biocompatible materials generally consists of calcium and phosphorus oxides or other constituents of the material that help to form chemical bonds with the bone and sometimes with the soft tissue, also. In this respect copper-calcium phosphate materials were produced with variable copper oxide concentrations.

Materials and methods. These materials were prepared using the conventional melt-quenching method. IR/Raman technique was used for the structural analysis of the materials. Elemental profile was also provided and antimicrobial effect was demonstrated on Staphylococus aureus (Gram positive) and Escherichia coli (Gram negative) bacteria.

Results. IR/Raman bands for phosphate groups are affected by the change in the concentration of copper oxide producing a depolimerization of the phosphate network. Elemental profile is strongly required in the study of materials with bioactive potential for the detection of impurities and toxic elements and such elements were not detected in the studied materials.

Conclusion. The antibacterial test of the studied glasses ($x \leq 20$ mol%) shows an inhibition in growth and a linear correlation between this effect and the amount of copper oxide, for both E. coli and S. aureus bacteria. Further tests in simulated biological fluid to evaluate the bioactivity of the material will be provided as next step in this study.

A NOVEL COMMON LARGE GENOMIC DELETION IDENTIFIED IN A GROUP OF ROMANIAN PHENYLKETONURIA PATIENTS, A POSSIBLE ROMANIAN FOUNDER EFFECT

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The mutation spectrum for the phenylalanine hydroxylase (PAH) gene was investigated in a group of 46 hyperphenylalaninemia (HPA) patients from Romania identified through neurometabolic investigations. Differential diagnosis identified 44 patients with classic PAH deficiency while 2 had tetrahydropterin cofactor deficiency and/or remained uncertain due to insufficient specimen.

PAH-genetic analysis included PCR-restriction fragment length polymorphism (RFLP) analyses for a small group, then a combination of Sanger sequencing of exons and exon–intron boundaries, Multiplex ligation-dependent probe amplification (MLPA) and Next Generation Sequencing (NGS) with genomic DNA, and cDNA analysis from immortalized lymphoblasts. The most prevalent mutation was p.Arg408Trp (or R408W) which was found in ~40% of all PKU alleles. A novel large genomic deletion EX6del7831 (c.509 + 4140_706 + 510del7831) that resulted in skipping of exon 6 based on PAH-cDNA analysis in immortalized lymphocytes. The genomic deletion was present in a heterozygous state in 11 patients of all the analyzed PKU alleles (~10%); the high frequency in the PKU population analysed here might hint towards a Romanian founder and/or a heterozygous advantage. According to Zschocke (2003) there have been numerous independent mutation events for PKU in Europe, and several mutations have independently recurred in different founders. Furthermore, it was proposed that a potential heterozygous advantage by an "over dominant selection" must have played an important role during the history of PKU in European population, although the exact nature of this effect remains unknown, and might have originated from a Romanian founder.

INFLUENCE OF RHODIOLA ROSEA PHYTOTHERAPIC PRODUCT ON TWO PARAMETERS IN MENTAL STRESS

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Introduction. Rhodiola Rosea (RR) influences the stress effects. The objective was to prove the RR product (RRP) action on two parameters in stress induced by an intense mental effort.

Methods. Volunteer healthy subjects (n=30 men) were organized into 3 groups: control (C=10) without treatment; which received placebo (P=10); which received RRP (RR=8). All groups were subjected to the same mental stress: a demanding mathematical exercise. The analyzed parameters were heart rate (HR) and salivary pH (SpH). Parameters evaluation (HR, SpH) was made: prior to P and RRP administration (T1); 15 min before (T2), 15 min (T3) and 24 hours (T4) after stress. Statistical evaluation was made on the basis of Student test.

Results. For C and P compared to RR: HR values were significantly higher at T2 and T3 and SpH values were significantly lower at T3 and T4.

Conclusions. 1) RRP influenced the two parameters, before and after the stress caused by an intense mental effort. 2) There were differences on dynamic developments between the three groups, for both analized parameters. 3) RRP influence was more intense on HR than on SpH. 4) RRP administration, in stress represented by an intense mental effort, could be useful, bng without side effects and having economic modulation path.

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ASSESSMENT OF MOBILE APPS' ADEQUACY FOR LEARNING ANATOMY: MEDICAL UNDERGRADUATES' PERCEPTION

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Introduction. Anatomy books and atlases have limited value by providing bi-dimensional images compared to mobile applications (apps) freely available to students via Smartphones. These could be used as teaching tools since the dynamic 3D images allow students to rotate and manipulate structures in different ways to identify anatomical architectures. The objective was to assess two anatomy apps used in second-year anatomy seminar, assess student satisfaction and advantages in using anatomy mobile apps on Smartphones.

Methods. A search of mobile medical anatomy apps available in English, free of charge, running both on Android and iPhone platforms was conducted. Based on students' recommendation and on the first year Anatomy curriculum, Essential Skeleton (ES) and Visual Body (VB) were selected. Each app was used during a distinct anatomy seminar on head structures. At the end of each seminar, students were given an adapted CRAAP (information Currency, Relevance, Authority, Accuracy, Purpose) questionnaire for evaluating mobile health applications, where we added a section on the benefits of anatomy apps. The Mann-Withney U test was used for comparing the scores of the apps.

Results. Regarding how current the information was the VB scores proved significantly higher than those for ES. On the relevance and on the accuracy of information ES scores proved significantly higher than those for VB. On the issues of authority, purpose, anatomy teaching benefits and over-all app evaluation there were no significant score differences between the two apps. Students stated that both apps offered information at an elementary level with no evident scientific support. When learning, 44% of students would choose the atlas, 30% the mobile apps and 26% would choose both. The most frequent advantages mentioned for both apps were better image visibility, easy access and use.

Conclusions. Freely available anatomy mobile apps need to be improved in order to use them for teaching purposes.

RETROSPECTIVE ANALYSIS OF PUBMED REFERENCES ON THE RELATIONSHIP BETWEEN ADAPTOGENS AND STRESS

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Introduction. The study of adaptogens (AD) is a growing scientific concern in recent years. The objective was the evaluation of research concerning AD and stress (S) relationship, by the retrospective analysis of PubMed publications.

Methods. 1979-2017 period was assessed, by the total number of publications (N), using keywords combinations: "AD and S" (ADS), "AD and oxidative stress" (ADOS), "AD and cortisol stress" (ADCS), "AD and anxiety stress" (ADAS). Analyzed filters: a) "species" with the sub-filters "other animals" (AN) and "humans" (H); b) "sex", with subfilters "male" (M), "female" (F). Statistical evaluation was made on the basis of the Student test.

Results. N for AD increased between 2000-2017. Publications were more numerous: a) for AN (42% of ADS) than for H (34% of ADS); b) for M (10.9% of ADS) than for F (7.4% of ADS); c) for ADOS (21.9% of ADS) than for ADCS (15.6% of ADS) and ADAS (12.5% of ADS).

Conclusions. 1) N for ADS for 38 years, was 64. 2) Studies with animals and human male predominated. 3) Publications on ADOS, ADCS and ADAS have shown interest since the 1980-1990s, and have steadily increased until now. 4) The relationship between bad aptogens and oxidative stress, cortisol stress, respectively anxiety stress, although it has shown a small number of publications, it is worthy of note from the point of view of the future research.

SURGICAL STRESS EVALUATION FROM THE PERSPECTIVE OF GLYCEMIA CHANGES IN NON-ENDOCRINE OPERATIONS

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Introduction. Stress (S) is commonly associated with the surgical act, and was investigated under various aspects, including modification of glycemia (GL). The objective was the evaluation of surgical stress (SS) from the perspective of G changes, in non-endocrine operations.

Methods. Volunteer operated subjects (n=71, 40 Male and 31 Female) were included. Evaluated parameter was GL: immediately before (BS) and after surgery (AS). The values analyzed were those usually determined by the operation. Selected surgical interventions had different degrees of complexity. Statistical evaluation was made on the basis of Student test.

Results. GL values were increased post-operation, and growth was more intense in the more complex operations, than in the minor ones. There were no significant differences between genres.

Conclusions. 1) The dynamics of peri-operator blood glucose levels was similar in patients analyzed, regardless the intervention type. 2) The patient's genre did not create differences in peri-operative dynamics. 3) The postoperative increase in GL may be associated with the severity of the intervention. 4) Glycemia could be a useful marker for assessing the intensity of surgical stress in non-endocrine interventions.

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MEDICAL SCIENCES

BĂILE TUŞNAD – A THERAPEUTIC EDUCATION AND MEDICAL REHABILITATION PROGRAM FOR PATIENTS WITH CHRONIC OCCLUSIVE ARTERIAL DISEASE

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Introduction. Băile Tuşnad spa resort is recognized for its role in the prevention and rehabilitation treatment of cardiovascular diseases, including chronic occlusive arterial disease, due to the presence of natural therapeutic factors: mixed carbonated mineral waters through their peripheral and central vasodilator effects, mofettes, a stimulating bioclimate.

Aim. The objective of the initiated program, which is in progress, is therapeutic education, as well as the assessment of the clinical efficacy of natural therapeutic factors alongside kinesiotherapy, by monitoring the duration of treatment effects, adverse effects, the reduction of therapeutic doses. The aim is to encourage walking, to reduce cardiovascular risk and to improve quality of life.

Material and method. Patients with chronic occlusive arterial disease attending spa treatments consisting of carbonated mineral water baths for 15 minutes, mofettes for 15 minutes, aerotherapy and special kinesiotherapy for 30 minutes daily, during 16 days. They will be monitored by phone over 6 months, while continuing daily exercises for 15 minutes and walking.

Results. At the end of treatment, we expect an improvement of the walking distance and speed, a significant improvement of gait, an increase of the walking perimeter, an amelioration of pain, the duration of the effects of these treatments being also important.

Conclusions. We aim to continue medical rehabilitation in spa resorts for the treatment of cardiovascular diseases by collaboration/partnerships with cardiovascular medical and surgical units.

DELETERIOUS EFFECT OF SINGLE CHAMBER PACING

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Introduction. Single chamber cardiac pacing is recommended for patients with atrial fibrillation (AF) and normal left ventricular ejection fraction (LVEF) and in those where a low pacing percentage is expected. However, a right ventricular percentage of pacing above 40% may induce LV adverse remodeling. The present case aims to highlight the effects of different pacing modalities on cardiac function.

Material and methods. A 61 year old man, with single chamber pacemaker (VVI) for trifascicular AV block and presyncope (implanted 4 years ago) was admitted for heart failure symptoms. The ECG revealed sinus rhythm, 60 bpm, with ventricular paced rhythm and AV dissociation. Transthoracic thoracic echocardiography (TTE) showed LV dilatation with severe dyssynchrony and LVEF=20% (TTE before VVI implantation: LV dimensions in the normal range with LVEF=60%).

Results. The case had indication for cardiac resyncronization therapy. An upgrade to triple chamber pacemaker with optimized AV and VV delays was performed. The 2-weeks follow up revealed no LV dyssynchrony (100% Biventricular pacing) with improved exercise capacity.

Conclusions. Single chamber pacing induces both AV and VV dyssynchrony potentially leading to LV adverse remodeling. Single chamber pacing should be reserved for patients with AF and normal LVEF or whenever a low percentage of pacing is expected; otherwise a more physiological device is recommended. In case of pacemaker induced cardiomyopathy an upgrade to triple chamber pacing might lead to reverse remodeling and symptoms improvement.

CARDIOVASCULAR PROFILE OF FEMALE PATIENTS WITH PERIPHERAL ARTERY DISEASE IN A CARDIAC REHABILITATION CLINIC

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Introduction. Peripheral artery disease (PAD) was thought to be almost an exclusively male disease. Current data show an increased prevalence of the disease in females, even surpassing that of men after 75 years of age.

Methods. 257 consecutive patients admitted in the Cardiology Department, previously diagnosed with symptomatic PAD, were enrolled. The mean age was 66.34±9.54 years. PAD was defined according to ESC criteria, cardiovascular risk factors associated comorbidities and treatment type and outcome were all registered.

Results. 33% of our cohort were female patients. There were no significant differences in cardiovascular risk factors, with the exception of smoking, more frequent in men: 81.6% vs 44.57% (p=0.0001). Diabetes was more common in female patients, short of statistical significance (45.7 vs 33.3 %, p=0.07). HDL-cholesterol levels were slightly higher in women (45.07±14.1 vs 42.09±9.66 mg/dl, p=0,08), while uric acid levels (6.54±1.85 vs 6.05±2.03 mg/dl, p=0.06) and creatinine (1.00±0.59 vs 0.98±0.55 mg/dl) were found to be elevated in men. Female patients presented with critical limb ischemia more often than men, while the majority of males had intermittent claudication (p=0.013). Multivariate statistical analysis found ABI (p<0.0001), diastolic BP (p=0.02), obesity (p=0.04), LDL-cholesterol (p=0.001), HDL-cholesterol (p=0.009) and serum creatinine (p<0.0001) to be independent predictors for PAD severity. Regarding anatomo-pathological features of PAD, women exhibited complete occlusions on imagistic study more often than men (60.24 vs 56.32%, p=0.016). Treatment wise, medical therapy was similar between the two groups, PTA was more often used for women (42 vs 28%, p=0,026), while surgery for men (38.5 vs 21.6%). Limb amputation was slightly more frequent in men (3.44 vs 1.2%, p=0,02).

Conclusion. Women with PAD have a particular cardiovascular profile, which often requires a different approach for this category of patients.

PREDICTED INDIRECTLY RECOGNIZABLE HLA EPITOPES CLASS II SCORE IN PEDIATRIC KIDNEY TRANSPLANTATION – EXPERIENCE OF A SINGLE CENTER

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Introduction. Donor-specific HLA antibodies detected post-transplant are an independent risk factor for late deterioration of renal allograft. A novel tool to predict an allo-immune response is the PIRCHE algorithm. In our study, we hypothesized that the PIRCHE II algorithm can be an independent predictor for the development of de novo dnDSA.

Methods. We systematically reviewed the electronic patient record for all renal transplantations from January 2010 to August 2016. We included 70 pediatric recipients (mean age at transplantation 11.23±3.86 years) with complete HLA typing, as well as HLAab follow- up.

Results. The cohort included first kidney transplantations mainly from deceased donors (61 patients) with a mean waiting time for the graft of 0.93 years ±0.61 years. The PIRCHE II score ranged between 2 and 193, with a mean of 76.05±36.92. There was a significant correlation between the number of HLA mismatches and PIRCHE II score with a $p<0.001$ and $r2=0.19$. The mean PIRCHE II score for patients with ABCDRDQ mismatches < 5 was 61.24 ±24.89 and for patients ≥5 was 86.53 ±40.57, with a $p=0.004$. A total of 8 patients (11.42%) developed dnDSA during the first year after transplantation. The mean PIRCHE II score for patients who developed dnDSA in the first year after transplantation was 61.50 ± 23.90 vs 77.93 ± 38.01 for patient who did not develop dnDSA. We divided the dnDSA negative patients into 2 groups: one with low risk (mismatches <5, n=25) and high risk (mismatches ≥5, n=37). The PIRCHE II score was 60.2 ± 24.44 in low risk vs 61.50±23.90 in dnDSA + patients ($p=0.89$), respectively 89.91 ± 41.04 in high risk vs 61.50±23.90 in dnDSA + patients ($p=0.06$). There is a statistical difference between negative dnDSA patients with low risk and high risk, $p=0.001$.

Conclusions. In our study the highest PIRCHE II scores were not associated with dnDSA development. The PIRCHE II algorithm is a promising tool for the allocation of organs but still needs improvements.

ASSESSMENT OF PATIENTS USING INSULIN PUMP AFTER SHORT AND MEDIUM TERM USE

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Introduction. Patients with Type 1 DM are confronted with limitations in the optimization of glycemic control: symptomatic hypoglycemia, ineffective adjustment of bolus and basal insulin according to physical effort and health, the down/dusk phenomenon. The alternative is continuous subcutaneous infusion of insulin. The aim of this paper was to evaluate short and medium term metabolic control and the quality of life of CSII patients.

Material and methods. Between Jan 2016-Mar 2017, CSII was installed in 32 patients with type 1 DM, the mean age was 21 years old (7;63), and mean disease duration 8.5 years, having a mean HbA1C of 8.12%, and a mean hospitalization of 5 days. The reasons for switching to CSII were glycemic imbalance, predominantly nocturnal hypoglycemia, glycemic fluctuations and the desire to perform sports. Those who didn't present at the regular evaluation and discontinued the use of pump were excluded. Quality of life was assessed through questionnaires.

Results. The 19 patients evaluated periodically chose CSII due to hyperglycemia 68.4%, reduction in number of injections 78.9%, frequent hypoglycemia 31.6%, lipodystrophy 26.3%. The baseline insulin dose was significantly reduced (mean ins.basal=20.96±11.6; $p < 0.001$; ins.basal mean at discharge=16.18±7.1; $p < 0.001$). HbA1c at 3 months decreased by 0.64% (baseline HbA1c 8.02, 3M HbA1c 7.34, $p < 0.001$). 68.4% did not experience glycemic variability, 89.5% nocturnal hypoglycemia, only 21.1% had severe hypoglycemia, 73.7% had more flexible meals, 21.3% had hypoglycemia <70 mg/dl, but only 52.6% used bolus advisor. Accommodation period with the pump was 4.5 weeks, 6 patients started sport activities after the pump was installed.

Conclusion. CSII has demonstrated optimization of glycemic control and increased quality of life by reducing the frequency of nocturnal hypoglycemia, increasing the safety of practicing sports, the flexibility of the meal timetable. Long-term control is essential.

EVALUATION OF GLICEMIC CONTROL AND USE OF "BOLUS ADVISOR" IN PERSONS WITH INSULIN PUMP V.S. INSULIN PUMP AND CONTINUOUS GLUCOSE MONITORING

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Introduction. Evaluation of paraclinical and clinical glycemic control following the use of the Bolus advisor (BA) with the automatic bolus calculation based on: capillary glycaemia, daytime glycemic targets, correction and sensitivity factor, active insulin, compared to sensor users (CGM) and those without a sensor.

Material and methods. The observational study included 22 people with type 1 diabetes (T1D) who had the insulin pump (AccuChekSpiritCombo) and the meter (remote control) installed between 2016-2017, then evaluated at 3 and 6 months after initiation. The mean age of the group was 17.9 years (±9), with a mean disease duration of 6.91 years (±6) and mean baseline HbA1c of 8% (±1). Users of CGM at the time of installing the pump or in the first 3 months were included. We compared two groups: with sensor (P+S) and without (P). Data related to the use of BA and the frequency of hypo-/hyper-/glycemic variability were obtained by questionnaire.

Results. In the P+S group, the age and duration of the disease was lower [n=13; (14.69±5.7) (4.89±5)] than in the P group [n=9 (9.8±6.4)]. Autoimmune thyroiditis 38.5% and celiac disease 7.7% had P+S. The most commonly used sensor was Abbot 76.9%, Dexcom 15.4% and Medtronic 7.7% with a mean difference from capillary glycaemia ±54.4 mg/dl. The mean HbA1c was lower both initially, at 3 and 6 months in the P+S (in=7.75±1) (3M=7.19±1, p=0.00) (6M=7.23±1.3, p=0.003)] vs. P [(in=8.40±0.9); (3M=7.62±0.9, p=0.008) (6M=7.61±0.85, p=0.36)]. BA used 44% of the P group and 23.1% of the P+S group. For prandial bolus, BA used only 44% P and 38.5% P+S. Weekly mild hypoglycemia was more common in the P+S (22.2% vs 53.8%). Hipo <54 mg/dl had more frequent P (55.6% vs 30.8%). Glycemic variability was similar (33.3% vs 38.5%)

Conclusion. Glycemic control was better in those using CGM even if they didn't used BA. Severe hypoglycemia rarely underwent P+S, but it was more frequent in those without a sensor due to the non-use of BA.

TOOTHPASTE TUMOR, TO BE OR NOT TO BE OPERATED

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Introduction. Caseous calcification of the mitral valve annulus is a less known entity, defined as chronic degeneration of the mitral valve fibrous ring, involving mainly the posterior annulus. Many cardiologists are not familiar with this condition, therefore, it is easily confused with a tumor or abscess.

Material and methods. We present two unusual cases of caseous calcification of the mitral annulus in a 63-year-old female patient, and one in a 67-year-old female. The masses were detected during TTE and further evaluated with a full spectrum of cardiac noninvasive imaging modalities.

Results. In both cases the diagnosis was made by incidental findings of an intracardiac mass during TTE, defined as heterogeneous tumor masses at the posterior mitral valve base, with regular margins and relative internal hypoecogenicity. In the first patient the mass was initially measured 17 mm in dimensions, and multimodality imaging, including ETE, MRI imaging were performed and demonstrated non-homogeneous structure with hypointense center on T2-weighted MRI sequences, and reduction in size over time. In the second case the mass was measured 5 cm square on TTE, confirmed on MRI T1-weighted MRI sequences, as tumor mass in the left ventricular myocardium in relation to the posterior mitral valve with hypo-intense center, without intratumoral contrast intake. Further a computed tomography was used and showed coarse calcification in the ventricular myocardium in relation to the mitral valve. The patient underwent cardiac surgery and the diagnosis was confirmed intraoperatively.

Conclusion.

1. The clinical presentation needs complimentary imaging modalities which can clearly differentiate it from other lesions.

2. The natural evolution may have a dynamic course, it can resolve spontaneously or even recur after surgical excision.

3. TTE is the most reliable method for diagnosis, it can be completed with cardiac CT, and MRI, to confirm the diagnosis and avoid unnecessary surgery.

METACHRONOUS MULTIPLE PRIMARY NEOPLASMS - SURVIVAL AND PATIENT CHARACTERISTICS

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Introduction. There is an increased interest in identifying the most frequent cancer associations, possible risk factors and the implications of multiple primary neoplasms (MPN) in the outcome of oncological patients given the significantly increased incidence of MPN over the last few years. The aim of this study was to evaluate the survival and clinic-pathological characteristics of patients with metachronous MPN (mMPN) diagnosed and treated in The Oncology Institute "Prof. Dr. Ion Chiricuta" Cluj-Napoca (OICN).

Material and methods. Patients with mMPN diagnosed and treated in the OICN between 2008-2012 were included in this study. The medical charts of the patients were reviewed and the data were retrospectively collected and analyzed.

Results. 158 patients with mMPN were treated in the OICN between 2008-2012. The median interval between the diagnosis of the primary and subsequent tumor was 30.98 months. 92% of the patients presented with metachronous tumors < 5 years. 54% of the patients were females and 46% were males. Most patients presented with early stage primary tumors and advanced stage secondary tumors. The most frequent cancer associations observed were breast cancer-ovarian cancer, breast cancer-thyroid cancer, head and neck cancer-lung cancer, prostate cancer-lung cancer, lung cancer-colorectal cancer, colorectal cancer-prostate cancer and uterine body cancer-breast cancer.

Conclusion. During the follow-up of oncological patients physicians should be aware of the possibility of MPN occurrence in the patients they have in their care and closely monitor them in order to diagnose secondary tumors in early stages.

BREST CANCER AND PSYCHOSOCIAL INTERVENTION STRATEGIES FOR IMPROVING QOL. A SURVEY

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Introduction. Many of the patients diagnosed with breast cancer experience a myriad of psychological, medical and social challenges. Just like there is no doubt that "the attraction of Tolkien's Ring is the complex and haunting journey of his fellowship," (Saunders, 2003: 13), it is clear for us that our Ring is represented by the quality of life of patients and consists of three parts: improving the quality of medical care, improving the quality of psychological care and that of social care.

Material and methods. In all, 20 patients diagnosed and treated for breast cancer in the Oncology Institute "Prof. Dr. Ion Chiricuţă" Cluj-Napoca, agreed to participate in the survey. They have all given their approval by signing the informed consent form. As such, they have completed the functional assessment of cancer therapy for breast cancer (FACT-B) form, (Romanian version), and a 20 question questionnaire regarding their specific needs at the moment of its completion.

Results. The FACT-B scale is appropriate for use in oncology clinical trials, as well as in clinical practice. It demonstrates ease of administration, brevity, reliability, validity, and sensitivity to change. On the other hand, the questionnaire regarding the specific needs of the patients showed that psychosocial strategies such as the main types of effective interventions that can be performed by the clinical psychologist together with the social worker for these patients include: training regarding treatment options and appropriate decisions in this regard, long-term stress management strategies (Smith & Toonen, 2007). In addition, a very important social intervention is the behavioral one.

Conclusion. Overall, psychosocial care during breast cancer treatment, and in the survival stage, should be carried out in routine clinical practice as an important cure strategy.

CERVICAL CANCER IN ROMANIA - KNOWLEDGE, PREVENTION AND EXPOSURE TO RISK FACTORS AMONG STUDENTS

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Introduction. Cervical cancer is the fourth most common cancer in women. Decreasing cervical cancer incidence could be done by improving knowledge levels concerning the disease and by facilitating the access to preventive services. The aim of this study was to evaluate the level of awareness and preventive behavior for cervical cancer among undergraduate students in Romania.

Material and methods. A cross-sectional study using a survey consisting of 4 sections was conducted. First part consisted of questions about demographic information, second tested the knowledge about human papillomavirus (HPV) and cervical cancer, third part had questions about applied preventive methods and the last part investigated the possible exposure to risk factors among respondents. 125 undergraduate students from Romania aged 19-25 years old, both men and women, participated to this survey.

Results. Majority of respondents (81.6%) were female. The mean age of the respondents was 21.93±1.88 years old. Most of participants (87.2%) were medical students. 88.8% of participants said that knew what HPV is and 91% of these knew that it may affect men and women alike. Students who knew what HPV is, went to gynecologist (64.9%) more frequent then those who did not know (21.4%, p=0.002) but just 9.9% awarded HPV students underwent the HPV vaccination compared to 0% of unaware students (p=0.611). High number of sexual partners and history of sexually transmitted diseases were pointed as being the most frequent risk factors for cervical cancer. Most of the respondents were sexually active (72%), starting sexual intercourse around 17.93±1.76 years old and 68.8% mentioned that they used contraception (60.8% condoms and 21.6% hormonal pills).

Conclusions. Romanian undergraduate students have a good knowledge about HPV, prevention and exposure to risk factors of cervical cancer but even so, vaccination coverage has low rate among them. The most popular contraceptive method among students are condoms.

EFFICACY OF IRON CHELATION THERAPY ON POLYTRANSFUSED PATIENTS

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Introduction. Chelation therapy is recommended for transfused patients that have an elevated serum ferritin level, evidence of iron overload or received over 20 units of red blood cell transfusions (RBCT). We assessed the results of Deferasirox efficacy, side effects and to study if the number of RBCT decreased after starting Deferasirox.

Material and methods. Retrospective study including adult polytransfused patients treated with Deferasirox in three counties.

Results. We included 40, age average 63. The baseline value of ferritine was between 1075 - 6187 microg/l. There was a significant reduction in serum feritine from baseline for all the patients. Ferritine median at start, 3631 microg/l decreases at 1537 microg/l after 6 months of treatment and at 994 microg/l after 12 months of treatment.

Digestive adverse events appeared in three cases. In all these cases the treatment was temporarily discontinued. In three cases, treatment was stopped because low ferritin level.

RBCT were administered beforeand after starting Deferasirox, the difference is statistically significant (Student Test, $t(39)=6.98$, $p<0.001$). After starting Deferasirox treatment mean number of RBCT decreased, mean of differences (95% CI) was 1.04.

We analyzed the group of 23 patients treated with Deferasirox less than 12 months, and the patients treated more than 12 months, 15 patients. In both groups the difference of RBCT means (before and after the start of the treatment) are statistically significant (for the patients treated less than 12 months: Student Test, $t(23)=8.12$, $p<0.001$ and for the patient treated more than 12 months: Student test, $t(15)=3.03$, $p=0.008$).

Conclusion. Analyzing our group of 40 patients, Deferasirox proves to be effective and safe. Adverse effects that determined a temporary stop of the treatment were mild/medium short time digestive reactions. The number of red blood cell transfusion significantly decreased after starting Deferasirox treatment.

A CASE OF PSYCHOSIS PRECIPITATED BY SPORTS SUPPLEMENTS

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Introduction. As sports supplements are widely used, their potential side effects are becoming more frequent. There have been some reports in the literature of onset of acute psychosis following excessive consumption of energy sports supplements containing high amount of caffeine and taurine.

Material and methods. We present the case of a 28 year old man admitted to the Psychiatric Clinic for disorganized and bizarre behavior and speech, paranoid delusions and delusions of influence, olfactory hallucinations and severe insomnia. His symptomatology with a sudden onset after the patient significantly increased his daily intake of sports supplements (in addition to several types of amino acid and protein powders, he took excessive amounts of caffeine and taurine to maximize his workout).

Results and discussion. From accounts from his family and after completing the SCID II (The Structured Clinical Interview for DSM-IV Axis II Disorders), the patient was diagnosed with premorbid schizotypal personality disorder. Even though he was a successful computer engineer, he held magic beliefs (since adolescence, together with his younger brother, he started studying buddhism and witchcraft books, practiced occult rituals). Since his unusual way of thinking developed over his entire adult life, but only recently he used higher amounts of supplements, the current psychotic episode could have been precipitated by them.

Conclusion. The likelihood that certain supplements could trigger acute psychotic disorder may be higher in individuals with preexisting psychiatric conditions, such as schizotypal personality disorder, which are part of the spectrum of psychotic disorders.

EVALUATION OF THE SAMe-TT2R2 SCORE TO PREDICT THE QUALITY OF ANTICOAGULATION CONTROL IN A COHORT OF PATIENTS WITH NONVALVULAR ATRIAL FIBRILLATION TREATED WITH VITAMIN K ANTAGONISTS

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Background. Atrial fibrillation (AF) is the most common cardiac arrhythmia with an increasing prevalence and incidence worldwide. Vitamin K antagonists (VKAs) therapy is an effective anticoagulation option for stroke prevention in patients with nonvalvular atrial fibrillation. The SAMe-TT2 R2 score was developed to predict the quality of anticoagulaton control in patients with atrial fibrillation treated VKAs.

Objective. To evaluate the SAMe-TT2 R2 score in a cohort of patients with nonvalvular atrial fibrillation treated with vitamin K antagonists and determine its usefulness.

Methods. Retrospective cohort study including all consecutive patients with nonvalvular AF treated with VKAs for > 90 days in a tertiary care hospital between January 2015 and January 2016. We investigated all variables included in the SAMe-TT2 R2 (female sex, age < 60 years, medical history [>2 comorbidities], treatment [interacting drugs, eg, amiodarone for rhythm control], tobacco use [doubled], race [doubled]) score and analyzed the relationship between the SAMe-TT2R2 score and time in therapeutic range (TTR) determined by the percentage of INR determinations.

Results. We studied 256 patients (mean age 70.13 ± 9.96, 54% women). The median number of INR values per patient was 3 (2–8). The mean TTR was calculated as 63%. The low-risk group (score 0-1) had a better median TTR as compared with the high-risk group (score ≥ 2): ($p = 0.036$). Similarly, the percentage of patients with TTR ≥ 65% or 70% was higher in the low-risk group ($p = 0.001$ and $p = 0.003$, respectively).

Conclusions. The SAMe-TT2R2 score is useful to predict quality of anticoagulation control in patients with nonvalvular atrial fibrillation treated with VKAs.

IMPACT OF CAROTID ARTERY UNDERSIZED BALLOON POSTDILATION ON SHORT-TERM PROGNOSIS

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Introduction. Recent clinical trials proved the non-inferiority of carotid stenting as compared to carotid endarterectomy. Our study compares two different carotid angioplasty techniques in terms of cerebral ischemic complications and restenosis rate.

Material and methods. Between 2001 and 2011, 180 patients admitted to "Niculae Stãncioiu" Heart Institute were treated by carotid angioplasty, using a simplified protocol that tracked the avoidance of pre- and post-dilation. If necessary, stents were post-dilated either with smaller diameter balloons than usual (undersized) or with normal diameter ones (nominal post-dilation). The desired result was a less than 30% residual stenosis. The patients were evaluated immediately after the procedure, at 30-days and after one year, in terms of stroke and restenosis.

Results. 161 patients benefitted from direct stenting, while 19 of them were pre-dilated. Self-expanding, nitinol stents were used. A distal embolic protection filter was used in all cases. Patients were grouped in three categories: no post-dilation – 13.33%, undersized post-dilation – 38.88% and nominal post-dilation – 47.77%. Stroke rate at 30-days follow-up was 1.43% in the undersized post-dilation group, while the rate of restenosis at 1-year was 2.86%. In the nominal post-dilation group, the 30-days rate of ischemic complications was 3.49% and the 1-year restenosis rate was 3.48%. Although the result did not reach statistical significance, there was a positive trend in case of undersized post-dilation, in association with direct stenting.

Conclusions. Undersized carotid post-dilation, in association with direct stenting, reduces the rate of cerebral ischemic complications and the rate of restenosis.

QUALITY OF LIFE IN RELATION TO CARDIOVASCULAR RISK IN AN AVERAGE AGE POPULATION WITH ARTERIAL HYPERTENSION

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Introduction. Arterial hypertension (HTN) is a condition commonly found in modern society. This brings an increased risk for cardiovascular events and mortality. But the impact on the quality of life (Qol) of these people is not negligible. The present study aims to assess Qol in relation to cardiovascular risk in an average age group with HTN.

Material and Methods. We have conducted a prospective observational study in patients diagnosed with HTN hospitalized from April to June 2017 in the Departments of Internal Medicine and Cardiology of the Cluj-Napoca Municipal Clinical Hospital. The inclusion criteria were 40-65 years of age, diagnosis of HTN and antihypertensive treatment for at least one month, and the exclusion criteria - the refusal to participate and / or the presence of an associated psychiatric condition. Data were obtained by anamnesis, physical examination and laboratory tests. For the assessment of the risk of death at 10 years, the corresponding SCORE chart for Romania was used. To assess Qol, the MINICHAL questionnaire was used, specific for the population with HTN, structured from two sets of questions regarding somatic and mental influence.

Results. We retained just patients who had a 100% response rate (97%). The final group consisted of 40 (67%) women and 21 (33%) men, with an average age of 58.11 + 5.95 years. The 10-year risk-of-death rate estimated by the SCORE chart was 3.442 + 3.057%. The MINICHAL total Qol score in the study group was 18.245 + 7.671. Total regression graph SCORE_MINICHAL had a linear distribution. In terms of the ROC curve of the MINICHAL - SCORE correlation, the cut-off threshold of > 7 corresponded to a high risk level of death at 10 years, with a sensitivity of 94.1% and specificity of 66.7%.

Conclusions. In an population diagnosed with HTN, the application of a Qol questionnaire specific to this condition identifies statistically significant correlations between Qol and the risk of death at 10 years.

THE ASSESSMENT OF SERUM OXIDATIVE STRESS MARKERS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND NON-ALCOHOLIC STEATOHEPATITIS

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Background and objectives. The association of non-alcoholic steatohepatitis (NASH) and type 2 diabetes mellitus (DMT2), generates a phenotype of high cardiometabolic risk. The objective of this study was to assess a set of protein oxidative stress markers, lipid peroxidation and serum uric acid in patients with DMT2 & NASH, and the correlations with clinical & biochemical patient characteristics.

Material and methods. Group I (35 patients with DMT2 & NASH); Group II (40 patients with DMT2 without NAFLD); and 30 controls (Group III), were clinically & biologically assessed. A panel of serum markers of systemic oxidative stress (protein carbonyls, malondialdehyde, 8-isoprostane, uric acid) were measured and statistically processed by correlation analyses.

Results and discussion. Gr. I vs. Gr. II exhibited significantly higher serum levels of oxidative stress markers: protein carbonyls (Gr. I: 1.112 ± 0.42 nmol/dl vs. Gr. II: 0.508 ± 0.35 nmol/dl, $p = 0.01$, vs. Gr. III: 0.417 ± 0.38 nmol/dl, $p = 0.001$), Malone dialdehyde (Gr. I: 6.181 ± 1.81 ng/ml vs. Gr. II: 4.258 ± 1.54 ng/ml, $p = 0.002$, vs. Gr. III: 2.393 ± 1.75 ng/ml, $p = 0.001$), 8-isoprostane (Gr. I: 338.6 ± 98.5 pg/ml vs. Gr. II: 269.92 ± 88.7 pg/ml, $p = 0.014$, vs. Gr. III: 195.94 ± 45.3 pg/ml, $p = 0.001$), and uric acid (Gr. I: 7.10 ± 1.65 mg/dl vs. Gr. II: 5.58 ± 1.48 mg/dl, $p = 0.001$, vs. Gr. III: 4.74 ± 1.02 mg/dl, $p < 0.001$). Gr. I patients exhibited increased prevalence of obesity, poor control of diabetes, and a high UKPDS CV risk. Correlation analysis results showed a significant association between the increase of oxidative stress markers and clinical, biochemical parameters of cardiovascular risk, in Gr. I.

Conclusions. Serum levels of oxidative stress markers are significantly increased in Gr. I (NASH & DMT2), indicating an imbalance in the oxidative stress status. The systemic inflammatory, oxidative stress profile, and the clinical and biochemical patient characteristics, are associated with a high CV risk.

STIGMA AND INSIGHT IN SCHIZOPHRENIA

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Background and aims. Stigma and Insight in patients with schizophrenia are very important aspects of the disease because they both relate with seeking and accepting health care for their disease.

The aim of our study was to investigate the relationship between stigma, insight and symptoms of the disease in outpatients with schizophrenia.

Material and methods. 70 outpatients diagnosed with schizophrenia, stable from the point of view of the symptoms for at least 3 month were included in our study. Stigma was evaluated using the Internalized Stigma for Mental Illness Scale (ISMI), insight and symptoms of the disease were evaluated Positive and Negative Syndrome Scale (PANSS).

Results. The patients were classified in two subgroups as having or lacking insight of the disease. Our findings suggest that in patients with schizophrenia having insight on the disease is associated with higher levels of internalized stigma and symptoms severity. Logistic regression analysis found a the lack of insight on the disease is a predictor for decreased experiences of stigma and also for decreased adherence to treatment.

Conclusions. Our study supports previous findings which report a correlation between increased experience of stigma and patients with better insight. Also it is clear that the two variables: stigma and insight have very important roles in predicting the adherence to treatment.

PROGNOSTIC VALUE OF THE VALUE OF SVC FLOW IN THE FIRST DAY IN THE PREMATURE NEWBORN ≤32 WEEKS OF GESTATION

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Introduction. The relationship between the systemic flow and different organs injuries during the transition period remains a challenge. Clinical markers used for the assessment of cardiac function are insufficient for a correct evaluation during the transition period. Evaluation of superior vena cava flow (SVC) can be used as an indirect marker of systemic flow.

Material and methods. A prospective study took place Emergency Hospital of Cluj-Napoca, in the 1st Neonatology Department between July 2015 and April 2016, enrolling 51 preterms with GA ≤ 32 weeks. Examination was during the first 24 hours, following parameters being noted: anthropometric, clinical, laboratory and ultrasonography data (resistive index and SVC flow). Were analyzed using the IBM SPSS version 23.

Results. Gestational age was 28.49±2.64 weeks with weight of 1141.27±450.61 grams. The ultrasound was performed at 16.69±15.83 hours of live. SVC flow was not be influenced by gestational age (p=0.685), birth weight (p=0.590) or by dimension of arteriosus duct (p=0.930). SVC flow were lower in preterm from mothers with chorioamnionitis:73.17±36.50 vs. 140.32±138.76 ml/kg/min (p=0.046). SVC flow had no significant differences between a different type of respiratory support. Significant correlation was found between SVC flow and intraventricular hemorrhage (p= 0.017) and periventricular leukomalacia (p=0.043). SVC Flow was significant lower in the decesed group, p=0.046.

Conclusions.

1. SVC flow in the first day of life is independent of GA, weight, size of PDA
2. SVC flow is significantly lower in children from mothers with chorioamnionitis
3. SVC flow can be considered as a prognostic factor for hemorrhagic and ischemic events
4. SVC flow be used as prognostic factor in death.

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HEART RATE VARIABILITY IN PATIENTS WITH DIABETES MELLITUS

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Introduction. Heart Rate Variability (HRV) is a non-invasive method to investigate the adaptability of the heart to various needs of the body and can predict potentially lethal arrhythmias. Diabetes Mellitus (DM) is a wide-spread disease that affects an important percentage of the people. We aimed to check the relations between diabetes and HRV.

Material and methods. We studied a group of 91 type 2 diabetics mean aged 61 that had diabetes for an average of 9 years without documented neuropathy. We also considered patients of similar age without diabetes as controls. We excluded those patients that needed insulin, had arrhythmias, ECG signs of coronary ischemia or signs of left ventricular or global heart failure, renal failure or respiratory chronic diseases.

We performed echography of the heart, including the measurements of the size of the ventricles, motility, isovolumic relaxation time, ejection ratio and other parameters. Parameters that were considered for HRV analysis were: the mean duration of normal R to R wave intervals (MNN), standard deviation of those normal RR intervals (SDNN), variability coefficient (CV), standard deviation of normal RR intervals (SDANN), and the percent of normal RR successive intervals different by more than 50 ms (pNN50). We followed those HRV time and frequency parameters and did some calculations.

Results. The echocardiography parameters revealed thickening of the septum, reduced diastolic diameter of the left ventricle (LVDD), altered systolic function (EjR), increased time of relaxation of the ventricles in diabetics that also exhibited some impaired parameters of HRV.

Conclusion. Diabetes has a detrimental effect on heart adaptability; most diabetics had HRV affected for their corresponding age and those parameters seemed to be linked with some abnormal echocardiography findings. The age, duration of the diabetes also had a tendency to relate to the alteration of the HRV.

CHARACTERISTICS OF PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION IN THE CLUJ REGIONAL CENTER

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Objective. We investigated the characteristics of people living with HIV infection in care in the Clinical Immunodepression / HIV-AIDS Compartment at the Clinical Hospital of Infectious Diseases Cluj-Napoca.

Methods. We conducted a cross-sectional study involving 514 patients in care in December 2016 regarding the following characteristics: age, gender, way of transmission and antiretroviral treatment.

Results. 254 patients are from Cluj, 94 from Maramureş, 17 from Sălaj, 37 from Satu-Mare, 58 from Bihor, 35 from Hunedoara, and 19 from other counties. More than half of in care patients were men (350 subjects, 68%, 95%CI [64-72]). The age distribution was as follows: 50 patients under 25 years, 213 between 25-35 years, 171 between 35-45 years, and 80 over 45 years old. Most of the participants were heterosexual (262 patients, 51%, 95%CI [46-55]), 154 MSM (men who have sex with men - 30%, 95%CI [26-34]), 5 were intravenous drug users (1%, 95%CI [0.4-2]), 82 belongs to the Romanian cohort (16%, 95%CI [13-19]), and 11 were with perinatal transmission of HIV (2%, 95%CI [1-4]). The majority of patients (462) were under antiretroviral therapy (89.88%, 95%CI [78-92]). The highest at the first line, 108 the second line, 58 are at the third line, 152 have had more than three lines of antiretroviral therapy.

Conclusions. Heterosexual transmission is the main route in the investigated cohort, closely followed by MSM transmission. The 25-35 age groups is representative. There is an imperative need to have an earlier HIV diagnosis.

HIGHLIGHTING THE INFLAMMATORY SYNDROME IN PATIENTS WITH DIABETES: A RETROSPECTIVE STUDY

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The overall prevalence of diabetes has increased dramatically over the past two decades, given the current trends, over 360 million people will have diabetes by 2030. The chronic complications of diabetes are retinopathy, neuropathy and nephropathy. All the complications of diabetes, both, vascular and non-vascular events, are accompanied of micro inflammation manifestations.

This study is descriptive, retrospective, and was carried out on 276 patients from Center of Diabetes, Nutrition and Metabolic Diseases Cluj, with type 1 and type 2 diabetes and its aim is to highlight the inflammatory syndrome trough C-reactive protein and its link with the main marker used to evaluate the patients with diabetes, glycosylated hemoglobin.

For this purpose we determined in both groups the Pearson correlation index between the values of glycosylated hemoglobin and C-reactive protein and have obtained a $r = 0.51$ ($p < 0.001$) for patients with type 1 diabetes and a $r = 0.53$ ($p < 0.001$) for patients with type 2 diabetes. After exclusion from analysis of the patients with PCR values below 1 mg/dl, values considered normal, we found a significant statistical difference between PCR values between the two diabetes types, $p < 0.001$ (Mann-Whitney U test), patients with type 1 diabetes been less affected (median value and Q1-Q3 of 1.53, 1.26-2.92 vs. 1.70, 1.63-3.68).

Since the correlation coefficient obtained in both groups indicated a moderate correlation, statistically significant, we can support the study hypothesis of association between the inflammatory syndrome with the diabetes complications.

For a better evaluation this retrospective study will be continued with some others, more sensible markers of the micro inflammation induced by diabetes evolution, such as chitotriosidase and neopterin, with the purpose of the early diagnosis of their presence in order to correct the baseline treatment of the disease and to trying to prevent them.

PAROXYSMAL ATRIAL FIBRILLATION WITH MINIMAL CHANGES IN THE STRUCTURE OF THE LEFT ATRIUM - A CASE REPORT

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Introduction. Atrial fibrillation is a frequent rhythm disorder that lowers the quality of life, increases the number of hospitalizations, complications and mortality. Ablative therapy is superior to antiarrhythmic medication.

Case report. A 66-year-old female, with numerous episodes of paroxysmal atrial fibrillation, which started in 2013, a resistant arrhythmia to class IC and III antiarrhythmic drugs. Due to existing indication, we performed the invasive procedure consisting of anatomical and electrical mapping of the left atrium and pulmonary veins. We found the existence of a healthy atrial tissue, both in the anterior and posterior walls, but also in the inter-atrial septum. The isolation of the ipsilateral pulmonary veins, in bulk, was performed. There were no complications post-procedurally. At follow-up, after clinical evaluation, Ecg and Holter monitoring, there were no relapses.

Conclusion. Ablation of atrial fibrillation, in the early stages of the disease, before structural atrial changes occur, is considered to be an effective procedure.

METABOLIC DISORDERS IN ACUTE LIVER FAILURE SECONDARY TO MUSHROOMS POISONING IN CHILDREN

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Introduction. Acute liver failure (ALF) is rare in children, but in our region (North-Western part of Romania) was an important cause of death among children, being directly proportional with the large number of mushrooms poisoning encountered in our country. Disorders of acid-base balance and electrolytes are frequently found in ALF and represents prognostic markers in the evolution of these cases.

Objective. The aim of our study was to analyze the metabolic disturbances presented among children admitted with ALF secondary to mushrooms poisoning.

Material and methods. We have analyzed retrospectively the laboratory parameters in patients with wild mushrooms poisonings hospitalized between 2000 and 2015 in our hospital, the main Toxicology Centre in North-West Romania.

Results. From 320 children with mushrooms poisoning, 84 patients presented ALF. Venous blood pH, glycaemia and electrolytes were analyzed in these cases. In our study, the most common type of acid-base disturbance was metabolic acidosis (70.23%). This was compensated just in 4 cases (6.8%). 14 of these cases (16.6%) presented at the moment of the admission clinical and laboratory evidence of impaired renal failure. Metabolic alkalosis was present in only 4 cases (4.76%) and probably was induced by the administration of diuretics (most of these cases being transferred from other hospitals where they were initially treated). Most of the cases presented hypoglycaemia (78.57%) and this was frequently accompanied by hyponatremia (85%).

Conclusion. ALF in mushroom poisoning is associated with a high mortality in children, despite optimal medical therapy (54.21% in our study). The metabolic imbalance and electrolytes disorders represent important and early markers of prognosis in the evolution of ALF, most of the fatal cases presenting significant changes to these parameters.

DISCRIMINATION OF MELANOMA LESIONS SEVERITY BY REAL-TIME ELASTOGRAPHY MEASUREMENTS

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Introduction. Relative elasticity or rigidity (stiffness) of the tissues can be assessed by real-time elastography (RTE) and RTE appearance proved to significantly correlate with strain ratio (SR) of lesion to dermis and hypodermis. We aimed to investigate the accuracy of real-time elastography measurements (SR of lesion to normal dermis and hypodermis) in discriminating melanoma lesions severity.

Material and methods. The same radiologist evaluated 42 cutaneous melanoma lesions in 39 adult subjects by real-time strain elastography. Semi-quantitative measurements expressed as SR of lesion to normal dermis and hypodermis were recorded. The classification of the lesions was made based on pathologic results regarding Breslow depth. We used three different classifications of melanoma lesions based on Breslow depth: ≤ 1 mm (including in situ lesions), between 1.01 mm and 4 mm, and > 4 mm. ROC (receiver operating characteristic) curve analysis was conducted to assess accuracy of SR of lesion to normal dermis and hypodermis into categorizing melanoma lesions.

Results. The SR of lesion to dermis proved to be statistically significant at a significance level of 6% in discriminating the lesions with Breslow depth higher than 4 mm. The AUC (area under the curve) was 0.731 (95%CI [0.519-0.942]) with a sensibility of 42.9% and a specificity of 97.1% for the threshold of SR lesion to dermis equal to 1.440. The SR of lesion to hypodermis proved to be statistically significant (p=0.0137) in discriminating the lesions with Breslow depth higher than 1 mm. The AUC (area under the curve) was 0.798 (95%CI [0.569-0.999]) with a sensibility of 94.3% and a specificity of 71.4% for the threshold of SR lesion to hypodermis equal to 0.950.

Conclusion. A value of strain ratio of cutaneous melanoma lesion to hypodermis, measured by real-time elastography, higher than 0.950 indicates an intermediate or thick melanoma.

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HOW DOES MINIMALLY INVASIVE HEMODYNAMIC MONITORING INFLUENCE THE 3- AND 6-HOURS FLUIDS BUNDLES IN THE INTENSIVE CARE UNIT IN SEPSIS AND SEPTIC SHOCK?

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Introduction. The 2016 Surviving Sepsis Campaign (SSC) introduced a new target of 30 ml/kg crystalloids in the management of sepsis induced hypotension which should be administered in the first 3 hours after the diagnosis. This comes in contrast to the previous SSC recommendations which targeted central venous pressure , mean arterial pressure , urine output and central venous oxygen saturation for a specific fluid resuscitation. The aim of our study is to assess whether minimally invasive hemodynamic monitoring affects this new 3 hours fluid bundle.

Methods. We conducted a prospective observational study in a mixed surgical and medical ICU, between October 2015 and July 2017. We included 68 patients with sepsis and septic shock, with no comorbidities that may influence the hemodynamic parameters. We assessed the fluid status both by static and dynamic parameters during the first 3 hours of fluid resuscitation and used advanced hemodynamic minimally invasive monitoring to evaluate the results after the initial 3 hours.

Results. Our research showed that only 47% of the patients included in the study received the 30 ml/kg fluid bolus as recommended by Surviving Sepsis Campaign guidelines. As regarding the vasoactive therapy, 52 patients, representing 76.5% were already on vasoactive support at the moment of study inclusion, and the Norepinephrine infusion dose was tapered up during the six hours volume resuscitation period.

Conclusion. Minimally invasive hemodynamic monitoring influences the volume resuscitation in septic and septic shock patients in the way of reducing the total fluid load and by increasing the vasoactive support, minimizing the 3rd space fluid loss. By the third hour of resuscitation all hemodynamic parameters targeted are in the desired interval.

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CONVERSION DISORDER IN CHILDREN

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Introduction. Conversion disorder is defined by the presence of symptoms involving voluntary motor or sensory function that suggests a neurological condition. Amaurosis may be a manifestation of this pathology and there is no explanation for the symptoms. In the presence of normal ophthalmological and neurological findings psychiatric disorders have to be considered.

Case report. We present a case of a 15 years old female with a history of repeated traumatic events during the last two years, otherwise healthy adolescent, who presented to our clinic with acute bilateral vision loss and nausea. The symptoms appeared 30 minutes after the ingestion of a glass with an unknown substance. Ophthalmological and neurological examinations showed no evidence of trauma or organic disorders. Intoxication with methanol was excluded by the absence of metabolic acidosis or hypoglycemia. The literature review revealed the connection between amaurosis fugax and methamphetamine, cocaine and phencyclidine abuse, but the toxicology screen from blood and urine was negative for these drugs. Supportive therapy was administered in order to facilitate the clearance of the unidentified substance. Full vision recovery occurred after three days of being hospitalized in our Clinic without any specific therapy. Therefore, in the absence of any arguments that could explain the clinical findings the diagnosis of conversion disorder was proposed and the patient was referred to a Psychiatry Clinic.

Conclusion. Acute vision loss requires immediate assessment in order to evaluate possible ophthalmological and neurological causes. In the same time, drug abuse can not be ignored especially in young patients. The diagnosis of conversion disorder is a diagnosis of exclusion which should be taken into account in front of a patient with signs and symptoms warranted by the laboratory investigations.

A RARE TUMOR OF THE SCAPULAR REGION – CASE REPORT

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Introduction. Primitive neuroectodermal tumors (PNET) are a group of extremely rare and highly malignant round cells tumors of neuroectodermal origin, affecting soft tissues and bones. Over the last several decades they were classified as part of Ewing family of tumors (EFT). They present under the age of 20, with a slight male predominance. Ultrasonography is a very useful tool in tumor diagnosis, evaluation of its extension in the surrounding tissues and post-treatment surveillance, enables percutaneous core needle biopsy, and is considered the appropriate method of diagnosis.

Case report. We report the case of a 72 years old woman presenting with a tumor of the right scapular region, of 10/12 cm that appeared several months earlier, accompanied by weight loss. At the physical exam we identified a non-tender, firm tumor with adherence to the underlying plans. Blood test showed increased lactate dehydrogenase. Ultrasound examination of the right scapular region revealed a large solid tumor with poor delimitation of the surrounding tissues, with inhomogeneous structure (hyper- and hypoechoic areas) and moderately vascularized. Due to the numerous calcification areas (small and large calcifications) the delimitation from the scapular bone was difficult. No malignant lymph nodes were found. A Magnetic Resonance Imaging was performed and showed a large infiltrating tumor, with necrosis areas, and extension in the surrounding muscles, and scapular bone edema. An ultrasound-guided percutaneous core needle biopsy was performed and the histopathological examination revealed the aspect of a primitive neuroectodermal tumor. The patient was referred to the surgery department and the tumor was resected. The final diagnosis was peripheral primitive neuroectodermal tumor pT2bNxL1V1R1.

Particularities. The primitive neuroectodermal tumor is very uncommon in elderly patients.

Conclusion. Ultrasonography enables rapid evaluation and diagnosis tumors with superficial location.

ROLE OF PARTICULAR INFLAMMATORY BIOMARKERS IN RISK ASSESSMENT IN METABOLIC SYNDROME PATIENTS

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Introduction. Metabolic syndrome (MS) is a cumulative pathogenetic process that causes vascular damage and generates chronic inflammation with a major role in MS progression. Recently it has been assumed that pentraxin-3 (PTX3) and tumor necrosis factor alpha (TNF-α) are main factors in MS pathophysiology, but further studies are required to pinpoint their role. The aim of the study was to determine the association between levels of biomarkers and severity of MS, to seek their ability in MS risk stratification. Also, we endeavoured to establish if the combined use of these biomarkers provides significant value for prognosis assessment.

Material and methods. We conducted a prospective study on forty male and forty female patients, matched for age. The patients were further separated into 4 age groups, 10 men and 10 women matched for age. All patients were evaluated by the same protocol, including history taking, clinical examination, 6MWT, heart and vascular ultrasonography and measurements of PTX-3 and TNF-α, in addition to standard biochemistry tests.

Results. TNF-α was significantly increased with age ($p<0.001$) and with number of MS components. PTX-3 dynamics according to age was less linear, with a decrease in 55-64 years group by comparison with other groups ($p<0.001$). PTX3 and TNF-α were correlated with hs-CRP levels. In univariate analysis, significant correlations were found between the presence of atherosclerotic plaques and age ($p<0.001$), PTX-3 levels ($p<0.003$), CCA-IMT, PWV and stiffness index β, but only the correlations to age and PWV persisted after multivariable analysis ($p< 0.05$).

Conclusion. PTX-3 and TNF-α were not associated to the development of atherosclerotic plaques after regulation for intricate factors, despite an initial correlation to PTX-3 levels.

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ACUTE PANCREATITIS IN A GIRL WITH SEVERE HYPERTRIGLYCERIDEMIA: TREATMENT CHALLENGES

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Introduction. Acute pancreatitis in children is a disease with an increasing incidence. Although uncommon, metabolic abnormalities like hypertriglyceridemia can be associated with the development of acute pancreatitis. Familial hypertriglyceridemia is an autosomal dominant disease, which does not usually manifest until adulthood.

Case report. We present the case of an 8 years old girl with two episodes of acute pancreatitis, one requiring surgery with appendectomy. Her brother has type 1 diabetes mellitus, with slightly elevated triglycerides (TG), and her father has had an episode with increased level of TG, that resolved with diet and lipid-lowering treatment. When presenting to our clinic, she had a high level of serum TG (2647 mg/dl, then 4811 mg/dl), with slightly elevated level of cholesterol and low HDL cholesterol. The lipoprotein electrophoresis showed high pre-beta lipoproteins, with absent beta lipoproteins and chylomicrons. The patient underwent a low fat and low carbohydrates diet (less than 15-20% of calories from fat, low-fat milk and dairy products, avoiding fast-release carbohydrates) and Omega 3-6 treatment. At the first monthly follow-ups, she continued having elevated serum TG, but admitting that she didn't respect the diet firmly. Her laboratory parameters improved after an infectious episode that entailed decreased appetite. Latest, accordingly to her adherence to the diet, her serum TG, cholesterol and HDL-cholesterol levels were normal (TG=93 mg/dl).

Conclusion. Hypertriglyceridemia is a less common cause of acute pancreatitis in children. The first line of treatment includes low fat and low carbohydrates diet and Omega 3 dietary supplementation, followed by introduction of nicotinic acid or fibrates treatment, if needed. Following a strict diet can be a great challenge for a child and his family. Familial hypertriglyceridemia is not thought to be highly atherogenic, but it can determine acute pancreatitis episodes.

HANSEL AND GRETEL IN NEURORADIOLOGY: FOLLOWING NEUROANATOMY AND NEUROLOGICAL FINDINGS

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Introduction. Being inquisitive is one of the most important qualities in a physician, more so for one who deals with the nervous system. Each bundle of fibers and cell population has a specific purpose. If a dysfunction is noticed, the neuroradiologist verifies if imaging matches with the neurological findings.

We present a peculiar aspect on brain MRI that may be confused with normal neuroanatomy.

Case presentation. A 44 year old female patient with no prior history presents to the Emergency Room with headache, decreased muscle strength in all limbs, balance disturbances and swallowing difficulties.

Neurological examination revealed postural and kinetic tremor in upper limbs, neck stiffness, decreased sensibility in left ear conduct, positive Romberg maneuver, neurosensory hypoacusis, decreased gag reflex, tetraparesis, bilateral Babinski sign.

A brain MRI was performed and deemed normal at first. Upon closer inspection, an extraneuraxial solitary mass with a round shape, homogenous, isointense signal to gray matter on T1 and T2 sequences was observed anterior to the medulla oblongata, which was actually displaced posteriorly. A diagnosis of WHO grade I meningioma was given.

Discussion. Meningiomas are mostly benign tumors. 5-10% are located in the infratentorial region and are isointense on T1 and T2 sequences to gray matter, making it difficult to distinguish from surrounding nervous tissue.

In this case, the mass appeared as if it was the medulla oblongata, due to its localization, homogenous, well defined shape and apparent continuity with the pons and medulla.

Signs that highly suggest an extraneuraxial mass in such cases are: CSF cleft, gray matter between mass and white matter, displaced subarachnoid space and a broad dural base.

Conclusion. Abnormal neurological findings need imaging assessment with the utmost diligence. Given that imaging is not always crystal clear, one needs a trained eye for neuroanatomy, neuropathology and differential diagnosis.

PRIMARY HYPOTHYROIDISM AFTER RADIOTHERAPY FOR SUPRAGLOTTIC LARYNGEAL CARCINOMA

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Introduction. Primary hypothyroidism can affect 20-30% of patients that undergo curative radiotherapy applying minimum doses of 40Gy to the neck region. A higher incidence has been noticed in patients treated using telecobalt therapy than in patients treated with a linear particle accelerator. The pathogenic mechanisms that can explain the thyroid injuries are: vascular damage, cellular lysis and autoimmune reactions with antibody formation.

Case report. We present the case of a 54-year old woman diagnosed with supraglottic squamous cell carcinoma (cT2N1M0) and treated with telecobalt radiotherapy (50Gy/38days), chemotherapy (Cisplatin 30 mg/m2/week) and surgery (laryngectomy+right thyroid lobectomy) in 2006, a patient that later on underwent permanent tracheostomy. She was admitted to our clinic with complains of inspiratory dyspnea, fatigue, muscle weakness with myalgia and loss of appetite.

In 2017, a CT scan showed pleural and massive pericardial effusion of unknown origin.

The clinical examination revealed poor general state of health, full moon facies with dry, cold skin, periorbital puffiness, macroglossia, hoarseness, short neck with tracheostomy, straw-like hair, loss of axillary and pubic hair, abdominal distension, bradicardy, tightened vesicular murmur with basal crackles and hypotonia. The work-up confirmed primary hypothyroidism (TSH↑ and FT4↓) with minimum thyroid tissue on the left side and negative antibodies. The replacement therapy with levothyroxine 100µg/day was started, triggering significant clinical improvement and a decrease of the liver and muscle enzymes values.

Conclusion. Early hypothyroidism recognition and treatment prevents associated complications. The effect produced by RT is progressive: 50% of the cases occur within the first 5 years. The follow-up procedures include at least annual evaluation with a history for signs and symptoms of thyroid dysfunction and measurement of thyroid hormones.

HEART FAILURE WITH PRESERVED EJECTION FRACTION IN VERY ELDERLY POPULATION - CLINICAL PROFILE AND TREATMENT MANAGEMENT IN A TERTIARY CARE HOSPITAL

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Background. With increase in both survival rate and prevalence of hypertension (HT), type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD), heart failure with preserved ejection fraction (HFpEF) has gained epidemic proportions in the elderly population.

Objectives. We evaluated the clinical profiles and treatment management of 206 consecutive patients with heart failure for whom hospitalization was required in the cardiology department between January 2016 – December 2016.

Material and method. This was a retrospective observational study. All the patients diagnosed with HFpEF (NYHA II-IV, EF> 50 %, echocardiographic patterns of diastolic heart failure) were included in the study.

Results. The mean age on admission was 72.16 +/- 8.64 years, 41.6% men. Women with diagnosed HFpEF were more symptomatic than men and are typically older with more comorbidities. HT, CAD and T2DM were present in 61%, 51.9% and 10.4% respectively. The commonest presenting symptom was breathlessness (57.1%) Most frequently observed clinical feature was pedal edema (83%) followed by tachycardia (48.1%). 75.3% of patient received diuretics. Beta-blockers were used in 64.9%, 51.2% and 35.4% of the patients with NYHA classes II, III and IV respectively. Spironolactone were used in 55.8% of patients before discharge.

Conclusions. HFpEF is more common in elderly patients. Better recognition of the clinical profile and therapeutic management are needed to develop improved methods for prevention and management.

CLINICAL AND IMMUNOLOGICAL PHENOTYPES IN AUTOIMMUNE HEPATITIS

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Introduction. Due to heterogenicity of clinical, laboratory and histological manifestations of autoimmune hepatitis (AIH), we wanted to assess the clinical phenotypes and immunological features of this disease.

Material and methods. 56 patients (40 females and 16 males, 20-73 years old) with positive diagnosis of AIH from the 2nd Medical Department were analysed in a retrospective study (2012-2016) from clinical, biological and histological point of view. Inclusion criteria consisted in immunological (autoantibodies >1:40) and/or histological confirmation of AIH. All patients underwent clinical, biological, immunological and ultrasonographic examination, and some of them liver biopsy and histology (n=7).

Results. Among patients, 45/56 were of urban provenience, 40/56 were females. 35/56 patients had positive ANA, 12/56 had positive SMA, 4/56 had ANA+SMA positive, 1/56 had negative and the rest were not mentioned. Speckled fluorescent ANA pattern was the predominant type (12/56). 40 of 56 patients had another associated autoimmune disease (Hashimoto thyroiditis, SLE, rheumatoid arthritis, serum negative spondylartrhopathy, autoimmune thrombocytopenia). Hepatocytolytic syndrome revealed an average value of 51.4 U/l (GOT), and 54.8 U/l (GPT). Steatosis and homogeneous structure were the main liver features in ultrasonography.

Conclusion. Associated autoimmune diseases, together even with an atypical clinical or immunological picture in follow-up, should bring AIH as diagnosis possibility in patients that were priorly classified as cryptogenetic hepatitis.

ULTRASONOGRAPHY AS AN INTEGRATED TOOL IN CLINICAL DECISION-MAKING IN THE EMERGENCY DEPARTMENT

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The aim of this retrospective study was to identify the role of ultrasonography as a decision-making and screening tool in emergency patients with pathological changes.

Material and method. The study was carried out for 28 months in the Emergency Department of the County Emergency University Hospital, Cluj-Napoca. An ultrasound examination was performed as part of the clinical algorithm within the first hour of treating non-critical patients after they had been triaged. The diagnostic decision based on the results of the ultrasound examination was compared with the final diagnosis at discharge from Emergency Department.

Results. 1565 patients with a mean age of 50.61±19.21 years were included in the study. Ultrasound changes were detected in a statistically significant number of patients from all the examined subgroups ($p \leq 0.002$). The concordance between clinical and ultrasound findings was of 54.06%. Of all the examined patients, 20.63% were referred to surgery based on the results of the ultrasound examination. Surgery was the final therapeutic decision in 5.06% of all the patients with normal ultrasound findings.

Conclusions. 1. Ultrasonography as an integrated tool in the clinical examination algorithm allowed the identification of non-critical patients who required emergency surgery. 2. The integration of point-of-care ultrasound into the clinical examination allows the management of emergency patients through the ranking of decisions: hospital admission for surgery and medical treatment, other diagnostic investigations, referral to outpatient care and family doctors.

A RARE CAUSE OF DIFFICULT-TO-CONTROL ASTHMA IN CHILDREN, DISCOVERED 4 YEARS AFTER ASTHMA DIAGNOSIS

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Introduction. Asthma is the most common chronic disease in childhood, affecting an estimated 7 million children. Although asthma is a widely controllable disease with correct treatment and adherence to it, there still are some particular cases difficult to control.

Case report. We describe the case of a 8 year old boy, born prematurely, with low birth weight and mild cerebral palsy due a hypoxic incident at birth. He followed kinetotheraphy sessions, he had minor motor disorders and no mental deficits. He had an atopic background, multiple allergies and was diagnosed at the age of 4 years with asthma and chronic allergic rhinitis. Although his asthma treatment was correctly followed up, he was hospitalized multiple times for exacerbations and pneumonias. Outside acute episodes he had persistent wheezing and was on a low weight-for-age percentile. Upon one of the follow-up thoracic echographic examinations a hyperechoic mass was discovered in the left lung, near the diaphragm. A CT scan was performed and the 20/18 mm mass was interpreted as a retroperiotoneal fat herniation through a 8 mm diaphragmatic defect (a Bochdalek hernia). Before this diagnosis at least 9 chest X-rays were performed; there were no modifications that suggested local mechanical issues. This diaphragmatic hernia is in observation and awaiting a future surgical opportunity (parents refused to consider a surgical approach).

Discutions. Late-presenting congenital diaphragmatic hernias can be a cause of persistent wheezing, recurrent pulmonary infections and failure to thrive. With this case, we want to assess if the poor control of asthma symptoms is solely determined by the multiple predisposing factors presented by this patient (prematurity, low birth weight, cerebral palsy, atopic background, multiple allergies) or can be partly attributed to this newly discovered condition.

Conclusions. When we have a difficult to control asthma, we should consider mechanical problems, such as a Bochdalek hernia.

THE IMPACT OF A SELF-DESIGNED NURSING INTERVENTION ON THE QUALITY OF LIFE IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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Introduction. The aim of our study was to evaluate the quality of life in patients with Irritable Bowel Syndrome in a hospital-setting and one-month after applying a self-designed plan of nursing interventions.

Material and methods. The study was performed during January 2017-April 2017 in the CF Clinical Hospital, and was approved by the hospital`s ethics committee. We included in the study 52 patients diagnosed with Irritable Bowel Syndrome. They were interviewed and helped to complete a validated tool for evaluating the general quality of life (the SF-36 questionnaire), the IBS-QoL and the Birmingham IBS questionnaires for evaluating the quality of life in patients with irritable bowel syndrome. We applied a self-designed nursing intervention. We did a one month phone-visit and recorded the results of the same questionnaires. The results were analyzed using Microsoft Office and an online descriptive statistics instrument.

Results. Patients were an average 58 years old. 48% of these patients had constipation as the predominant symptom. We recorded the results from the 3 questionnaires during the index of hospitalization. We designed and applied a nursing intervention combining 3 different non-pharmacological approaches. Each of them showed improvement in the symptoms and quality of life of patients with IBS after one month. There was a significant improvement in all health concepts concerning the total score of the SF-36 questionnaire ($p<0.01$). The IBS-QoL questionnaire has shown that the total score of quality of life was improved ($p<0.05$), except the sexual-related issues scale. The total score of symptoms as assessed by the Birmingham IBS symptom questionnaire was decreased significantly after one month follow up ($p<0.01$).

Conclusion. The present study showed that a self-designed plan of nursing intervention increased the quality of life in patients with Irritable Bowel Syndrome, one-month after hospital discharge.

LARGE NON-FUNCTIONING PITUITARY ADENOMA PRESENTING DE NOVO IN PREGNANCY WITH VISUAL FIELD DEFECTS WITH AN EXCELLENT FINAL OUTCOME

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Introduction. Nonfunctioning pituitary adenomas (NFPA) are very rare during pregnancy since fertility is usually impaired.

Case report. A 31 year old woman was referred to the endocrine clinic for the investigation and management of a large pituitary tumor, discovered at 35 weeks of gestation. She complained of a progressively increasing headache and abnormal vision, in particular in her left eye, in the last few weeks. An MRI scan showed a pituitary mass of 3.1 ×2.7 ×1.8 cm (LL/CC/AP) with suprasellar extension, displacing and stretching the optic chiasm, especially on the left side. Serum prolactin, as well as other endocrine investigations were normal, so she was diagnosed as having a NFPA. Both inducing labour or giving medication (bromocriptine) while proceeding to a safe term for pregnancy were considered. However, we chose just to follow her closely. There was no further deterioration and at 38 weeks a caesarian section was performed, a healthy boy being delivered. Within 2 days, the visual field defects and headache improved. Two weeks after delivery, she underwent craniotomy (right lateral subfrontal approach) with resection of the NFPA, followed by complete regression of the visual disturbances. The postoperative MRI demonstrated empty sella and no residual tumor, while the hormonal evaluation detected no significant pituitary insufficiency.

Conclusion. As far as we know, this is the largest reported NFPA diagnosed de novo in pregnancy. The case illustrates an unusual and challenging endocrine pathology – that may pose a challenge especially for endocrinologists and gynecologists, but also for neurosurgeons – that had an excellent final outcome.

KILIMANJARO MEDICAL EXPEDITION WITH LUNG TRANSPLANT PATIENTS AT 5895 M

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Introduction. Lung transplant is a procedure performed on patients with end-stage pulmonary diseases. The patients who undergo such a procedure are oxygen dependent and house or hospital bound prior to the operation.

The purpose of this expedition was to prove that lung transplant not only saves the lives of these patients but allows them to live a normal life and even to climb the highest mountain in Africa.

Material and methods. The expedition party consisted of 34 people, 10 lung transplanted patients together with physicians, kinetotherapists and psychologists from 5 countries (Austria, Hungary, Romania, Italy and Greece).

During the ascent, which started at 2100 m from the base of Mount Kilimanjaro, all the way up to Uhuru Peak at 5895 m, a series o tests were performed as presented next: blood gas testing, creatinine levels, immunosuppressant blood levels, sleep testing, muscle strength testing, optic nerve and chest ultrasonography.

Results. Preliminary results show that drug levels are not influenced by altitude, thus ascending a high mountain does not influence the immunosuppressive therapy. On the other hand, the blood gas level was significantly influenced by altitude with low CO2 levels. The most interesting fact was that in case of the transplantees the oxygen saturation and blood gas levels were higher than in the control non-transplanted group by an average of 4%. Another interesting find was the sleep pattern of the entire group, with severe desaturation during the night but with no significant obstructive events, merely hypoxemic conditions. The ultrasonography of the chest and optic nerve did not reveal any signs of oedemas in the brain or lung, although headache and nose bleeds became more and more frequent as the altitude increased.

Our partial conclusion is that transplanted patients exhibit higher tolerance to altitude and hypoxemic conditions, with approximately 4% better values. However, for now, the reason for this remains unclear.

IBRUTINIB EFFICACY AND SAFETY IN RELAPSED/REFRACTORY CHRONIC LYMPHOCYTIC LEUKEMIA – SINGLE CENTER EXPERIENCE

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Introduction. Chronic lymphocytic leukemia (CLL) management remains a considerable challenge despite many therapeutic regimens introduced recently. The patients with relapsed/refractory disease have limited therapeutic options and poor overall survival. It was an urgent need to discover a novel, less toxic and more effective targeted treatment for CLL patients. Ibrutinib is an oral inhibitor of Bruton's tyrosine kinase that has been shown to be beneficial for B-cell malignancies with overall response rates of 71% in initial clinical trials for CLL.

We conducted a transverse, retrospective study to evaluate the efficacy and safety of Ibrutinib in patients with heavily treated, relapse/refractory CLL.

Materials and methods. 12 CLL patients were included, the first group of Ibrutinib treated patients in our center. It was analyzed the demographic characteristics of the patients, the stage of the disease at the beginning of Ibrutinb treatment, the overall survival, the response rate to the treatment, the adverse events.

Results. 12 cases (11 male, 1 female) were included in the study, patients received Ibrutinib 420 mg daily. The median age of the study population was 64 years (range 40-76 years), and 41% of the patients were age 70 years or older. 66% of the study participants were diagnosed in advanced stage (IV). Among the 12 of cases, 9 patients received two or more previous therapies. The overall response rate was 58%. The 12 month overall survival was 75%. Ibrutinib was well tolerated, adverse reactions leading to temporary treatment breaks occurred in 16% of patients. 1 patient discontinued the treatment. Blood lymphocytosis occurred in 5 patients.

Conclusion. Ibrutinib is well tolerated and effective in refractory/relapse patients.

EVALUATION OF COMMONLY USED HEMATOLOGICAL PARAMETERS AS PROGNOSTIC FACTORS IN OVARIAN CARCINOMA

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Introduction. Ovarian carcinoma remains the first cause of mortality by gynecological cancers and the 5th death cause by cancer in women. A series of hematological parameters have proved their efficacy as prognostic factors in serous ovarian carcinoma (SOC). The present study has tried to verify whether some commonly used hematological parameters may have a prognostic value in SOC.

Materials and methods. The study evaluated 43 female patients, aged 40-73 years, treated in „Ion Chiricuta" Oncology Institute in Cluj-Napoca. Commonly used hematological parameters: absolute neutrophil count, leucocytes, platelets, CA-125 tumor marker, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR) where assessed. Correlations with tumor stage, grade, response to treatment, related toxicity where evaluated to provide data on their prognostic value.

Results. Clinical and surgical staging revealed 3 patients with stage I, 5 patients stage II, 23 patients stage III and 12 patients stage IV SOC. Pathological evaluation identified 4 patients with grade 1 tumors, 14 patients with grade 2 tumors and 25 patients with grade 3 tumors.

After treatment, 49% of patients presented complete response, 25% partial response, 7% stable disease and 19% progressive disease.

Absolute neutrophil count, leucocytes, platelets, NLR, and PLR did not correlate with tumor stage and grade. There was no association between the value of CA-125, NLR, PLR and the gastrointestinal and neurological toxicity. Statistically significant difference was observed between absolute neutrophil count and the type of response to treatment.

The decreased percentage of CA-125 after the treatment correlated with the type of response to chemotherapy.

Conclusions. Absolute neutrophil count can be considered a prognostic factor in differentiating complete response from partial response in SOC.

The decreased percentage of CA-125 after the treatment can be a useful predictor of the patient's response.

HEMATOLOGICAL DIAGNOSTIC FACTORS IN BLADDER CANCER

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Introduction. Bladder cancer is the second most common cancer of the urinary tract, representing 7% of total cancers in men and 2% in women each year. A high recurrence rate, in spite of complete resection, is a particularity of early phase bladder cancer requiring the use of new markers for prognostic and diagnostic factors.

Materials and methods. 45 patients, 38 men and 8 women, with a median age of 67 years were included in the study. 56% were non metastatic invasive bladder cancer (NMIBC) whereas 55% where metastatic invasive bladder cancer (MIBC). Blood count was evaluated before diagnosis and treatment procedures, transurethral resection of bladder tumor (TURBT) and radical cystectomy.

Neutrophil/lymphocyte ratio (NLR) and thrombocytes/lymphocyte ratio (TLR) were assessed.

Correlations between hematologic parameters, tumor stage and malignancy were evaluated by t-student test and U-Mann-Whitney test.

Results. After cystoscopy and TURBT, 15 patients were Ta, 10 patients pT1, 11 patients pT2, 5 patients pT3 and 4 patients pT4, 51% of tumors being low-grade and 49% high grade. There was a statistical significant correlation between platelet number and tumor stage (p=0.0057). Moreover, a borderline significant correlation was revealed between neutrophil count and tumor stage (p=0.0595). No correlations were observed between red blood cells, lymphocytes, NLR, TLR and tumor stage.

Conclusions. These results demonstrate a real potential for hematological parameters in diagnosis and evaluation of muscle invasion in bladder cancer, confirming results in the literature.

CONCOMITANT ACUTE STROKE AND ACUTE MYOCARDIAL INFARCTION – CASE REPORT

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Introduction. Acute ischemic stroke and acute myocardial infarction have the same risk factors; it is yet uncommon for a patient to present in the Emergency room with these conditions with simultaneous onset. The literature on this topic is sparse, there are no guidelines regarding therapeutic intervention in this setting.

Material and methods. We present the case of a 73 years old man presenting with acute ischemic stroke in the Emergency Department. The diagnostic workout revealed an acute myocardial infarction associated with the acute neurological condition (left anterior descending coronal artery). Since the patient was 2 hours and 15 minutes from the onset of the clinical neurological deficit we decided to perform iv thrombolysis using Actilyse.

Results. The patient had a 16 mm cerebral ischemic lesion located in the right middle cerebral artery territory with an initial NIHSS score of 6. Two hours after the procedure the neurological state worsened (NHISS score 8), but without any radiological sign of hemorrhagic transformation.

The neurological state improved over time (NIHSS score of 7 at 24 hours, 6 at 7 days and 5 at 3 months after onset). The patient did not present any hemorrhagic complications associated with thrombolysis.

Conclusions. The acute myocardial infarction did not add significant complications during iv thrombolysis for acute ischemic stroke in our patient.

EVALUATION OF PAIN LEVELS AND PSYCHOLOGICAL SYMPTOMS OF DISTRESS IN PATIENTS WITH COLORECTAL CANCER

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Introduction. Colorectal cancer (CRC) is one of the most prevalent causes of cancer associated deaths worldwide, with a 5 year rate of survival about 60%. Half of the patients develop metastatic disease, with a life expectancy of about 30 months. In these patients, psychological distress (PD) can interfere with the compliance with treatment, perception of pain and quality of life.

The objective of our study was to determine pain levels and the extent of PD manifested by anxiety and depression in a group of patients with advanced or metastatic CRC undergoing oncological treatment in The Oncology Institute "Prof. Dr. Ion Chiricuţă" Cluj-Napoca.

Materials and methods. Forty-nine patients, 24-78 years old with a mean age of 63 were included in the study. 63% of patients had colon tumors, 33% had rectal tumors and 4% had anal canal tumors.

Visual Analogue scale (VAS) vas used to evaluate pain intensity.

Type of pain and localization was assessed by applying McGill inventory with the projection of pain on the silhouette. Anxiety was evaluated by State-Ttrait Anxiety Inventory (STAI) and depression by Beck Depression Inventory (BDI). Correlations between demographic characteristics, pain evaluation and symptoms of PD were analyzed using Chi-squared test $\chi 2$.

Results. More than half of patients had depression while the anxiety was mostly mild to moderate. There were statistically significant correlations (SSC) between the type of pain and pain intensity. A SSC was also observed between the tumor site and level of anxiety.

There was SSC between the tumor site and level of anxiety assessed by STAI.

Conclusion. Anxiety and depression in cancer patients are not routinely assessed in daily practice and current methods of evaluating PD are heterogeneous. There is little data on the assessment of PD in cancer patients and even less on their association with pain. Methods used in our study have been validated in other non-oncological pathologies.

TUBERCULOSIS PLEURAL EFFUSION IN KARTAGENER SYNDROME: AN UNCOMMON DUO

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Introduction. Kartagener syndrome (KS), is a rare, ciliopathic, autosomal recessive genetic disorder that causes a defect in the action of the cilia lining the respiratory tract and fallopian tube. Most males with this syndrome are usually infertile. The association of tuberculosis pleural effusion and KS is rarely reported in the literature. The aim of this paper is to present a case of KS associated with tuberculosis pleural effusion and male fertility.

Material and method. 22 year old male, known with Kartagener Syndrome since childhood, presents to pulmonology ward for the evaluation of a massive pleural effusion that recurred despite repeated drainage and broad spectrum antibiotics. The liquid was exudative, with important lymphocytosis and elevated adenosine deaminase (46 IU/L). The examination for mycobacterium tuberculosis was negative. The CT revealed dextrocardia, bronchietasia in the inferior left lobe and pleural effusion. Considering the age, the liquid characteristics and the persistence of pleural effusions despite treatment the case was interpreted as a tuberculosis pleural effusion and antituberculosis treatment was started with the completed remission of the liquid. The urology consult revealed that he is fertile.

Discussions. A pleural effusion in a patient with Kartagener syndrome poses numerous problems of differential diagnosis, and a bacterial etiology should always be suspected first. But tuberculosis should be kept in mind especially in recurrent effusion.

Conclusions. Although rare tuberculosis, pleural effusion can appear in a Kartagener syndrome patient. Infertility in men, although frequent among this patients it's not universal.

BEHAVIORAL AND CORTISOL RESPONSES TO STRESS IN NEWBORN INFANTS: EFFECTS OF MODE OF DELIVERY

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Introduction. Suboptimal birth characteristics have been associated with altered reactivity to stress in infants. However, previous studies have not controlled for mode of delivery, which may influence the neonatal onset of stress responses.

Materials and methods. The present study assessed stress-related behavior and salivary cortisol before and after an inoculation at two hours after birth, and compared infants born through VD (N = 70) and elective CS (N = 72). Behavioral assessments and saliva collection were done during a routine Hepatitis B inoculation in the first two hours after birth. Behavioral stress assessments were made by trained nurses, at three time points: two minutes before, immediately after and fifty minutes after inoculation. Stress-related behaviors before and after inoculation were assessed using the Modified Behavioral Pain Scale and the cortisol was assayed using the Salimetrics Cortisol Enzyme Immunoassay Kit (Salimetrics LCC, Philadelphia, USA), following the manufacturer's protocol.

Results. The results indicated that overall stress behavior and body movements were increased immediately after inoculation in infants born through CS compared to VD. Infants born through CS did not show significant cortisol increases following inoculation and their overall cortisol reactivity (i.e., AUCG) was lower compared to infants born through VD. However, unexpectedly, cortisol levels in infants born through VD were highest before inoculation and subsequently decreased. Cortisol was significantly related to behavior in both groups, but in opposite directions.

Conclusion. These results support the view that mode of delivery influences neonatal stress reactivity, although future studies should try to disentangle the effects of mode of delivery and related variables.

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DIAGNOSIS CHALLENGES IN PULMONARY CAVITARY LESIONS

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Introduction. Cavitary lesions are uncommon findings on chest X-rays, usually associated with tuberculosis in endemic areas, but other infections or tumors should be considered.

Material and methods. We present a case of a 34 years old woman, admitted in our hospital for further investigations of a cavitary lesion in lower left pulmonary lobe. The patient was prior diagnosed with tumoral lesions of the liver. 6 months ago, when she was 5 moths old pregnant she developed intracranial hypertension with severe cephalea. MRI findings were multiple cystic cerebral disseminated lesions, metastatic lesions being considered. Biological findings: inflammation with leucocytosis and neutrophilia, normal level of eosinophils, normal levels of beta-HCG hormone, negative serology for parasites. Abdominal echoghraphy suggests the presence of hepatocarcinoma.

Results. The excision of an intracerebral lesion reveals the presence of cerebral echinococcosis. Albenazol treatment was initiated, with stationary lesions after 3 months and good clinical outcome. Surgery of hepatic , pulmonary, other cerebral lesions is under discussion.

Conclusion. Echinococcosis is an infectious disease caused by cestodes of Echinococcus genus, family Taeniidae. In human pathology, Ehinococcus granulosis and Echinococcus multilocularis (alveolar) are involved. Out of all cerebral tumors, hydatic cyst is responsible for 0.32-3% of intracranial space occupying lesions.

SURGICAL SPECIALTIES

PROGNOSTIC FACTORS IN THE FIRST TRIMESTER PREGNANCY WITH POTENTIALLY RESERVED EVOLUTION

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Introduction. The incidence of embryonic demise is 25%. Complications of the first trimester pregnancy are a current health problem. The etiology of the embryonic demise is multifactorial, with chromosomal abnormalities being the most common (40%).

Material and method. The study is a case-control prospective analysis that took place at the „Dominic Stanca" Clinic of Obstetrics and Gynecology, Cluj-Napoca that includes two groups of patients: 81 patients with first-trimester pregnancy in evolution and 89 patients with embryonic demise, all of the patients having amenorrhea between 6-11 weeks. Endovaginal ultrasonographic exploration was performed in order to evaluate the parameter sought: the distance between the embryo and yolk sac. From each subject enrolled in the study, 20 ml of blood was collected for beta human chorionic gonadotropin (beta hCG) dosing.

Results. Regarding the distance between the yolk sac and the embryo in the case group, lower values were observed compared to the control group, the difference being statistically significant. In statistical analysis of serum β-hCG values, statistically significant differences were observed between the two groups ($p < 0.05$). Analyzing the correlation between the two parameters it was observed that for the control group the correlation was weak in almost all weeks of amenorrhea, except for week 6 and 7, where an acceptable correlation was observed and for the case group were observed very good correlations between the indicators in all the weeks of amenorrhea.

Conclusion. The correlation between these 2 parameters increase the effectiveness of screening methods in prenatal monitoring and improve diagnostic methods for first trimester pregnancies whose evolutive potential can be reserved.

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SOFT TISSUE GIANT CELL TUMOR OF LOW MALIGNANT POTENTIAL: A RARE CASE REPORT

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Introduction. Giant cell tumors of soft tissue (GCT-ST) are extremely rare neoplasms. GCT-ST and bone giant cell tumors have similar histopathological and immunohistochemical characteristics. Frequently, it is found in the lower extremities, especially the thigh. We report here a case of GCT-ST diagnosed on histopathological examination after surgical excision.

Case presentation. A 66-year-old man presented with a superficial, ulcerated, non-tender mass, approximately 10×15 cm in size, involving the upper part of the left thigh, near the gluteal region. The patients' medical history revealed three surgical excisions for a recurrent tumor of unknown origin localized in the same part of the body. Magnetic resonance imaging (MRI) scan showed a tumor around 15 cm in size with multiple calcifications, localized in the proximal third of the left thigh. Accordingly to the MRI scan, no bone involvement and no infiltrative characteristics were present. A complete surgical excision of the tumor was performed. The histopathological diagnosis revealed a GCT-ST of low malignant potential. The patient recovered without complications after surgery. Considering the high risk for local recurrence, radiotherapy was recommended. No signs or symptoms of recurrence were reported at the six-month follow-up.

Conclusion. To sum up, soft tissue giant cell tumor of low malignant potential can have a benign clinical course if complete surgical excision is combined with radiotherapy.

ARTICULAR CARTILAGE LESIONS TREATMENT USING SCAFFOLDS WITH NANOSTRUCTURED BIOMATERIALS AND STEM CELLS

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Abstract

Introduction. This study analysis the effect of biological autologus treatment in the cartilage lesions using cell stems and collagen scaffolds.

Material and methods. The purpose of this study is to evaluate and compare the chondro-regenerative properties of lipoaspirant fluid (LAF) cells, extracted by a simple mechanical procces, and the cells from the processed lipoaspirate (PLA), on a preclinical model of cartilage defect in the rabbit. LAF cells can be quickly separated by minimal tissue manipulation, so they are cheaper and more suitable for one-step surgical procedures. The study was performed on a white rabbit animal model divided into 3 groups with an osteochondral defect in the femoral trochlea: group A: control – collagen I/III membrane (ChondroGide®), group B: membrane + LAF cells (24 hours seed), group C: membrane +PLA cells (24 hours seed).

Results. The analysis of the result evaluated macroscopic, histological, micro-CT and gene expression changes. The macroscopic evaluation after Wayne score showed a statistically superior restoration in groups B and C, compared to the control group. Gene expression analysis responsible for the cartilage proliferation, such as COL2A1, ACAN and SOX9, showed statistically significant differences between fluid liposuction fluid group B and the other groups. This changes are sustained also by the histological changes that showed in groups B a hyaline cartilage more abundant and a better reconstruction of the subchondral bone. Micro-CT allowed visualization of the osteochondral defect repair as well as three-dimensional reconstruction of the segments involved.

Conclusions. This study brings real benefits, and this stem cells therapies are a hope for the future of the focal joint cartilage treatment and also in the treatment of osteoarthritis, delay in bone consolidation, pseudoarthrosis, osteoarticular infections etc.

COMPARATIVE STUDY REGARDING BONE CONSOLIDATION BY USING PHYSICAL AND BIOLOGICAL ENHANCING FACTORS

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Introduction. Fracture of the lower limb are very common in the traumatology and are often associated with other injuries, especially the fracture of the femur caused by high energy forces. Lower limb bones have an essential role in stability and motion, and their fractures will lead to prolonged disability and important morbidity, despite of optimal treatment.

Material and methods. The experiment was performed on 20 murine models, with a femoral shaft fracture. Group 1 (5 rats) treated with uncovered titanium nails without exposure to short pulse electromagnetic waves (control group), Group 2 (10 rats): uncovered titanium nails with exposure to short pulse electromagnetic waves and Group 3 (5 rats): hydroxyapatite-collagen coated titanium nails with exposure to short pulse electromagnetic waves. After the second day of the intervention, the murine models from the second and third groups were treated for two weeks with short pulsed waves provide by DIAPULSE machine, ten minutes per day at 4/400 pulse/sec. The bone consolidation and bone marrow space were evaluated, by identifying the macroscopically changes and using micro-CT 3D reconstruction images. Furthermore, alkaline phosphatase and osteocalcin were analyzed before the intervention, after two and eight weeks.

Results. It was found that, clinically the bone healing was faster in the studied group and also the micro-CT showed an extended area of bone apposition around the nails compared with the control group. Moreover, alkaline phosphatases and osteocalcin were higher in the studied groups at two weeks compared to the controlled group.

Conclusions. Collagen coated titanium nails and short pulsed electromagnetic waves showed a faster and better bone consolidation with a superior osseointegration of the intramedullary nails.

TWIN PREGNANCY WITH TRAP SEQUENCE COMPLICATED WITH RETROPLACENTAL HEMATOMA – A CASE REPORT

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Introduction. Twin reversed arterial perfusion (TRAP) sequence is a rare (1/35.000 pregnancies) and severe complication specific to monochorionic twin pregnancies, involving the presence of an acardiac twin and a structurally normal co-twin (pump twin). The normal twin has a high mortality rate (50-70%), especially due to congestive heart failure.

Case report. We report on the case of a IIG IIIP 33 year-old patient who was referred to our institution form another service with the initial diagnosis of multiple pregnancy with one dead twin. Ultrasound revealed 24 gestational weeks intrauterine biamniotic monochorionic twin pregnancy with TRAP sequence and polyhydramnios. Therapeutic amniocentesis was performed for polyhydramnios, evacuating 430 ml of amniotic fluid. A fetoscopic intervention was decided, with the occlusion of the umbilical cord of the acardiac twin, followed by the evacuation of another 700 ml amniotic fluid. The patient was readmitted to our institution at 34 gestational weeks for preterm premature rupture of membranes and vaginal bleeding. Ultrasound revealed intrauterine growth restriction of the living twin, corresponding to 31 gestational weeks and retroplacentar hematoma, reaching 8.5/5 cm. The patient gave birth through cesarean section to a living female fetus, weighing 1480 g, Apgar score 6, 7, 8 at 1, 2 and respectively 5 minutes.

Conclusion. TRAP sequence is a rare entity, requiring early diagnosis and careful ultrasound monitoring, in order to select the best management option for the pump twin. To the best of our knowledge, this is the first case reporting a twin pregnancy with TRAP sequence complicated with retroplacentar hematoma.

PROGRESSION OF EVENTS IN MULTI-VESSEL DOPPLER STUDIES IN A FETUS WITH GROWTH RESTRICTION

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Introduction. Intrauterine growth restriction (IUGR) represents a challenge because diagnostic certainty of its cause is difficult to reach. The purpose of the obstetricians is to plan the management for IUGR according to the severity of the condition and the gestational age.

Clinical case. A case of a 31-year-old patient with history of preeclampsia in her previous pregnancy and IUGR with suggestive Doppler alterations during her current pregnancy will be highlighted.

Umbilical artery (UA) Doppler study represents the gold standard in the management of IUGR. An ↑ pulsatility index (PI)>95th percentile and absent end-diastolic flow (AEDF) was non-assuring. The↑PI of the uterine artery (Ut.A) in our high-risk patient was considered predictive for IUGR. Abnormal ↓ in cerebral vascular resistance was depicted by a ↓ in the middle cerebral artery (MCA)PI<5th percentile. Ductus venosus (DV) Doppler is used in the assessment of IUGR when UA Doppler is abnormal. An ↑PI, the absence or reversal of flow during fetal atrial contraction being suggestive for inadequate oxygen supply to vital organs.

The progression of multi-vessel Doppler studies indicating placental dysfunction pointed out the following events: ↑Ut.A PI accompanied by notching at 22 weeks' gestation (WG), UA PI>95th percentile from 29 to 31 WG, AEDF on the UA at 32 WG and a MCA PI < the 5th percentile. As the AEDF between 29 and 31 WG represents fetal extraction criteria, the fetus was delivered by C-section 48 hours after maternal corticotherapy administration. The newborns' weight was 1580g, Apgar score was 7/8/9 and the newborn's status did not required admission to neonatal intensive care unit.

Conclusion. The combined assessment of multi-vessel Doppler studies, fetal movements, fetal biometry, cardiotocographic patterns, amniotic fluid volume are complementary in detecting fetal compromise that might entail fetal extraction.

SQUAMOUS CELL CARCINOMA OF THE THYROID. A RARE CASE REPORT

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Introduction. Primary squamous cell carcinoma (SCC) of the thyroid gland is an extremely rare entity representing <1% of all primary carcinomas of the thyroid gland. It is described as a very aggressive tumor, with a poor prognosis (OS of 6 months) due to its complications, just a few cases being reported in the literature. The optimal treatment includes surgical excision of the thyroid gland and chemo and radiotherapy, even if the malignancy has a poor response to chemotherapy and in many cases is radio-resistant. The aim of this poster is to report the therapeutic management in the case of a SCC of the thyroid gland in a 66 years old woman.

Case report. A 66-year-old female with a history of normo-functional thyroid goiter was admitted to our clinic due to progressive neck enlargement and progressive dyspnea. On physical examination, a mobile, elastic, insensitive thyroid nodule in the right lobe was palpable. In the right latero-cervical region, a 1.5 and 1 cm, mobile, elastic, insensitive lymph nodes were palpable. Thyroid ultrasound was performed revealing a mass of the right lobe of 3 x 2.3 x 2.4 cm and the presence of two enlarged lymph nodes in the right neck. The patient underwent total thyroidectomy and excision biopsy of the right laterocervical lymph nodes. The recurrent nerves were identified and preserved in both sides. No infiltration of adjacent organs was noted intraoperatively. The histopathological diagnosis was: SCC of the thyroid, nonkeratinized, poorly differentiated. Subsequently, the patient underwent tracheostomy and was submitted to adjuvant chemotherapy and concomitant external radiotherapy.

Conclusion. SCC of the thyroid gland is a rare and aggressive entity with poor prognosis. The only prognostic factor is the complete surgical resection of the tumor, whereas efficacy of adjuvant treatment remains controversial. A fatal outcome is usually a result of its complications, due to loco-regional spread of the disease.

THE ROLE OF ANTENATAL DIAGNOSIS IN CONGENITAL HEART DISEASE. CASE PRESENTATION

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Introduction. Interrupted aortic arch is a rare congenital heart disease (1% of congenital heart diseases), very rarely diagnosed in the fetus. Of the three types, B type (aortic arch interrupted between left common carotid artery and left subclavian artery) is the most frequent (55% of cases). It is associated with ventricular septal defect (VSD) in 90% of cases and Di George Syndrome in 50% of cases.

Case raport. We present a newborn antenatally diagnosed with interrupted aortic arch and VSD. Amniotic fluid genetic testing revealed the deletion of 22q11.2 (Di George Syndrome). Spontaneously born at term, with good postnatal adaptation, he was transferred in a pediatric cardiac surgery unit, under prostaglandin treatment.

Echocardiography confirmed type B interrupted aortic arch, VSD, bicuspid hypoplazic aortic valve, patent foramen ovale and patent ductus arteriosus. Surgical intervention in the 5th day of life reconstructed the aortic arch and closed the VSD, atrial septal defect and ductus arteriosus. After surgery the newborn was hemodynamically stable with moderate inotrope support. The evolution was slowly favorable, in the 19th postoperative day he was transferred to the pediatric cardiology unit.

3 weeks after surgery he developed a Staphylococcus epidermidis sepsis, which resolved under antibiotic treatment.

The final postoperative echocardiography revealed a good cardiac function.

The short and long term cardiac prognosis is good, but in this newborn it is encumbered by the association of 22q11.2deletion.

Conclusion. The antenatal diagnosis and prompt surgical intervention in a specialized unit offers a good survival chance for children with rare congenital heart disease.

USING DYNAMIC INFRARED THERMOGRAPHY (DIRT) FOR PREOPERATIVE MAPPING OF CUTANEOUS PERFORATORS

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Introduction. The high technical demands associated with perforator flaps demand a precise preoperative identification and evaluation of perforator vessels. Dynamic Infrared Thermography (DIRT) is a relatively new technique used for preoperative perforator mapping. The purpose of this paper is to analyze the value of using DIRT for preoperative mapping of cutaneous perforators.

Materials and methods. DIRT was used for preoperative perforator mapping in 10 pigs. The results were compared to intraoperative findings. Total number of perforators, localization, and identification of the dominant perforator was analyzed for the method.

Results. Each quadrant was distinctly analyzed. The location and number of perforators identified by DIRT was compared with the intraoperative findings. The total number of perforators identified during surgery was 202. DIRT visualized 238 perforators, with 192 confirmed by surgery. The sensitivity of DIRT in identifying perforators was 95.05%. The positive predictive value of the method was 80.67%, due to an increased number of false positive results attributable to perforator branching. Superimposition of the images acquired during DIRT showed that the positions of "hot spots" on the skin were located within a mean radius of 0.9 cm (N=192) from the point where the perforator was observed to pierce the fascia. The dominant perforator identified by DIRT correlated with surgical findings in all cases.

Conclusion. Preoperative perforator mapping has become a compulsory step in nearly all reconstructive procedures. The method has a high sensitivity and positive predictive value in identifying perforators, and has accurately identified the dominant perforator in all cases. Correctly identifying the dominant perforator preoperatively reduces operative time, lowers complication rates and ensures an overall better result.

A CASE REPORT OF PHARYNGEAL AMYLOIDOSIS

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Introduction. Amyloidosis is a clinical disorder caused by extracellular and/or intracellular deposition of insoluble abnormal amyloid fibrils.

Case report. A 71 year old patient presented in our hospital with a complaint of bilateral nasal obstruction, hyposmia and bilateral hearing impairment. On clinical examination he was found with bilateral hypertrophy of the tonsils, bilateral hypertrophy in rhinopharynx. On audiometry was found with bilateral mixed hearing loss and Weber lateralized on the right side.

The patient underwent a CT scan that visualized the presence of a tumor mass in oro- and rhinopharynx. Also an endoscopic biopsy from rhinopharynx and oropharynx was performed. The histopathology result with Congo red staining established a diagnosis of pharyngeal amyloidosis.

Conclusion. Amyloidosis localized in pharynx is a rare condition that imposes differential diagnosis with other pharyngeal benign or malignant tumors.

OTOACOUSTIC EMISSIONS STUDY IN TWINS NEONATAL HEARING SCREENING

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Introduction. Using TEOAE and DPOAE, the study aims to compare the results of neonatal hearing screening for the twin population with those obtained by the general pediatric population.

Material and methods. The study group consisted of 58 pediatric patients with a mean age of 1.9 months (0.2 to 4.1 months), divided into two groups: group 1 (11 pairs of twins) and group 2 (36 patients, the single births). Statistical analysis involved using student t test and Pearson correlation.

Results. When analyzing the average values of SNR TEOAE recorded on each frequency for the two groups, the significant values were obtained for the right ear, solely on frequency of 2 kHz (p=0.04) and the left ear, the low frequencies of 1 and 1.5 kHz (p=0.04 or 0.03). There were no statistically significant differences for TEOAE SNR between the two ears in any study group. Comparing the average values of DPOAE SNR's right ear, recorded on each frequency for the two groups, we recorded significant values only for the frequency of 2 kHz (p=0.03). There were no statistically significant differences for DPOAE SNR both ears in any group.

Conclusion. Twin pregnancy is not a risk factor for congenital hearing loss, instead the twin or multiple pregnancy risks are those that could strike the risk of congenital hearing loss.

IMAGING COMPUTER ANALYSIS (CT SCAN) OF THE RHINOBASE - RADIOANATOMICAL STUDY

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Introduction. The purpose of this study is to determine and statistically analyse important anatomical variations of rhinobasis describe by computed tomography (CT).

Material and methods. Retrospective review of 150 direct coronal and reconstructed sagittal images of paranasal sinus computed tomography (CT) scans. The CT scan was evaluated emphasizing the anatomical variations of rhinobase including ethmoid fovea, olfactory fossa, lateral lamella and anterior ethmoid artery.

Results. Of the 150 patients, 23 patients (15.3%) present asymmetric ethmoid fovea. Among 23 patients, 15 patients (56.52%) showed low fovea on right side and 8 (43,48%) showed low fovea on left side. 72 patients (48.0%) showed a contour asymmetry with „flattening" of the ethmoid roof on one side, 38 (52.7%) on the right and 34 (47.3%) on the left side. A statistically significant difference was detected between the right and left sides in the height of the lateral lamella ($p < 0.05$). In present study we noticed that anterior ethmoid artery (AEA) passes through ethmoidal air cells in 123 patients (82%) and along anterior skull base in 27 patients (18%).

Conclusion. CT scans allowing comparison of the right and left ethmoidal roofs should always be made before endoscopic sinus surgery. Differences in height of the skull base between right and left sides, especially in the anterior ethmoid sinus, may be an important surgical consideration.

NECROTIZING SCLERITIS REVEALING POLYCHONDRITIS AND COMMON VARIABLE IMMUNE DEFICIENCY

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Introduction. Necrotizing scleritis is a severe ocular complication of systemic diseases, that may rarely be inaugural. Relapsing polychondritis (RP) is a rare disease evolving with recurrent cartilage inflammation, but also with ocular, respiratory, cardiac and vascular involvement. Associations of RP with various autoimmune disorders and hematological diseases, mainly leukemia, lymphoma and myelodysplastic syndrome and rarely with hemolytic anemia, have been described.

Common variable immune deficiency (CVID) is a rare disease manifesting with low concentrations of immunoglobulins, mainly IgG and IgA, and with inefficient production of antibodies to different pathogens.

Material and method. We report a 53-year patient with thyroiditis and pernicious anemia in whom a left eye necrotizing scleritis led to the diagnosis of RP and common variable immune deficiency. The necrotizing scleritis was successfully operated with dura mater plastia. However, the disease control was difficult to be achieved with glucocorticoids and various immune suppression regimens tried (including cyclophosphamide, cyclosporine, azathioprine, leflunomide and infliximab) along with immunoglobulin substitution.

Results. The patient was treated surgically with sleral plastia. Also, systemic therapy with methylprednisolone pulses and cyclophosphamide monthly, cyclosporine – stopped due to severe hypertension and renal insufficiency, azathioprine – stopped due to intolerance, then cyclophosphamide orally. The visual acuity returned to normal and she had less episodes of auricular and respiratory chondritis, but persistence of severe episodic arthritis. Leflunomide and a single infusion of infliximab were given, stopped because of prolonged diarrhea revealing an E. coli sepsis and she was continued on low-dose glucocorticoids and leflunomide 10 mg/day, along with immunoglobulins.

Conclusions. The association of RP and CVID or CVID-like diseases is rare, another 4 cases having been reported.

AN UNCOMMON AND INSIDIOUS PRESENTATION OF CLEAR CELL RENAL CARCINOMA WITH TUMOR EXTENDING INTO THE INFERIOR VENA CAVA: A CASE REPORT

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Indroduction. Renal cell carcinoma (RCC) is a potentially lethal cancer with aggressive behavior, tendency to metastasize and it involves the inferior vena cava (IVC) in approximately 15% of cases. Surgical resection of RCC is the benchmark for long-term cure of the disease. The open or laparoscopic radical nephrectomy is considered the gold standard for stage T1b-T4 tumors.

Case presentation. A 53-year-old man was referred to our hospital for macroscopic hematuria and right low back pain. An abdominal and pelvic CT scan showed a 11x7.5 cm enhancing right renal tumor with tumor thrombus extending into the right renal vein. Therefore, we diagnosed the tumor as a clinically classified pT3bNxMx right RCC. Open radical right nephrectomy with en bloc resection of the entire kidney as well as the surrounding perinephric fat, the ipsilateral adrenal gland, the regional lymph nodes and renal vein thrombectomy was performed. The pathological diagnosis was Clear Cell Renal Carcinoma, a renal cortical tumor typically characterized by malignant epithelial cells with clear cytoplasm and a compact-alveolar (nested) or acinar growth pattern interspersed with intricate, arborizing vasculature.

Conclusion. Advanced extension of RCC can occur with no apparent symptoms and be detected incidentally. In rare circumstances, atypical presentation of RCC should be considered in a patient presenting with Inferior Vena Cava Syndrome. For advanced RCC with tumor thrombus extension into the IVC, lateral venorrhaphy and primary IVC repair avoids complicated caval reconstructions and results in high patency rates with a low local tumor recurrence rate. RCC with IVC thromb invasion is a complex surgical challenge, but excellent results can be obtained with proper patient selection, meticulous surgical techniques, and close perioperative patient care.

INTRASCROTAL EXTRATESTICULAR LIPOMA: A RARE CASE REPORT

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Introduction. Intrascrotal lipomas are rare benign mesenchymal tumours. Although lipomas found in other parts of the body are not uncommon, scrotal lipomas, which have the highest frequency among the nontesticular intrascortal tumours, are still considered rare in the literature. They can originate from the epididymis, spermatic cord and also from the tunica vaginalis.

Case presentation. We discuss the case of a primary intrascrotal lipoma presenting as a painless swelling of the left scrotal region and local discomfort. The physical examination uncovered an elastic, irreducible, non-tender, regularly shaped mass on the left side of the scrotum apart of the testicle. Both spermatic cords and testicles were normal. Ultrasound examination of the left hemiscrotum describes a scrotal mass of parenchymatous structure, having a trabecular model, without invasion in the testicle. No vascularization was detected on the Doppler imaging. Magnetic resonance revealed an adipose structure, situated left extratesticular, surrounding the spermatic cord, with dimensions of 70/82 mm, without any evidence of herniation of adipose tissue from the peritoneum. We therefore considered, based on the imagistic aspect, the diagnosis of extratesticular left intrascrotal lipoma. Complete excision was performed through scrotal incision. No drainage was placed. The histological report confirmed the diagnosis: the tumoral mass was formed of mature cells of adipose tissue with fine conjunctive septa, without lipoblasts, nuclear atypia, mitosis or necrotic areas.

Conclusion. Although intrascrotal lipomas are rare, they should be considered as differential diagnosis of scrotal masses. Clinically, it imitates inguinal herniation and haematoma and it is hard to distinguish malignancy. Ultrasound and magnetic resonance help establish an accurate diagnosis and guide the surgical management.

INITIAL RESULTS OF FLEXIBLE URETHEROSCOPY AND LASSER LITHOTRIPSY FOR KIDNEY STONES

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Introduction. Minimally invasive procedures have become the first choice of treatment for urinary pathology, especially urolithiasis. Flexible ureteroscopy has been through significant technological advancements in the previous decades for the treatment of upper urinary tract lithiasis. The aim of this study is to evaluate the effectiveness of flexible ureteroscopy for the treatment of renal stones.

Materials and methods. We conducted a retrospective study of 27 pacients with kidney stones treated in the Urology Department of Clinical Institute of Urology and Renal Transplant Cluj Napoca, over a period of 5 months. 29 procedures were conducted using a flexible ureteroscope and intracorporeal laser lithotripsy was performed, using a Sphinx jr. Holmium laser.

Results. The immediate postoperative renal stone-free rate was 93%. 52% of the stones were located in the right kidney and 48% in the left kidney. Out of these 62% had sizes between 10-20 mm, 15% were < 10 mm and 23% > 20 mm. 64% were multiple stones, 24% were single stones and 12% staghorn stones. Among the renal stones, 48% were located in the inferior calyx, 26% were located in the mid calyx and 26% in the upper calyx.

Conclusions. Flexible ureteroscopy for kidney stones is a favorable treatment option which offers high stone-free rate and low post-operatory morbidity. Flexible ureteroscopy it is an efficient diagnostic and curative method of treatment for upper urinary tract pathology.

EYE TRACKING – A NEW TECHNIQUE TO QUANTIFY THE SEVERITY OF OCULAR MOTILITY DYSFUNCTION IN PATIENTS WITH TRAUMATIC BRAIN INJURY

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Introduction. Traumatic brain injury (TBI) represents a major cause of morbidity and disability, especially in the young population. Apart from mortality, which seems to decrease after the implementation of acute management of TBI guidelines, morbidity in TBI also represents a major public health problem, disregarding of the severity of the injury.

Due to the complexity of factors that interact in the pathology of TBI and the heterogeneity of clinical presentation, there is need for a multidimensional approach regarding both evaluation of outcome and treatment.

Material and methods. Eye tracking implies looking at targets on a computer screen while a special system records eye movements and changes in pupil diameter in response to the movement of the targets. Patterns of eye movements offer information about what a person is processing at a particular moment and the time course of processing visual information. We can use standard, validated, computerized eye tracking protocol, fixation, saccades and smooth pursuit eye movements for patients with TBI to identify diffuse axonal injury.

Results. Eye tracking identifies the patients with known brain trauma, including milder concussion that have been missed on CT scans, such as those associated with diffuse axonal injury.

Some people recover completely while others, especially those with multiple concussions, develop chronic headache, neurodegenerative diseases and psychiatric disorders. One of the reasons concussion is difficult to treat is its difficult diagnosis. Diffuse axonal injury is common in TBI and is presumed to contribute to persistent motor problems.

Conclusion. Disconjugate eye movements have been associated with TBI. Ocular motility dysfunction may be present in up to 90% of patients with concussion or blast injury. Eye tracking may help quantify the severity of ocular motility dysfunction associated with concussion and structural brain injury.

ADVANCED PERIAURICULAR CUTANEOUS CARCINOMAS WITH TEMPORAL BONE INVOLVEMENT-SALVAGE SURGERY

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Introduction. The auricle and periauricular area are the site of origin in 5% to 10% of all nonmelanoma skin cancers. Basal cell carcinoma is the most common histological type, accounting for 85% of all skin cancers, whereas squamous cell carcinoma accounts for 10% of skin cancers. Many of these advanced tumors become difficult to treat because of local spread and regional metastasis. Those tumors that are not treated early often require more aggressive treatment with ear canal resection, partial temporal bone resection, or even parotidectomy and radiation therapy.

Material and methods. We report on a series of 3 patients with advanced periauricular cutaneous carcinomas with temporal bone involvement, which presented to E.N.T. Department University of Medicine and Pharmacy Cluj-Napoca. All the patients were classified as T4 status according to current the American Joint Committee on Cancer system staging criteria. Surgical salvage was attempted in 3 patients due to unresectable skull base involvement in order to treat the unbearable pain and the recurrent bleeding.

Results. These 3 cases attempts at local salvage were successful in all cases, defined as achieving survival of at least 24 months.

Conclusions. Advanced periauricular cutaneous carcinoma is a rare disease with little available literature regarding epidemiology, prognostic markers, and management protocols. Aggressive surgical resection is the best solution in these cases. Surgical salvage may be an option for unresectable skull base involvement tumors.

OLFACTORY REHABILITATION AFTER TOTAL LARYNGECTOMY

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Introduction. The absence of airflow after total laringetomy causes a decreased sense of olfaction and thereby a decrease in the fine nuances of taste. Olfactory rehabilitation helps patients recover their olfactory, and also the sense of taste. The aim of this study is to determine the efficacy of the nasal airflow-inducing maneuver (NAIM), also known as „polite yawning", as a method of olfactory rehabilitation in laryngectomized patients.

Materials and methods. A prospective study was conducted on patients with total laryngectomy at the Ear, Nose and Throat Department of the Emergency County Hospital of Cluj-Napoca, between September 2016 and March 2017, using NAIM or „polite yawning" rehabilitation olfactory technique. Olfactory function assessment was performed using olfactory tests („Sniffin'Sticks" test) before and after the technique NAIM or „polite yawning." We trained the patients in this manoeuver, and its effectiveness in inducing nasal airflow was checked with water manometers.

Results. Olfactory tests are related to patient age and sex and categorize sense of smell in three diagnoses: normosmia (30-48 points), hyposmia (16-30 points) and anosmia (≤15). Based on the threshold, discrimination and identification (TDI) score patients were functionally diagnosed into „smellers" for hyposmia, and „nonsmellers" for anosmia. Before treatment there were eleven nonsmellers and 1 smeller. After intervention there were 6 nonsmellers (50 %) and 6 smellers (50%).

Conclusion. NAIM technique is an effective and inexpensive method for olfactory rehabilitation of laryngectomized patients. NAIM is easy to learn and quickly improves the ability to smell, and also the taste.

PHARMACY
FUNDAMENTAL RESEARCH

ELECTROCHEMICAL DETECTION OF VANCOMYCIN

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Introduction. Vancomycin is a glycopeptide antibiotic, indicated parenterally for the treatment and prophylaxis of severe infections caused by Gram-positive bacteria. The main drawback of the treatment with vancomycin is the relative high occurrence of nephrotoxicity, ototoxicity and the spread of bacterial resistance to antibiotics.Therefore, there is an increasing need of analytical tools for the therapeutic drug monitoring of vancomycin, in order to maximize efficacy and improve the clinical outcome for the patients and to minimize the emergence of antibiotic resistance. The purpose of this study was the development of a fast and sensitive electrochemical method for the analysis of vancomycin.

Material and methods. The electrochemical behaviour of vancomycin was studied using different electrochemical techniques, like cyclic voltammetry and differential pulse voltammetry and different electrodes: glassy carbon electrode, boron-doped diamond electrode, carbon-based screen printed electrode (SPE) bare or modified with carbon nanotubes or graphene.

Results. Vancomycin presents just one irreversible electrochemical oxidation peak. The electrochemical oxidation of vancomycin is influenced by the pH of the supporting electrolyte, the electrode material and by electrochemical parameters. The electrochemical method allows quantitative analysis of low amounts of vancomycin and it proved to present good selectivity.

Conclusion. The electrochemical behavior of vancomycin was investigated at different electrode materials, with best results at the SPE modified with graphene. The optimized electrochemical method presented good sensitivity and selectivity for the detection of vancomycin.

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HOST-GUEST COMPLEXATION BETWEEN TETRAZINES-B-CYCLODEXTRIN STUDIED BOTH IN SOLUTIONS AND FILMS

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Introduction. Tetrazines are electroactive heterocycles with a very high electron affinity and with interesting fluorescence properties that can be electrochemically monitored.

Material and methods. Four tetrazines derivatives were successfully solubilized in water by using β-cyclodextrin (β-CD) and gold nanoparticles modified with β-CD (AuNPs-CD) due to the formation of inclusion complexes. The behavior of these supramolecular assemblies was investigated by electrochemical and fluorescence methods. Tetrazines were also immobilized onto polypyrrole film functionalized with β-CD.

Results. The tetrazine immobilization onto polypyrrole-β-CD film was achieved due to the host-guest interactions between tetrazine derivatives and β-CD cavity maintaining the electrochemical and fluorescent properties of tetrazines. This immobilization was examined using fluorescence microscopy and cyclic voltammetry measurements. These new molecular architectures allowed the immobilization of β-CD-tagged glucose oxidase showing thus promising perspectives for the development of new biomolecular sensors with electrochemical and fluorescence properties.

Conclusion. Tetrazines solubilization in aqueous solutions was successfully achieved by using β-CD and AuNPs-CD due to the formation of inclusion complexes. Tetrazine derivatives were also immobilized onto electrogenerated films of polypyrrole functionalized with β-CD.

POLY-(PYRROLE-3-CARBOXYLIC ACID) BASED NANOSTRUCTURED PLATFORM FOR THE DETECTION OF CARCINOEMBRYONIC ANTIGEN

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Introduction. A nanostructured platform based on pyrrole 3-carboxylic acid (P3CA) was developed and it was used for the detection of carcinoembryonic antigen (CEA), a biomarker for gastro-intestinal tract cancers. Apart from the cost-related advantages, this conductive polymer offers possibilities for functionalization due to the presence of the carboxylic group.

Materials and methods. The nanostructured platform was tailored by polymerizing P3CA at the surface of a graphite-based screen-printed electrode by using multiple pulse amperometry and cyclic voltammetry. The carboxylic groups were activated with N-hydroxysuccinimide in the presence of 1-ethyl-3-(3-dimethyl aminopropyl) carbodiimide hydrochloride. The activation of carboxylic groups facilitates the formation of amide covalent bonds with the terminal amine groups from the anti-CEA antibody. Each step's optimization was tracked by performing electrochemical impedance spectroscopy. The immunosensor was successfully applied for the detection of CEA in synthetic samples.

Results. The polymerization of P3CA led to an increase of the charge transfer resistance (Rct) compared to the bare electrode. The increase was inversely proportional with the concentration of the monomer solution. The activation of the carboxylic groups decreased the Rct of the sensor by providing more polar groups at the surface of the platform. By comparing P3CA with pyrrole, significantly greater increases of the Rct were achieved by using the functionalized monomer. The binding of the anti-CEA antibody was reproducible and directly proportional with its concentration. The increase of the Rct after the incubation with CEA could not be correlated with the concentration of the sample and it remains open to further investigations.

Conclusion. A simple nanostructured platform for the label-free detection of a carcinogenic biomarker molecule was developed, thus holding great opportunities for clinical diagnostics and other biosensor applications.

A NOVEL IMMUNOSENSOR BASED ON GRAPHENE OXIDE/CHITOSAN MODIFIED SCREEN PRINTED ELECTRODE FOR THE DETECTION OF SEROTONIN

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Introduction. The affinity sensors for selective targeting of certain biomolecules have been intensively studied as alternative detection methods for the existing ELISA based immunoassays. These biosensors received a particular attention due to their numerous advantages such as: low cost instrumentation, time effective analysis and highly selective and sensitive testing potential. Serotonin is a neurotransmitter found not only at central nervous system level, but also at peripheral one. Besides the impact over ones emotions, serotonin is involved in bowel movement, nausea, blood clotting, bone health and sexual function. Its deficiency or excess could influence numerous functions across ones body. Hence, the development of an inexpensive, sensitive and selective detection method for serotonin is highly needed. This work presents an innovative platform for the detection of this biogenic amine.

Material and methods. The first step in the development of the biosensor was the activation of the screen printed electrode surface using chronoammperometry, followed by chitosan - graphene oxide mixture deposition. Next, the incubation with serotonin antibody is performed, proceeded by the surface blocking with BSA. The biosensor was electrochemically characterized through cyclic voltammetry, differential pulse voltammetry and electrochemical impedance spectroscopy.

Results. A reproductible nanostructured serotonin selective surface was developed along with the determination of its analytical parameters. The biosensor was tested in biological samples and in the presence of different interferents, where good recovery rates were obtained.

Conclusion. The results are expected to be a starting point for creating a quicker, cheaper and more sensitive and selective tool for serotonin detection.

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NEW PYRENE-DIAZIRINE PHOTOACTIVABLE ELECTRODE MATERIALS FOR BIOSENSING APPLICATIONS

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Introduction. By combining electrochemical and photochemical properties, a versatile tool for biomolecules photografting (eg. enzymes, antibodies, aptamers) onto nanostructured surfaces can be developed. Diazirines are of particular interest and often preferred to other photoreactive crosslinking reagents as they exhibit more advantages, including its small size, short lifetime upon UV irradiation and higher subsequent reactivity [1], than benzophenone.

Material and methods. The development of a new immobilization platform based on the use of a new diazirine derivative (pyrene-diazirine) for proteins binding was achieved. To get this purpose, a new compound has been synthesized allowing its π-stacking onto multi-walled carbon nanotubes (MWCNT), and its electropolymerization at both Platinum (Pt) and MWCNT/Pt electrodes [2].

Results. The electropolymerization parameters were optimized and the electrogenerated films of poly(pyrene-diazirine) were characterized by cyclic voltammetry. Different modified electrode configurations are described. In order to prove the photoreactivity of these electrogenerated architectures, glucose oxidase and polyphenol oxidase were photografted by irradiation, and tested by amperometry for the detection of glucose and catechol, respectively.

Conclusion. An original interfacial hybrid cross-linker molecule combining electrochemical and photochemical properties by substitution of two functional groups, pyrene and diazirine was described.

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NEW SENSING PLATFORMS FOR ENZYME IMMOBILIZATION BASED ON HYBRID FILMS OF POLY(METHYLENE BLUE) FROM DEEP EUTECTIC SOLVENTS AND CARBON NANOTUBES

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Introduction. Deep eutectic solvents (DES) are a new class of "green" designed solvents that offer an inexpensive, biodegradable and robust alternative as innovative solvents for polymerization, in the synthesis of electroactive/conducting films for the development of biosensors. Hybrid composites consisting of poly(methylene blue) films (PMB) made by electropolymerisation in DES and carbon nanotubes (CNT) were developed [1,2].

Material and methods. A uniform and reproducible PMBDES film was obtained by cycling for 30 scans in the potential range 0.6–+1.2 V; (v = 50-500 mV s-1) from a solution of methylene blue (5mM) dissolved in ethaline. For comparison purposes, PMB was also prepared in aqueous medium.

Results. The DES synthesized polymer shows nanostructured features which increased its electronic conductivity/ redox activity compared to the aqueous analogue, and together with CNT enabled the construction of highly performance electrochemical sensors. Low LoD of 13.8 μM and 1.6 μM were obtained, with excellent sensitivities of 2.2 μA cm-2 μM-1, and 68.7 μA cm-2 μM-1, for ascorbic acid and acetaminophen, respectively, outclassing other similar sensors found in the literature.

Conclusion. New hybrid nanostructured platforms based on carbon nanotubes and redox polymer films formed in deep eutectic solvents were prepared and characterized showing good sensitivity, reproducibility, and high recovery factors when used in pharmaceutical formulations representing a new possible strategy for the development of enzyme-based biosensors.

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GUEST – HOST INTERACTION STUDIES BETWEEN PROPRANOLOL AND β-CYCLODEXTRIN AT SOLID/LIQUID INTERFACE

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Introduction. Gold nanoparticles are an excellent platform for selective and/or sensitive bio-detection offering unique optoelectronic and catalytic properties. As such, they continue to attract considerable interest in electrocatalysis and in the design of chemo- and biosensors. The present study aimed to investigate the interaction at the solid/liquid interface between AuNPs, the enantiomers of propranolol and cyclodextrin using electrochemical techniques.

Material and methods. AuNPs were potentiostatically (-0.4V vs. Ag/AgCl, 3M KCl) electrodeposited on the surface of a glassy carbon electrode, in the presence or the absence of cysteine. Following the spontaneous adsorption of propranolol's enantiomers on the gold surface β-cyclodextrin was added. The electrooxidation of enantiomers was performed in phosphate buffer (pH=7.00) by differential pulse voltammetry.

Results. It has been observed that, the gold deposition on the eletrode surface is achieved in a more controllable and reproducible manner by using cysteine. Increasing the time exposure to the cyclodextrin, there is a cathodic shift of potential and an increase of the oxidation peak intensity. There is a chiral discrimination of the enantiomers in the presence of cyclodextrins.

Conclusion. In conclusion, we have seen that the enantiomers adsorption on the electrode surface modified with gold nanoparticles it's non-chiral. The considerable differences in the peak potential and current intensity of the two enantiomers would enable a very simple and convenient way in the chiral probing of drugs with potential applications in the biomedical field.

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OPTIMIZATION OF SAMPLE PRETREATMENT PHASES IN GC-MS ANALYSIS OF FATTY ACIDS

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Abstract

Introduction. Fatty acids are important components of the human body, having biological, structural and functional roles. Omega-3 and omega-6 polyunsaturated fatty acids (PUFAs) seem to be the most important. Their plasma levels have been shown to be altered in different type of diseases. The fatty acids plasma profiles have been used to identify potential biomarkers for several pathologies, mostly by using a gas-chromatography (GC) method. The derivatization of fatty acids into their methyl esters (FAME) may have different drawbacks, therefore the aim of our study was to develop a fast and efficient derivatization and extraction method.

Material and methods. The pretreatment of fatty acids consists of derivatization and then extraction of FAME in hexane. In the first step we used two different reagents: BF_3/MeOH and HCl/MeOH, and applied the following procedures: (1) derivatization and extraction (LLE) in the oven at 70°C/5 min, (2) in the water bath at 70°C/5 min, (3) using the microwave oven/ 5 sec, (4) at the room temperature and (5) derivatization followed by SPE.

Results. Results have shown significant differences between the tested procedures. In all cases when the derivatization was combined with the LLE the bias and accuracy was improved. Using the microwave oven the pretreatment time was also significantly shortened, without losing efficiency.

Conclusion. In conclusion, we have developed a fast and fully optimized pretreatment for the fatty acids, which can also be applied on human real samples.

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THE MULTI-REGULATORY PATHWAYS OF SECURIDACA SAPONIN INDUCED ANTICANCER ACTIVITY ON CERVICAL CANCER CELL LINES

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Introduction. Over 90% incidents of cervical cancer are caused by hpv infection, particularly the high-risk subtype 16 and 18. The molecular oncoproteins E6 and E7 of this virus have been implicated in the primary etiology and progression of malignant phenotype in cancerous cells. Plant-derived Saponins have been identified as potent inhibitor of E6 and E7, targeting their functions in cervical tumor cells.

Materials and methods. Two cytotoxic fractions labelled 4A3 and 4A4 were isolated from a purified root-extract of S. longipedunculata using preparative TLC (RP-18). The fractions were identified as triterpenoid saponins and activity investigated on tumor cell lines (Caski and BU25TK), positive with human papilloma virus. Specific tests carried out include MTT, scratch assay, RT-qPCR and fluorescence microscopy.

Results. Reduced cell proliferation was achieved in dose and time dependent manner by 4A3 and 4A4, with IC50 of 7.03 and 16.39 (µg/mL) respectively on Caski cells. The scratch assay presented a reduction in cell migration capacity in 48h, compared to the control. Late apoptosis was peculiar with cells treated with single dose of 4A3, while 4A4 indicated early apoptosis. Analysis by RT-qPCR revealed a fold-change expression of anti-apoptotic genes (MCL-1 and BCL2L1) for 4A3. AKT-3 was significantly inhibited, being known for multiple signal transduction involved in cell proliferation, apoptosis, angiogenesis, invasion and chemo-resistance. This data therefore supports the observed responses relating to low expression of VEGFA, MCL-1, BCL2L1 and CDH-1 via the PI3k-AKT/ mTOR/ NF-kB pathways.

Conclusion. The ability of these labeled fractions to kill tumor cells and induce apoptosis in manner involving multiple regulatory pathways makes them attractive, as candidate for anticancer development.

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DEGRADATION PROFILE OF ZEIN NANOPARTICLES AS TARGETED DELIVERY SYSTEMS

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Introduction. Zein, a protein obtained from corn endosperm is known for its hydrophobic character and the ability to self-assemble into nanoparticles (NPs) that can be exploited for the incorporation of hydrophobic pesticides.

The present study aims to examine the weathering and fate of zein nanoparticles (ZNPs) with various surface properties under environmentally relevant conditions.

Material and methods. Hydrodynamic size and surface charge measurements were performed on ZNPs synthesized with various cationic and non-ionic surfactants, followed by accelerated degradation studies. Degradation profiles of ZNPs were obtained at extreme pH values (pH 4 and 9). The change of the parent compound over time was monitored by capillary gel electrophoresis with UV detection, where the rate constants of the hydrolytic degradation allowed the approximation of zein NPs persistence in aqueous media at a chosen temperature.

Results. In general, zein NPs demonstrated a longer persistence time in acidic media (~3918 days at 20ºC) in comparison with a more alkaline environment (~205 days at 20ºC, pH=9) for zein-DMAB. The exception was NPs obtained in the presence of DBDM (~1392 days at 20ºC, pH=4 and ~3028 days at 20ºC, pH=9). Degradation rate constants were directly correlated with the studied temperature and pH values.

Conclusion. In conclusion, the nature of surfactants in zein NP formulations influenced their physical properties and chemical stability over time. A better understanding of the surfactants' impact on zein nanodelivery systems may allow for fine tuning of their specific interaction with targeted plants and pests, as well as their environmental fate, assuring a more rational and environmental friendly use of these nanopesticides.

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LABEL FREE ELECTROCHEMICAL IMMUNOSENSOR FOR SENSITIVE DETECTION OF MUCIN4

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Introduction. Mucin 4 (MUC4) is normally expressed in airway epithelial cells, in breast milk, saliva, ear and eye fluids, while its aberrant expression has been reported in pancreatic, breast, lung, ovarian, colorectal, and bladder carcinomas. The development of an electrochemical immunosensor for MUC4 detection, using electrochemical reduction of diazonium salts for the covalent attachment of the antibody is presented [1].

Materials and methods. The sensing platform was obtained by electrochemical grafting onto a graphite-based electrode of in-situ generated aryl diazonium salt from p-aminophenyalcetic acid (p-APAA). The nanoscale film was then functionalized by amino-terminated MUC 4 antibody. An additional blocking step was introduced in order to block the open spaces, and also to stabilize the biomolecules previously bound to the electrode surface, by incubation of 0.5 % bovine serum albumin solution. In the end, different concentrations of MUC 4 were applied on the surface of the functionalized immunosensor for the quantification of the O- Glycoprotein. MUC 4 was also detected from combinations of Mucin 16 and Interleukin-6 with MUC4 and serum samples. All the results were obtained using electrochemical measurements.

Results. Every single step made to obtain the immunosensor was optimized, testing different concentrations of (p-APPA) and MUC 4 antibody at different incubation time. The optimal results were: 30 s chronoamperometry grafting of a 5 mM p-APAA solution, and a 30 min incubation time for a MUC4 antibody 5 mM solution. For the detection of MUC4 a detection limit of 0.33 µg mL-1 was estimated based on a signal-to-noise ratio of 3.

Conclusions. The novel label-free immunosensor allows the sensitive and selective electrochemical detection and quantification of MUC4 in spiked human serum samples proving its potential for biomedical and clinical applications.

RECENT ADVANCES ON THE OXIDATIVE BIOTRANSFORMATION OF SEVERAL BETA-BLOCKERS

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A full comprehension of the hepatic biotransformation pathways of a pharmaceutical substance represents an essential key in the evaluation of safety profiles in drug development. In addition to the conventional in vivo and in vitro methods using biological matrices, biomimetic, non-enzymatic investigational approaches are gaining an increased importance and popularity. These fast, efficient and cost-effective methods offer the possibility to electrochemically generate metabolites, further separated and identified by chromatographic or electrophoretic techniques coupled to mass spectrometry (MS), offering important advantages in mimicking and understanding of the underlying mechanisms for phase I reactions as part of the oxidative transformation of drugs in the human liver due to cytochrome P450 enzymatic activity.

This study is focused on revisiting the oxidative metabolization processes of several beta-blockers. Therefore, the electrochemical oxidation products of propranolol, atenolol, oxprenolol, alprenolol, obtained with an electrochemical flow cell are compared to metabolites formed during microsomal incubation (human liver microsomes). The separation and detection of the emerging oxidative products was accomplished by CE/MS methods.

The performed experiments re-endorse the possibility of using electrochemical simulation in the predication of oxidative species formation during metabolic conversions.

To the best of our knowledge, in case of atenolol and oxprenolol such biotransformation studies were performed for the first time. Furthermore, new findings arose related to the electrochemical oxidation pattern of the studied beta-blockers (aromatic-hydroxylation, O-dealkoxylation and N-dealkylation). Moreover, some relevant differences in comparison with the biotransformation process were also pointed out.

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METAL ION MEDIATED MOLECULAR IMPRINTED POLYMERS FOR ATENOLOL

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Introduction. Molecular imprinting allows the design of highly cross-linked polymeric materials able to mimic natural recognition processes. The choice of the appropriate functional monomer, cross-linker and the nature and specificity of template - monomer interactions are critical for the imprinting process. The use of a metal ion (pivot) has proven to offer a high fidelity of imprint by inducing a higher degree of organization in the prepolymerization mixture, especially when non-covalent imprinting fails (atenolol (ATNL)).

Material and methods. The pivoting effect of two transition metal ions (Cu(II), Co(II)) was tested in different porogenic solvents (DMF, ACN) using (S)-ATNL as template. The bulk molecular imprinted polymers (MIPs) were obtained by electropolymerization or photoinitiation (-18°C) using 4-vinylpyridine (Vp) or N,O-bismethacryloyl ethanolamine (NOBE) as single cross-linking monomer. For comparative reasons (S)-ATNL imprinted methacrylic acid and trifluoromethacrylic acid based MIPs were also synthesized.

Results. Non-covalent interaction of NOBE with S-ATNL in DMF does not seem to offer efficient molecular imprinting. The compromise of solubilizing the ternary metallic complex in DMF annulled the expected advantages of metal pivot mediated molecular imprinting. Switching to a better porogen (ACN) by adding acidic functional monomers (MAA or TFMAA) granted enantioselectivity of the MIP towards ATNL's enantiomers (ion pairing mechanism).

Conclusions. Results showed that in spite of the expected favorable non-covalent interaction between the template and NOBE, acrylate based MIPs showed superior enantioselectivity under the tested conditions. Nevertheless, the studied Co(II) pivot showed improvement in enantioselectivity when paired with Vp in a MIP film modified electrode setup.

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SYNTHESIS AND CHARACTERIZATION OF NEW THIAZOLE AURONES BY OXIDATIVE CYCLIZATION OF ORTHO-HYDROXYCHALCONES

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Introduction. Aurones and chalcones are natural compounds whose therapeutic potential has been highlighted with studies that revealed their antioxidant, anticancer, anti-inflammatory and antimicrobial properties. In the continuation of our researches regarding the synthesis of analogues of natural products such as chalcones and their cyclization products, our aim was the synthesis of new thiazole aurones in order to evaluate their biological potential.

Material and methods. Thiazole ortho-hydroxychalcones were synthesized via Claisen-Schimdt condensation of thiazole aldehydes with ortho-hydroxyacetophenones in basic media. Their oxidative cyclization with mercury(II) acetate in pyridine afforded the corresponding thiazole aurones. The compounds were purified by column chromatography and analyzed by 1H NMR, 13C NMR, IR and MS. The capacity of inhibition of the DPPH free radical was evaluated for the synthesized thiazole ortho-hydroxychalcones using ascorbic acid and butyl-hydroxytoluene as standards.

Results. The thiazole ortho-hydroxychalcones were obtained with 28-68% yields. The thiazole aurones were obtained with 70-85% yields by oxidative cyclization of the corresponding thiazole ortho-hydroxychalcones. The structures of all synthesized compounds were confirmed by 1H NMR, 13C NMR, IR and MS analysis. The synthesized thiazole ortho-hydroxychalcones showed weak inhibition towards the free radical DPPH, compared to the standards.

Conclusion. A series of new thiazole aurones was synthesized with good yields starting from thiazole ortho-hydroxychalcones. The structures of the newly obtained compounds were confirmed by spectral analysis. The thiazole ortho-hydroxychalcones showed weak inhibition of the DPPH free radical.

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SYNTHESIS AND BIOLOGICAL EVALUATION OF NEW THIAZOLO[3,2-b][1,2,4]TRIAZOLES BEARING BENZENSULFONAMIDE MOIETY

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Introduction. The aim of this study was the synthesis, characterization and biological evaluation of new thiazolo[3,2-b][1,2,4]triazoles and their corresponding thioethers bearing benzensulfonamide as well as other adequate moieties which led to anti-inflammatory and analgesic activities.

Material and methods. Thiazolo[3,2-b][1,2,4]triazoles derivatives were synthesized from 3-mercapto-5-benzensulfonamide-1,2,4-triazoles, which underwent a condensation reaction with α–halocarbonyls. According to reaction conditions, thiazolo[3,2-b][1,2,4]triazole derivatives were obtained directly, or via acyclic thioether intermediates. The synthesized compounds, characterized by 1H NMR, 13C NMR, IR and MS, were evaluated in vivo for their biological activities, using a pharmacological model of acute inflammation induced in rats. The anti-inflammatory activity was evaluated by a plethysmometric method and the analgesic activity was evaluated by Randall-Selitto test. The gastric toxicity of the new synthesized heterocycles was assessed by direct observation of the gastric mucosa.

Results. The spectral analysis confirmed the structures of the new polyheterocyclic compounds. Most of the synthesized molecules showed good anti-inflammatory activity (50 mg/kg, p.o.; max 51.3%) and analgesic activity compared to the positive control group (diclofenac 20 mg/kg, p.o.; 59.2%), without any evidence of gastric toxicity.

Conclusions. A series of new thiazolo[3,2-b][1,2,4]triazoles and their thioether intermediates were synthesized and characterized. The biological evaluation revealed good anti-inflammatory and analgesic activities for most of the tested compounds. Some of them will be considered for further investigations concerning their selective inhibition of COX1/COX2 and other inflammation mediators.

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ENZYME CATALYZED KINETIC RESOLUTION OF RACEMIC THIAZOLE BETA-AMINO ESTERS

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Introduction. Enantiomerically pure beta-amino acids have applications in medicinal chemistry, especially as key-intermediates in the synthesis of new chiral bioactive compounds such as peptides, polymer materials and other functionalized compounds. Thiazole derivatives are known to possess various biological activities that can be extended and improved by assembling them into chiral structures.

Based on these considerations, the aim of this study was the synthesis of new enantiomerically pure thiazole beta-amino acids, by enzyme catalyzed kinetic resolution of racemic beta-amino esters.

Material and methods. Several lipases were tested as biocatalysts for the enantioselective hydrolysis of thiazole derived beta-amino esters, in different organic solvents, in order to find the optimal conditions for the enzyme performance. The reactions were monitored by RP-HPLC with chiral stationary phase.

Results. The optimized kinetic resolution process was successfully applied at preparative scale, affording the thiazole derived L-beta-amino acids (ee>96%), as well as their corresponding D-beta-amino esters which remained untransformed during the kinetic resolution. The D-beta-amino esters were hydrolysed in acid catalysis, leading the corresponding thiazole D-beta-amino acids, without affecting the enantiopurity of the products (ee>98%).

Conclusion. A new series of thiazole beta-amino acids were obtained in both enantiomeric forms, with high enantiopurity, by lipase catalyzed kinetic resolution of racemic beta-amino esters.

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SYNTHESIS OF NEW 2-PHENYLAMINOTHIAZOLE DERIVED MANNICH BASES BY ENZYME CATALYZED MULTICOMPONENT REACTIONS

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Introduction. Multicomponent reactions have become powerful and versatile tools in drug discovery and modern synthetic chemistry because of their practical simplicity, rapidity and high atom economy. Besides their natural role, lipases are able to catalyze different multicomponent reactions, such as C-C and C-N bond forming, in Mannich type condensations [1].

Being aware of the biological potential of Mannich bases and 2-aminothiazole derivatives, our aim was to apply the lipase catalyzed Mannich type condensation in order to access new thiazole derived Mannich bases for medicinal applications.

Material and methods. The thiazole aldehydes necessary as substrates in the enzymatic reactions were synthesized starting from different aryl isothiocyanates, by treatment with ammonia, followed by the Hantzsch condensation of the obtained N-aryl thioureas with 1,3-dichloracetone. The obtained 2-arylamino-4-chloromethylthiazoles were transformed into the corresponding aldehydes by N-acetylation with acetic anhydride, followed by Sommelet reaction.

The thiazole Mannich bases were synthesized by trimolecular condensation of thiazole aldehydes with aniline and acetone, using lipase B from Candida antarctica as biocatalyst, in acetone/water mixture as reaction media, at room temperature and neutral pH.

Results. The biocatalytic Mannich type condensation of thiazole aldehydes with aniline and acetone afforded the target compounds with 55-76% yields. The obtained Mannich bases were characterized by melting point, MS, 1H NMR and 13C NMR analysis.

Conclusion. New thiazole Mannich bases were obtained by enzymatic multicomponent reactions in good yields, using mild and eco-friendly reaction conditions. Spectral analysis confirms the structures of the obtained compounds..

SYNTHESIS AND PHYSICO-CHEMICAL CHARACTERIZATION OF SOME THIAZOLE HYDROXYCHALCONES AND HYDROXYFLAVONES

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Introduction. Chalcones and their derivatives are natural and synthetic products with a vast biological potential. The thiazole ring is present in a large number of therapeutic agents with anticancer, anticonvulsant, antifungal and antibacterial properties. Starting from these premises, our aim was the synthesis of hydroxichalcones, 3-hydroxyflavones and their acetylated derivatives in order to assess their biological potential.

Materials and methods. The thiazole hydroxychalcones were obtained by Claisen-Schmidt condensation of 2-arylthiazole-4-carbaldehydes with ortho/para hydroxyacetophenones, in equimolar amounts. Ortho hydroxychalcones were cyclized to the corresponding 3-hydroxyflavones in the presence of urea-hydrogen peroxide complex or hydrogen peroxide. The obtained hydroxychalcones and 3-hydroxyflavones were acetylated by treatment with acetic anhydride in the presence of pyridine.

Results. For the synthesis of chalcones and 3-hydroxyflavones, it was studied the influence of the nature and the position of substituents grafted on the precursors on the reaction rates and yields. The reaction rates are not influenced by the nature and the position of substituents, while the presence of chlorine atom on the arylthiazole decrease the yield of the condensation and cyclization reactions. Oxidative cyclization of ortho hydroxychalcones to the corresponding 3-hydroxyflavones was more effective in the presence of urea-hydrogen peroxide complex when compared to the use of hydrogen peroxide.

Conclusions. A series of thiazole hydroxychalcones, 3-hydroxyflavones and their acetylated derivatives were synthesized and characterized to assess their biological potential. 1H NMR, 13C NMR, MS and IR confirms the structures of the synthesized compounds.

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DESIGN, SYNTHESIS, MOLECULAR DOCKING, AND ANTIBACTERIAL EVALUATION OF SOME NOVEL FLUOROQUINOLONE DERIVATIVES

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Introduction. Quinolone moiety is an important class of nitrogen containing heterocycles widely used as key building blocks for medicinal agents. It exhibits a wide spectrum of pharmacophores and has bactericidal, antiviral, antimalarial, and anticancer activities. In view of the reported antimicrobial activity of various fluoroquinolones, the importance of the C-7 substituents is that they exhibit potent antimicrobial activity. Our objective was to synthesize new fluoroquinolone analogues with different type of substituent at C-7 position of the main fluoroquinolone scaffold to monitor the variation in therapeutic effects of parent molecule.

Methods. A novel series of 7-substituted norfloxacin derivatives were synthesized and were characterized by IR, NMR, MS and elemental analysis techniques. All the synthesized compounds were evaluated for antimicrobial activity against both gram positive and gram-negative bacteria and the MIC and MBC values were calculated by the broth dilution method. To understand the interaction of binding sites with bacterial protein receptor, the docking study was performed using topoisomerase II DNA gyrase enzyme.

Results. Among all the synthesized compounds, some compounds showed potent antimicrobial activity.

Conclusion. A series of 7-substituted fluoroquinolone derivatives were synthesized and evaluated for antibacterial activity. The preliminary results showed a promising antibacterial activity for some of the tested compounds.

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HYPERTHERMIA AND CELL UPTAKE PROPERTIES OF HOLLOW SPHERE MANGANESE AND ZINC FERRITES MAGNETIC NANOPARTICLES

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Introduction. The remarkable magnetic properties of spinel ferrite nanoparticles offer their involvement in a broad spectrum of biomedical applications. In particular, manganese and zinc ferrites are nowadays thoroughly investigated as both hyperthermia and enhancement agents.

Materials and methods. By means of a polyol method, using chloride magnetic precursors, sodium acetate and ethylene-glycol, hollow-spheres of manganese and zinc ferrites magnetic nanoparticles (MNPs) were synthesized. They MNPs were systematically investigated by means of X-ray diffraction, transmission electron microscopy, vibration sample magnetometry and magnetic hyperthermia. Their cytotoxicity and cellular uptake has been investigated on four different cells lines: human retinal pigment epithelial cells, human lung carcinoma cells, human melanoma cells and mouse melanoma cells.

Results. The evolution of specific absorption rate (SAR) on the external alternating magnetic field amplitude of both types of MNPs presented a sigmoidal shape. Upon dispersion in water, MnFe2O4 MNPs exhibit a remarkable saturation SAR value of 1000 W/gFe, while ZnFe2O4 MNPs display only 400 W/gFe. Toxicity assays performed on four cell lines revealed almost no toxicity for both MNPs at a concentration of 0.05 mg/ml. Upon an increase in the concentration (up to 0.2 mg/ml), the MnFe2O4 MNPs exhibit a very small level of toxicity, while ZnFe2O4 MNPs show a gradually drop of 25% in the cell viability, most probably due to the formation of ZnO upon synthesis. Both types of MNPs penetrated the cells through endocytosis, in a time dependent manner and escaped the endosomes. Biodegradation of the MNPs inside cells was not observed.

Conclusion. Hollow-spheres MnFe2O4 MNPs are good candidates for magnetic hyperthermia therapy.

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SOLID SERS SUBSTRATES BASED ON SILVER NANOFLOWERS FOR ULTRASENSITIVE DETECTION OF PHARMACEUTICAL COMPOUNDS

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Introduction. Plasmonic nanoparticles are in the limelight of modern nanotechnology applications. The possible use of plasmonic nanoparticles as highly effective Surface Enhanced Raman Spectroscopy substrates led to the development of a plethora of synthesis methods for different types of noble metal nanoparticles. We propose in this study the synthesis of robust solid SERS substrates based on anisotropic silver nanoflowers synthesized using an original method developed in our laboratory, able to generate reproducible SER spectra for different pharmaceutical compounds having a very low Raman cross section.

Materials and methods. The nanoflowers have been synthesized using the chemical reduction of Ag+ ions by trisodium citrate molecules. This method has been previously employed for the synthesis of spherical nanoparticles by a great number of research groups but this is the first letter reporting the synthesis of anisotropic silver nanoflowers using only trisodium citrate as reducing and stabilizing agent. The key element of this method consists in the fact that the synthesis procedure has been performed in a sealed bottom flask homogenously heated and brought to boil in a microwave oven.

Results. UV-Vis absorption spectroscopy, TEM and DLS have been employed for investigating nanoflowers morphology. The vast majority of the nanoflowers consist of a central nanoparticle interconnected with several highly unidimensional individual arms. Their SERS activity has been evaluated using 4 different lasers: 532, 633, 785 and 830 nm. The amplified Raman spectra have been acquired for molecules of medical interest having different Raman cross sections (doxorubicine, 5-fluorouracil, atenolol, metoprolol).

Conclusions. Solid SERS substrates have been synthesized using as principal building blocks anisotropic silver nanoflowers. These substrates have been successfully employed for the detection of different pharmaceutical compounds in solutions using the SERS technique.

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STRONG PH DEPENDENCE OF SURFACE ENHANCED RAMAN SPECTRA OF METHYLENE BLUE ON SILVER AND GOLD COLLOIDS

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Introduction. Methylene blue (MB) is a molecule with many applications as a chemical indicator, marker, spectral sensitizer and biocompatible agent for photodynamic therapy. MB is also known to form dimers or higher order aggregates in its MB+ ionic form, in water. In the present study we report the pH dependence of the SER spectra of MB, complemented with FTIR, UV-Vis, DFT data aiming at elucidating the conditions leading to the formation of MB aggregates and the orientation of the molecule at metallic surfaces.

Material and methods. Several spectroscopic techniques (UV-Vis, FTIR, Raman, SERS) were used in order to evidence the dye's physico-chemical properties in different environments and the molecular geometry optimization was performed based on on density functional theory (DFT).

Results. The MB water solution UV-Vis spectra revealed an optical absorption band of the monomeric form of MB at 665 nm, most probably caused by the π-π* type transition at 10^{-6}M. At concentrations of 10-4-10-5M the formation of a second peak at ~610 nm was evidenced, indicating the dimer formation. For higher concentrations this peak is blue shifted as larger MB aggregates are formed. The SERS signals of MB on both silver and gold colloids is strongly dependent on pH. We report for the first time new vibration bands in the MB SERS in basic environments and an increase enhancement by one order of magnitude of MB SER spectra. The addition of KI in the colloidal solutions restored the neutral pH SER spectra.

Conclusion. The aggregation of MB in aqueous solutions was evidenced by the changes in the UV-Vis data. The SERS and DFT results revealed that at a neutral pH the molecule is oriented perpendicular to the metallic surface while in basic environments a flat configuration enhances the SERS signals.

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HYBRID NANOPLATFORM FOR RAPID IDENTIFICATION OF *PSEUDOMONAS AERUGINOSA* SIDEROPHORE

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Introduction. The rapid and accurate detection of pathogenic agents represents a milestone for precocious diagnosis and personalized therapy in nosocomial infections. The issue can be addressed by the rational identification of bacteria markers, siderophores, highly involved in its metabolism and in the interactions with the host. The development of sensors with a high sensitivity and selectivity towards this type of compounds could be an important outbreak in this direction.

Materials and methods. The detection platform was developed based on an association of carboxylic polypyrrole, graphene and Au nanoparticles due to their synergetic effect towards the detection of Pyoverdine (Pyo), the siderophore of *Pseudomonas aeruginosa*. The polymer was deposited on a graphite/graphene surface on screen printed electrodes, followed by the electrochemical deposition of Au NPs by cyclic voltammetry. The composite platform was characterized step by step by CV, electrochemical impedance spectroscopy (EIS) and scanning electron microscopy. The detection of Pyo was performed by differential pulse voltammetry in the presence of common interferents and in real samples: commercial human serum, saliva, and tap water.

Results. The CV and EIS characterization were complementary and showed an increased electroactive surface area and enhanced electronic transfer rate. The platform displayed a synergetic effect towards the electronic transfer rate and enhanced active surface area with good analytical performances: limit of detection of 333.33 nM and linear range of 1-100 μM. The sensor was successfully tested in the presence of interferent molecules, found in bioclinical matrix with excellent recovery rates and in real samples such as human serum, saliva and tap water.

Conclusion. The successful detection of Pyo with electrochemical sensors offers the premises for the development of simple and rapid decentralized detection device for different type of bacteria.

PHARMACY
PHARMACEUTICAL SPECIALTIES

IMPACT OF DIFFERENT BLOOD SAMPLE COLLECTION TUBES ON CLINICAL BIOMARKER DISCOVERY

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Introduction. Proteomics biomarker screening of body fluids has often lead to large variations caused by pre-analytical factors. The aim of this study was to investigate the impact of blood sample collection tubes on the blood protein profiling studies.

Material and methods. 24 blood samples were collected from 6 healthy blood donors in tubes containing EDTA, citrate and heparin as anticoagulant plasma, and silica particles. Subsequently, plasma and serum was obtained and proteins were analyzed before and after depletion of highly abundant proteins by nano-LC coupled with ultra-high definition Q-TOF mass spectrometry (UDMS^E).

Results. On the basis of the MSE spectra and protein intensities, the plasma and serum proteomes were characterized. Depletion was first evaluated and showed to be equally efficient in all samples. 300 non-redundant proteins were identified in the depleted protein fraction of each set, out of which 187 defined the blood core proteome. The sample collection method dependent coefficient of variation (CV) of proteins was higher in the EDTA (CV=0.28) and the citrate (CV=0.23) plasma samples, while heparin plasma and serum showed the lowest CV (CV=0.20). Moreover, in the core set, Complement Factor I constituted a suitable candidate for normalization, being one of the most stable proteins regarding both technical and biological variance.

Conclusion. In this study MSE detection was used to evaluate the impact of different blood sample collection tubes on the blood proteome pattern. A core blood proteome was defined independent of the sampling method and unique proteins were also characterized. Based on these findings, sample collection tubes need to be considered important pre-analytical factors for clinical biomarker discovery.

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CYTOTOXIC ACTIVITY OF RESVERATROL AND CURCUMIN ON COLORECTAL CANCER CELLS, AS SINGLE AGENTS AND IN COMBINATION

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Introduction. Colorectal cancer represents one of the most significant diet-related types of cancer. Curcumin and resveratrol are potent bioactive dietary compounds known for their anticarcinogenic and antioxidant properties. As single agents, they inhibit the growth of cancer cells and colon carcinogenesis. The aim of the present study was to assess the cytotoxicity of curcumin and resveratrol as single drugs and in combination, on two colon cancer cell lines.

Materials and methods. Human colorectal carcinoma cell lines Caco-2 and DLD-1 were seeded in 96-well plates. After 24 h, single compounds (resveratrol and curcumin) were added to each well at various concentrations (5-150 μM) and incubated for 48 h. To assess the combined effect of curcumin and resveratrol, both cell lines were treated with 9 successive concentrations of the combination treatment, at a 1:2.5 ratio (curcumin:resveratrol). The concentrations and the ratio to be tested were selected based on the IC50 values obtained for each agent alone. Cell viability was determined by using the MTT assay. All experiments were performed in triplicate.

Results. The results showed that resveratrol and curcumin significantly inhibited cell viability of both DLD-1 and Caco-2 cells in a dose- and time-dependent manner. The combination treatment of curcumin and resveratrol caused a greater cytotoxic effect compared to single compound treated cells. The IC50s for the combination treatment were 71.8 μM (20.5 μM curcumin + 51.3 μM resveratrol) for DLD-1 cell line and 66.21 μM (18.9 μM curcumin + 47.3 μM resveratrol) for Caco-2 cell line. Our data indicated that the combination treatment of resveratrol with curcumin may exert either a synergistic or an additive effect.

Conclusions. Based on our findings, both resveratrol and curcumin are powerful bioactive dietary agents, still the combination approach of curcumin and resveratrol is more effective in inhibiting cell viability in colon cancer cells in vitro.

IMPORTANCE OF FOOD GROUPS RICH IN BIOACTIVE DIETARY COMPONENTS IN COLORECTAL CANCER PREVENTION

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Introduction. Colorectal cancer (CRC) has become a global health problem being the third most common type of cancer worldwide. Frequent consumption of red and processed meat especially high temperature cooked meat has been associated with colorectal carcinogenesis, while a healthy dietary pattern based on adequate intake of fruit, non-starchy vegetables and whole grains can protect from developing CRC. The proposed mechanism is mostly attributed to the bioactive food components such as: resveratrol, curcumin, quercitin, Omega-3 fatty acids etc. known for their protective properties in CRC. The aim of the present study was to to investigate the possible CRC lifestyle risk or protective factors (physical activity, smoking, dietary habits) on a Romanian sample.

Materials and methods. A case control study was conducted from May 2016 – October 2017. Patients (n=151) recently diagnosed with CRC and undergoing conventional treatment were recruited from MEDISPROF Oncology Hospital. Controls (n=151) were selected randomly from generally healthy adults. Dietary and lifestyle data was collected during a face to face interview conducted by a trained dietitian. To assess dietary habits, respondents were asked to report frequency of consumption of a given serving of each food item.

Results. CRC patients have lower intakes of beans, leafy vegetables, nuts and whole grains. Intake of 3-5 servings / week of unrefined oils including extra virgin olive oil is higher in controls. Also, participants in the control group report drinking more red wine and green tea than participants in CRC group.

Conclusions. This study highlights that consuming more foods and drinks containing bioactive dietary components such as red wine, extra virgin olive oil, green tea and leafy vegetables may prevent colorectal cancer development. Also, we confirmed that fiber rich foods such as whole grains and beans are important constituents of a protective diet against colorectal cancer.

COMPARATIVE EVALUATION OF HYPERSENSITIVITY REACTIONS TO PLATINUM DERIVATIVES USING NCI-CTCAE AND RING-MESSMER SCALES

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Introduction. Oncology therapy is complex and requires a multidisciplinary approach. One of the challenges is the appearance of the hypersensitivity reactions (HSR), which by their severity may influence the course of chemotherapy. The increasing occurrence of HSR to platinum derivatives due to their more frequent use is a major problem of therapeutic management. Therefore, the aim of this study was to identify and evaluate the HSR to platinum derivatives using NCI-CTCAE and Ring-Messmer scales.

Material and methods. The retrospective analysis was conducted at the Cluj-Napoca Oncology Institute "Prof. dr. Ion Chiricuta", and included the HSR to platinum derivatives therapy (cisplatin, carboplatin and oxaliplatin) detected throughout the year 2013. The severity of the allergic reactions was assessed using the NCI-CTCAE v4.0 (Common Terminology Criteria for Adverse Event version 4) and the Ring-Messmer classification.

Results. The clinical symptoms were mainly located at cutaneous level (74.5%), respiratory tract (64.41%), circulatory system (37.29%) and digestiv system (23.9%). A total of 59 cases of HSR were detected: 33 cases to carboplatin, 24 cases to oxaliplatin and two cases to cisplatin. According to NCI-CTCAE v4.0, the distribution of severity of HSR severity was: six patients grade I, 19 patients grade II, 33 patients grade III and one patient grade IV. According to Ring-Messmer classification, the distribution of HSR severity was: eight patients grade I, 18 patients grade II, 32 patients grade III and one patient grade IV. The patients were mainly females (81.35%) and had a mean age of 53.2 years old.

Conclusion. Classifying the HSR using two different systems allowed a more complex analysis. The identification and prevention of the HSR to platinum derivatives represents a direction for future research that could directly impact the health of oncologic patients.

SYNTHESIS OF SOME NOVEL 1,2,4-TRIAZOLE-3-MERCAPTO DERIVATIVES AS POTENTIAL ANTIFUNGAL AGENTS

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Introduction. In the context of alarming incidence of systemic candidemia, corroborated with increasing number of multidrug-resistant Candida strains, it is mandatory to identify innovative antifungals. Docking simulation is a widely used structure-based drug design method due to its ability to predict the affinity of the ligands towards the active site of the biological targets. It can be used for the development of novel lead-like antifungal agents which act as lanosterol-C14α-demethylase inhibitors, a key enzyme involved in fungal ergosterol biosynthesis. A particular interest in the field of antifungal drug design was assigned to 1,2,4-triazole scaffold, as it is present in the structure of many clinically approved antifungals. Anti-Candida activity has also been reported for mercapto-substituted 1,2,4-triazole derivatives. Moreover, S-linker was reported to improve drug-like parameters, as lipophilicity and water solubility.

Materials and methods. A new series of 1,2,4-triazole-3-mercapto derivatives were synthesized via intramolecular cyclization of the corresponding N-substituted-acylthiosemicarbazides, followed by the S-alkylation of the triazole-3-mercapto intermediates with varia α-halocarbonyl compounds. The structural assignments of the synthesized compounds were based on their spectral (IR, 1H-NMR, 13C-NMR, MS) and elemental analysis. The interactions of the compounds with the catalytic site of lanosterol-C14α-demethylase were explored by molecular docking studies.

Results. The results of the docking simulation showed that the synthesized compounds might act as inhibitors of fungal lanosterol-C14α-demethylase.

Conclusion. In silico studies confirmed the anti-Candida potential of the synthesized compounds, so they can be further considered for optimization and developed as lead compounds.

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SYNTHESIS AND ANTI-CANDIDA EVALUATION OF A NOVEL SERIES OF 1,4-PHENYLENE-BISTHIAZOLE DERIVATIVES

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Introduction. In the last decades, there has been a dramatic increase in the incidence of nosocomial bloodstream infections caused by resistant Candida spp. Conventional antifungal agents are frequently associated with a lack of efficacy against resistant fungal strains, as well as severe side effects and many drug-drug interactions. In this way, it is of urgent need to discover novel antifungal compounds, which could be active against different Candida strains.

Material and methods. The 1,4-phenylene-bisthiazole derivatives were obtained in a five-step synthesis, starting from thioacetamide. The progress of all reactions and the purity of the intermediate and final compounds were monitored by thin layer chromatography. IR, MS, 1H-NMR and 13C-NMR spectra were recorded in order to characterize the new compounds. Evaluation of the anti-Candida activity was carried out using the broth microdilution method, against four different Candida strains.

Results. Novel 1,4-phenylene-bisthiazole derivatives were synthesized in good yields and their structures were confirmed on the basis of their elemental analysis and spectral data. Results obtained from the in vitro anti-Candida screening showed that some of the tested compounds possessed minimum inhibitory concentration and minimum fungicidal concentration values similar to the ones of fluconazole.

Conclusion. In this study, new 1,4-phenylene-bisthiazole derivatives were successfully synthesized and evaluated in vitro for their anti-Candida activity. The obtained results revealed that the new compounds have promising anti-Candida activity, which encourages us for further in silico studies in order to evaluate the pharmacokinetic and pharmacotoxicological profile and to predict a possible mechanism of action of these compounds.

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SYNTHESIS OF SOME THIAZOLIDINE-2,4-DIONE DERIVATIVES WITH ANTI-CANDIDA POTENTIAL

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Introduction. Infections with resistant fungal or bacterial strains are nowadays a big challenge of treatment in all health care systems worldwide. Especially in the immune-compromised hosts, it represents one of the most life-threatening complications, giving a poor prognosis to the infected patients. For example, the commensal Candida sp. common in humans, became frequent dangerous pathogen. It is imperative that new substances with antifungal properties to be found.

Material and methods. Thiazolidine-2,4-dione derivatives were synthesized under microwave irradiation. First, Knoevenagel condensation in position 5 of the thiazolidine-2,4-dione ring was performed using various phenolic aldehydes. Nitrogen and phenolic oxigen atoms were substituted using halogenated derivates. The purity of the new synthesized thiazolidine-2,4-dione derivatives was confirmed by thin layer chromatography. The structure of the new compounds was confirmed by spectral analysis: infrared spectroscopy, mass spectrometry, 1H-NMR and by quantitative elemental analysis. Compounds were screened in vitro for their ability to inhibit the growth of some standardized fungal strains. In silico evaluations were performed in order to find potential interactions of the novel molecules to lanosterol demethylase using AutoDock 4.2.

Results. The results of the in vitro anti-Candida screening showed that some of the tested compounds had minimum inhibitory concentrations similar of fluconazole.

Conclusion. Compounds were screened in vitro for their ability to inhibit the growth of some standardized Candida strains. In silico evaluations were performed in order to find potential interactions of novel molecules to fungal lanosterol demethylase. Our screening showed that some of the new compounds have promising antifungal activity.

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INVESTIGATION OF THE ANTIPROLIFERATIVE AND ANTIHYPERGLYCEMIC ACTIVITIES OF NEW THIAZOLIDINEDIONE DERIVATIVES

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Introduction. Cancer is a global threat, millions of persons losing their lives because of this disease [1]. For its limitation, an early diagnose, a careful monitoring and the finding of new efficient drugs, with limited secondary effects, are urgently needed. Diabetes is an important issue for the health system, due to its severe life-threatening complications [2]. Thiazole and its derivatives (thiazolidine, thiazolidinedione) are cited in literature for their antiproliferative [3], antidiabetic [4] and antioxidant activities. Thiazolidinediones are drugs already used in the treatment of type 2 diabetes [5]. This research project had as goals the investigation of the antiproliferative and antihyperglycemic effects of a series of newly synthesized thiazolidinediones.

Material and methods. The antiproliferative activity of 16 thiazolidinedione derivatives, previously synthesized [6], was evaluated by the MTT test, calculating IC50 on 2 tumor cell lines (B16 and CT26). For the antihyperglycemiant potential, an experimental model of diabetes was induced by the intraperitoneal injection of streptozotocin, in rats. After hyperglycemia was produced, animals received, suspensions of 6 thiazolidinedione derivatives, previously synthesized [7-9]. Their effects were compared with the reference antidiabetic pioglitazone.

Results. The compounds demonstrated promising inhibitory effects against the studied tumor cell lines. Thiazolidinediones 3, 7 and 9 exhibited best antiproliferative activity against B16 cells and compounds 1, 2 and 6, against CT26. Reduction of hyperglycemia was superior to pioglitazone, the antidiabetic drug used as reference.

Conclusion. The results obtained determine us to continue the synthesis of new series of thiazolidinedione derivatives with biological activity.

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THE RESULTS OF THE IMPLEMENTATION OF AN ANTIMICROBIAL STEWARDSHIP PROGRAM IN A PRIVATE HOSPITAL

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Introduction. Antimicrobial resistance represents a global health issue, caused mainly by the inappropriate use of antibiotics. Romania is one of the European countries with the highest antimicrobial resistance rates. This shows that the implementation of an antimicrobial stewardship program (ASP) is necessary. The main objectives are the reduction of inappropriate use of antimicrobials, the decrease of antimicrobial resistance and the increase of therapy effectiveness and patient safety.

Materials and methods. We conducted a quasi-experimental study in a 200 beds rehabilitation hospital. The study consists in a reference period and an intervention period aiming to compare antibiotic consumption and to assess the impact of the implementation of ASP measures.

An interdisciplinary team consisting of clinical pharmacists, epidemiologist, and an infectious disease specialist was created. A retrospective analysis of antibiotic consumption per antimicrobial class for each ward was conducted. Antibiotic consumption was reported as DDD/ 100 patient days (PD). After the analysis of the consumption data a list of restricted antibiotics was developed and implemented with the purpose of controlling and reducing inappropriate antibiotic consumption.

Results. For the reference period a high consumption was registered for fluoroquinolones (133.4 DDD/100 PD), penicilins (97.7 DDD/100 PD), third generation cephalosporins (50.1 DDD/100 PD) and aminoglycosides (35 DDD/100 PD). The total consumption for all classes of antimicrobials was 359.9 DDD/ 100 PD. The highest consumption of antimicrobials was recorded for the neurology and palliative care ward. The data for the intervention period showed a change of prescription patterns regarding the classes of antimicrobials used and a decreasing trend in overall consumption. The consumption decreased to 87.28 DDD/100 PD for fluorochinolones, to 33.1 DDD/PD for third generation cephalosporins. The total consumption decreased to 262.63 DDD/100 PD. Neurology and palliative care remain the wards with the highest reported consumption.

Conclusion. First ASP measures have been successfully implemented. Antibiotic consumption decreased, but continuous monitoring of the prescription pattern and the implementation of other educational and restrictive ASP measures are necessary in order to maintain a long term effect.

OBTAINING STANDARDIZED EXTRACTS WITH ANTITUMOR POTENTIAL FROM AJUGA GENEVENSIS AERIAL PARTS

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Introduction. The anticancer activity of natural extracts is attributed to their synergistically acting complex mixture of phytochemicals. Recent in vitro experimental results indicate that phenolic compounds, mainly antioxidants, exhibit anti-proliferative properties in cancer cells. Ajuga genevensis is an herbaceous flowering species used in Romanian traditional medicine for its anti-inflammatory, wound healing and hepatoprotective effects. The aim of this study was to obtain standardized extracts from A. genevensis (Ag) aerial parts and to evaluate the cytotoxic potential of the extract, by testing its effect on the proliferation of B16.F10 murine melanoma cells, as well as of C26 murine colon carcinoma cells.

Material and methods. The hydroalcoholic extract obtained by maceration was standardized in active compounds (polyphenols, iridoids). To determine the potential cytotoxic action on both cell types, Ag extract dilutions ranging from 225 µg/ mL to 650 µg/ mL were tested. The proliferative activity of the cancer cells after treatment was tested using ELISA BrdU-colorimetric immunoassay. Hydroalcoholic extract was spray dried and a dry Ag extract was prepared.

Results. The hydroalcoholic extract contains bioactive compounds with strong anti-proliferative effects on C26 murine colon carcinoma cell line and moderate anti-proliferative effects on B16.F10 murine melanoma cell line. The dry extract obtained was characterized in terms of its physicochemical parameters. The results showed that the adsorbtion process progressed smoothly and that an adequate quantity of active principles could be incorporated in the final product.

Conclusion. The dried extract from Ag aerial parts could be a promising intermediate phytopharmaceutical product with antitumor potential.

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NSAIDs DISPENSED FROM A COMMUNITY PHARMACY

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Introduction. Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used medicines, currently available to patients for the treatment of a wide range of conditions mainly due to their anti-inflammatory, analgesic and antipyretic properties. Community pharmacy is often the primary qualified source of healthcare services for patients [1]. In this context, the main objective of the study was to identify and evaluate NSAIDs dispensed from a community pharmacy and to highlight the dispensing modalities.

Materials and methods. The prospective study was conducted between March 1st and June 1st, 2017, and included patients who approached a community pharmacy in Cluj-Napoca to request NSAIDs without or on medical prescription.

Results. A total of 216 patients requiring NSAIDs without prescription, 61% women and 39% men, mean age 42.7 years (range 2-85 years), were included. The most commonly dispensed NSAIDs were ibuprofen (42.5%), diclofenac (19.9%), naproxen (11.5%) and ketoprofen (8.3%), mainly for relieving back pain (15.2% %), cold and flu symptoms (14.8%), headache and migraine (13.4%) and dysmenorrhea (10.6%). At the same time, 109 medical prescriptions for patients (46% women, 54% men) with an average age of 33.6 years (1-92 years) were included in the study. The most commonly prescribed NSAIDs were ibuprofen (44.0%), piroxicam (24.7%), ketoprofen (8.0%) and celecoxib (7.3%) for the treatment of arthritis (32.1%), pharyngitis and rhino-pharyngitis (23.8%), acute infections (8.2%) and otitis media (5.5%).

Conclusion. NSAIDs were dispensed from the community pharmacy, mainly without medical prescription. The most commonly dispensed NSAID was ibuprofen. Some of the dispensed NSAIDs have an increased risk of gastrointestinal and cardiac side effects, therefore the pharmacist's role in adequately counseling patients is essential to ensure safe and effective treatment.

ELEMENTS OF GREEN PHARMACY IN THE ROMANIAN LEGISLATION

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Introduction. Green pharmacy refers to managing all pharmaceutical activities in order to reduce their impact on the environmental quality. Among different environmental contaminants, researchers have found active pharmaceutical ingredients resulted from medicines use. Specific policies should be focused on creating appropriate regulations and founding ways to minimize the presence of medicines in the environment, such as preventing contamination, rational use and proper disposal. The aim of this paper is to identify and evaluate the elements of green pharmacy in the Romanian legislation.

Material and methods. The Romanian environmental and pharmaceutical legislation was investigated using methods of interpretation.

Results. In the environmental legislation, the elements of green pharmacy are: the need for an environmental impact assessment for any project involving production of basic pharmaceutical products, the obligation of pharmaceutical manufacturers to monitor the environmental quality status and to apply measures to avoid/reduce/offset major adverse effects, the obligation of any pharmaceutical unit to implement a waste management plan and to conclude contracts for the disposal of waste. In the pharmaceutical legislation, the elements of green pharmacy are: the need for an evaluation of the potential environmental risks posed by a medicine, an indication of those risks and of reasons for any precautionary or safety measures to be taken for the disposal of waste products in the application for a marketing authorization, the obligation of pharmacies to collect the expired or unused medicines brought by patients and to apply a standard operating procedure for the disposal of pharmaceutical waste.

Conclusion. The main elements of green pharmacy in the Romanian legislation are the provisions for preventing environmental contamination with medicines and for managing pharmaceutical waste disposal.

LIPOSOMAL CO-ENCAPSULATION OF DOX AND CURC: A NANOTECHNOLOGICAL APPROACH TO INCREASE ANTITUMOR ACTIVITY AGAINST COLON CANCER

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Introduction. A promising strategy to increase the therapeutic efficiency in colon cancer is combination anticancer treatment, which offers the possibility of synergism. Nanotechnological approaches, i.e. the use of drug delivery systems, can increase the accumulation of anticancer agent in tumor cells, thus increasing the antitumor activity. This study aimed at developing doxorubicin (DOX) and curcumin (CURC) co-loaded PEGylated liposomes (LCL-DOX-CURC) and assessing their effect on tumor growth in vivo.

Material and methods. Liposomes were prepared by the film hydration method and were characterized through size, polydispersity, Zeta potential, morpholology, DOX and CURC entrapment efficiencies and release profile. The effects of different experimental treatments (free DOX or LCL-DOX 2.5mg/kg; free CURC or LCL-CURC 5mg/kg; free co-administered, liposomal co-administered and liposomal co-encapsulated DOX and CURC at 2.5mg/kg and 5mg/kg, respectively) on tumor growth, were evaluated in a C26 murine colon carcinoma model in BALB/c mice, by measuring the tumor volume at day 11 and AUTC until day 11.

Results. Liposomes were nanosized, showed good stability and a prolonged release profile of DOX and CURC over 72h. Both LCL-DOX and LCL-CURC were very effective in suppressing tumor growth compared to control (PBS), while empty LCL had no such effect on this parameter. Notably, the liposomal co-encapsulation strongly augmented both DOX and CURC antitumor activity, as shown by the reduction with more than 50% of tumor volumes and AUTC, compared to control.

Conclusion. Based on the in vivo findings, this liposomal formulation co-delivering DOX and CURC, which is currently under mechanistic evaluation regarding its molecular tumor targets, exhibits an enhanced antitumor activity, which can be further exploited for the treatment of colon cancer.

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DEVELOPMENT OF AN IN-LINE NIR MONITORING METHOD FOR THE FLUIDISED BED GRANULATION PROCESS OF TWO APIs

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Introduction. The modern drug development and manufacturing is expected to be carried out following a quality by design (QbD) approach and applying in-line monitoring methods as process analytical technology (PAT). The aim of the present study was to apply an experimental design in order to optimise a fluid bed granulation process of 2 APIs simultaneously and to develop an in-line near infrared (NIR) method which would allow the water content monitoring along the process.

Materials and methods. The granulation runs were performed in a GEA Strea 1 fluid bed granulator and the NIR spectral data were recorded continuously during all the performed runs, using a Viavi microNIR PAT spectrometer.

Results. The developed D-optimal experimental design registered a G-efficiency of over 70 and a condition number of under 7.1, values which describe a good optimization design. The design contained 2 critical process parameters as quantitative factors and different sorts of APIs and microcrystalline cellulose as qualitative factors.

During the process, the registered relative humidity of the granules was between 1 and 19%. Those values were then used to calibrate the preprocessed NIR spectral data, developing an OPLS model with R2X greater then 0.9. The model allowed the in-line process control by predicting the water content throughout the process and the establishment of the granulation end point.

Moreover, during the in-line process monitoring, the changes of critical process parameters were well underlined, allowing the identification of the granulation steps, facilitating the process control and ensuring a high reliability of the process.

Conclusions. The described, systematic approach provided a thorough understanding of the fluid bed granulation and its variables, allowing the development of a robust, fully controlled process.

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MULTIVARIATE METHODS APPLIED FOR THE DEVELOPMENT (DOE) AND REAL TIME MONITORING (PAT) OF MANNITOL BASED GRANULATES LOADED WITH LORATADINE

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Introduction. The development of a pharmaceutical product relies on the identification and control of formulation and process variables that influence the product's critical quality attributes. This objective can be fulfilled by applying Design of Experiments and by implementing process monitoring instruments for real time quality testing as recommended by guidelines published for the industry.

Materials and methods. The solution layering process was performed in a Strea 1 fluid bed granulator (GEA, Switzerland). NIR spectral data were recorded continuously during all the performed runs, using a microNIR PAT spectrometer (Viavi, USA).

Results. To identify most relevant formulation and process variables five factors (atomizing pressure, pulverization rate, %Water, %PVP, raw material particle size distribution) were screened through a Fractional Factorial Design with resolution V. Mean particle size was influenced by atomizing pressure, pulverization rate and water content of the pulverized solution. Differences in granule flowing properties could be attributed mainly to atomizing pressure, water content and raw material particle size distribution. OPLS models with good predictive properties (Q2>0.7) were built from the spectra of pulverization phase for the real time monitoring of loratadine and PVP addition. Granule properties (% of sieve fraction size, PVP% and granule flowing properties) were predicted using models built on spectral data from the drying phase of the process.

Conclusions. This work demonstrates the advantages of applying Design of Experiments with Process Analytical Technology principles for improved process understanding and product quality control.

FORMULATION DEVELOPMENT OF AN OIL-IN-WATER HAND CREAM

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Introduction. The aim of the study was to formulate and optimize a oil-in water hand cream recommended for dry skin. The active ingredients (alantoin, sodium PCA, *Croton lechleri* extract) and the components of the cream base were chosen for beneficial properties to restore the hydrolipidic layer and to improve the hydration level of *stratum corneum*.

Material and methods. For the cream formulation, a factorial experimental design with three variables and two levels was used and the experimental trials were performed for all eleven combinations from the experimental design matrix. The variables selected were: the emulsifier type with the variables E1 (glucose laurate- Alfa Emulsifier® 7% and sucrose stearate- Hidractiv® 2%), E2 (cetearyl glucoside- Fluida® 1%), the percentage of lipophilic phase (10%-30%) and the percentage of glycerin (5-15%). The outputs analyzed in the experimental plan were: firmness, consistency, adhesive force, adhesiveness, stringiness work and spreadability, which were obtained using Brookfield CT3 Texture Analyzer, and viscosity, assessed with a rotational rheometer Brookfield DV-III Ultra.

Experimental design, coefficient calculation, statistic parameters calculation and evaluation of quality of fit were performed with Modde Pro software (Umetrics); results were evaluated by means of statistical analysis using ANOVA test.

Results. According to the experimental data, the high percentage of lipophilic phase influenced the physical properties of the creams, increasing the firmness, consistency, adhesiveness, stringiness and viscosity values and decreasing the spreadability values. The spreadability was also influenced by the emulsifier type (E1 enhanced spredability properties, whereas E2 led to less spreadable formulations). In order to evaluate the validity of the experimental design, the optimal parameters were selected and the optimal formulation was prepared and analyzed; a good correlation between the model predicted and the experimental response was obtained.

Conclusion. Therefore, the use of experimental design allowed setting the best ranges for the formulation factors that influence the preparation of the cosmetic creams in order to obtain a oil-in-water hand cream with optimal properties.

INFLUENCE OF FLUVOXAMINE ON CARVEDILOL METABOLISM AND PLASMA DISPOSITION – IN VITRO AND IN VIVO EXPERIMENTS

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Introduction. Carvedilol is one of the most used cardiovascular drugs, highly metabolized by CYP450 2D6, 1A2, 2C9. Fluvoxamine, an antidepressant agent, is a moderate/potent inhibitor of these enzymes. There is the risk of drug-drug interaction when these two drugs are concomitantly administered. The aim of this study was to investigate the drug-drug interactions between carvedilol and fluvoxamine in vitro and in rats.

Material and methods. There were two periods: reference and test. In the first period each rat received an oral dose of 3.57 mg/kg body weight [b.w.] carvedilol). In the test period, carvedilol was administered after a pre-treatment with multiple oral doses of fluvoxamine (14.28 mg/kg b.w.). HPLC-MS was the device used to determine the plasma concentration of carvedilol. The PK parameters were calculated by noncompartmental analysis. Rat liver microsomal incubation systems were used to investigate the effect of fluvoxamine on the metabolic rate of carvedilol.

Results. Fluvoxamine co-administered with carvedilol can change the PK parameters (increase AUC, t1/2, decrease the Cl). In vitro experiment showed that fluvoxamine decrease the metabolic rate of carvedilol.

The present study demonstrated the pharmacokinetic drug-drug interaction between carvedilol and fluvoxamine in vitro and in vivo.

Conclusion. Fluvoxamine significantly influenced the pharmacokinetic of carvedilol, due to its capacity of CYP2D6 and CYP1A2 inhibition. As a result of this interaction the exposure to carvedilol was significantly increased. This is the reason why co-administration of carvedilol and fluvoxamine needs precaution.

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THE EFFECT OF MULTIPLE-DOSE PAROXETINE ON THE PHARMACOKINETIC PROFILE OF CARVEDILOL IN RATS

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Introduction. The aim of the present study was to evaluate the effect of multiple-dose paroxetine upon the pharmacokinetic profile of carvedilol in rats.

Material and methods. Carvedilol was orally administrated in rats (3.57 mg/kg body mass (b.m.)) in the absence of paroxetine or after a pre-treatment with multiple oral doses of paroxetine (7.14 mg/kg b.m.). The plasma concentrations of carvedilol were estimated by high performance liquid chromatography-tandem mass spectrometry.

Results. After carvediol co-administration with paroxetine, an approximately 4.5-fold increase in the exposure of carvedilol was observed, considering the significantly elevated value of AUC0-∞. Furthermore, an increase by 72% of peak plasma concentration was found, as well as an augmentation by 91% of the half life time of carvedilol was observed.

Conclusion. Paroxetine co-administration led to a significant alteration of carvedilol's pharmacokinetic profile in rats, these effects could be explained by the existence of a drug-drug interaction mediated by CYP2D6 inhibition.

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SIMULTANEOUS DETERMINATION OF METFORMIN AND VILDAGLIPTINE IN PLASMA THROUGH HIGH PERFORMANCE LIQUID CHROMATOGRAPHY WITH MASS SPECTROMETER TANDEM. APPLICATION TO A PHARMACOKINETIC STUDY

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Introduction. Vildagliptin and metformin are two oral hipoglycemic agents with different mechanism of action. Simultaneous determination from bioanalytical point of view is a challenge that helps establish the therapeutic equivalence between different pharmaceutical products containing both agents. Having more products on the market ensures the treatment for a bigger number of patients with reduced costs.

Materials and methods. An HPLC chromatographic method with mass spectrometer tandem and electrospray ionization (LC-(ESI)/MS/MS) was developed and validated for simultaneous determination of metformin and vildagliptine in human plasma. After solid phase extraction of 0.100 ml plasma, the analytes were separated on Luna HILIC column, 5 µm, 4.6 x 150 mm, using a 20mM formate buffer: acetonitrile: formic acid mobile phase (40:60:0.005 v/v/v) with an isocratic debit of 1.2 mL/min. Retention time are 2.5, 2.5, 2.0 și 2.0 for Metformin, Metformin D6, respectively for Vildagliptine and Vildagliptine D7. Detection of compounds and internal standards was mass spectrometric with electrospray ionization (ESI), positive ion mode. The linearity of the method was validated using a range from 6.01 lto 6000.92 ng/mL and 15.27 la 2503.22 ng/mL for Metformin and for Vildagliptine respectively. Precision between batches for three analytical batches is from 0.49 % to 6.07 % for Metformin, and from 0.72 % to 7.06 % for Vildagliptine. This method does not present any matrix effect.

Conclusion. This LC-MS/MS validated method was applied successfully in order to establish the bioequivalence two formulations after a fixed oral dose of 50 mg Vildagliptine and 850 mg Metformin hydrochloride to 33 healthy volunteers.

THE PHARMACOKINETICS IN FED CONDITION OF A NEW DELAYED RELEASE FORMULATION WITH MESALAMINE

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Introduction. Mesalamine is an anti-inflammatory drug used to treat inflammatory bowel disease, such as ulcerative colitis and mild-to-moderate Crohn's disease. It has been developed a new formulation with mesalamine and assessed its bioavailability in comparison with an authorized reference product under fed condition.

Material and methods. An open, balanced, randomized, crossover fully replicate clinical study with 2 treatments and 4 periods were conducted on 24 healthy volunteers under fed conditions. 22 subjects completed the study. Washout period was 7 days. 48 blood samples for fed study were taken during each period. For determination of mesalamine in plasma it was used a validated HPLC method coupled with mass spectrometry. Non-compartmental pharmacokinetic analysis was performed using Pheonix® WinNonlin® version 6.3. Calculated pharmacokinetic parameters were AUC_{0-t}, AUC_{8-48}, C_{max}, T_{max}.

Statistical analysis was performed using SAS version 9.3.1 Type III ANOVA for calculating the least square means.

Results. It was evaluated the within reference intra-subject coefficient of variation, 90% confidence interval for the ratio of test/reference product averages and it's 95% Upper Confidence bound for the log transformed pharmacokinetic parameters: AUC_{0-t}, AUC_{8-48}, C_{max}. For C_{max} intra-subject coefficient of variation was 95.97 %, T/R ratio was 78.75%, with negative 95% Upper Confidence Bound of -0.12%. For AUC0-t intra-subject coefficient of variation was 52.52 %, T/R ratio was 72.96% with positive 95 % Upper Confidence Bound of 0.10%. For AUC_{8-48} intra-subject coefficient of variation was 53.53 %, T/R ratio was 80.18% with negative 95% Upper Confidence Bound of 0.01%.

Conclusion. Overall the results are positive for the fed study and it is suggested to increase the rate and the extend of absorption to increase the probability of meeting bioequivalence in a future pivot study.

BIOEQUIVALENCE OF TWO FORMULATIONS OF GLICLAZIDE IN A RANDOMIZED CROSSOVER STUDY IN HEALTHY CAUCASIAN SUBJECTS UNDER FASTING CONDITION

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Introduction. Sulfonylureas are the most frequently used oral hypoglycaemic agents. Trials of gliclazide modified release in varied populations have yielded very acceptable clinical results that support its first-line use in type 2 diabetes, including obese, elderly and mild-to-moderate renal insufficient patients. This study was aimed to investigate the bioequivalence of two formulations of gliclazide modified release tablets 60 mg in 48 healthy Caucasian volunteers under fasting condition.

Material and methods. A test product, Gliclazide MR (Ranbaxy Laboratories Limited, now Sun Pharmaceutical Industries, India), was compared with a reference product, Diamicron MR (Servier, France). The study was performed under a single-dose, two-treatment, two-period, and two-sequence crossover design in fasted condition with a washout period of 21 days. Blood samples were collected for 96 h after drug administration. Drug plasma concentrations were determined by a LC-MS/MS method. Analysis of pharmacokinetic characteristics was based on a non-compartmental model. The logarithmically transformed data of C_{max} and AUCs were analyzed for 90% confidence intervals using ANOVA.

Results. The mean values for the pharmacokinetic parameters were similar for the test and reference product. The ratios of LSM (with 90% confidence intervals) for the pharmacokinetic parameters C_{max}, AUC_{0-t} and $AUC_{0-\infty}$ for Gliclazide were 104.58% (96.42% – 113.42%), 99.55% (96.21% – 103.01%), respectively 99.43% (96.16% - 102.81%).

Conclusion. The investigated products are bioequivalent under fasted condition. The products can be interchangeable.

ANTIOXIDANT AND CYTOTOXIC ACTIVITY OF WALNUT (JUGLANS REGIA L.) SEPTUM EXTRACTS

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Introduction. Many studies show the benefits for human health of a diet rich in tree nuts and the positive impact on many diseases. Parts of the benefits extend to their by-products, such as walnut septum. Extracts from septum presented no in vivo toxicity. To the best of our knowledge, a characterization of chemical profile and a study of the effect of septum extracts on cancer cell lines have not been done. Our study assessed the antioxidant activity of several walnut septum extracts and their cytotoxicity on tumor cells.

Methods. The extracts obtained, based on experimental plans, were assayed for total phenolic, flavonoid and condensed tannins contents, and the total antioxidant activity analyzed. The extracts having the highest values were tested on three human cancer cell lines, A549 (lung carcinoma), HepG2 (hepatocellular carcinoma) and MCF-7 (breast adenocarcinoma), at increasing concentrations, at 24h/48h, to assess a possible cytotoxic activity. Cell viability was evaluated by measuring the capacity of the cells to reduce resazurin, a non-fluorescent dye, to resorufin, a fluorescent indicator.

Results. Septum extracts showed high content of phytochemicals, which positively related to the antioxidant activity. The extract with the highest values for bioactive compounds and antioxidant activity revealed significant cytotoxicity on all three cancer cell lines. On A549, cell viability decreased by 80% and 100%, after 24h and 48h exposure, respectively. The same cytotoxic dose response curve was observed for HepG2 at both time points. On MCF-7, a hormetic response was observed, significant increase in cellular metabolic activity at intermediate concentration levels and cytotoxic activity at the highest tested dose.

Conclusion. Our study proves that walnut septum can be a source of bioactive compounds for biopharma or food industry and warrant the continuation of the current research in further evaluating the anticancerous potential and the underlying mechanisms.

FLUOXETINE AFFECTS MIDBRAIN NEURONAL SPECIFICATION AND NEUROGENESIS IN VITRO

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Introduction. Recent meta-analyses suggest an association between prenatal exposure to the antidepressant fluoxetine (FLX) and an increased risk of autism in children. This study aimed to investigate if FLX affects processes involved in dopaminergic neuronal differentiation as a possible mechanism underlying this link, possibly via interference with the estrogen system.

Material and methods. Mouse neuronal precursors (wild-type (WT) and estrogen receptor β knock-out (BERKO)) were differentiated to midbrain dopaminergic precursor cells (mDPCs) and concomitantly exposed to therapeutically relevant FLX concentrations. Dopaminergic progenitors were then evaluated for expression of differentiation and stemness markers, as well as of nuclear estrogen receptors (ERs), using qPCR.

Results. In WT cells, FLX treatment led to a significant increase in early regional specification markers Orthodenticle homeobox 2 (Otx2) and Homeobox engrailed-1 and 2 (En1 and En2). On the other hand, two transcription factors essential for mDA neurogenesis, LIM Homeobox transcription factor 1 alpha (Lmx1a) and Paired-like homeodomain transcription factor 3 (Pitx3) were significantly down-regulated by FLX treatment. Finally, the stemness marker Nestin (Nes) was significantly increased and the neuronal differentiation marker β3-tubulin (Tubb3) significantly decreased in WT mDPCs.

Additionally, the expression of both ERα and ERβ was significantly down-regulated in WT cells after FLX treatment, suggesting an involvement of these receptors in the observed effects. Indeed, in BERKO cells, FLX had no or even opposite effects on the genes involved in mDPC specification, on Nes and on Tubb3.

Conclusion. These findings suggest that FLX increases induction of dopaminergic precursors, yet decreases the maturation of dopaminergic neurons. The effects seem to be partly ER-dependent as no or even opposite effects were observed in ERβ-deficient cells.

DENTAL MEDICINE

THE EFFECT OF LIVER FIBROSIS ON LIGATURE-INDUCED PERIODONTITIS IN WISTAR RATS - A PROOF OF CONCEPT STUDY

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Introduction. Experimental rat models are important tools to investigate mechanism of periodontal and liver pathogenesis. The ligature-induced periodontitis has been used to assess the response on tooth-supporting tissues under controlled conditions. Surgical ligation of the common bile duct has become a wide used technique to establish liver fibrosis with low variations and mortality.

The aim of this study was to evaluate the changes induced by liver fibrosis on the periodontium.

Material and methods. Female adult Wistar rats, were divided into four groups: C (control), EP (experimental periodontitis), BDL (bile duct ligation), EP+BDL. Liver fibrosis was obtained through the bile duct ligation procedure and experimental periodontitis through ligature around incisors.

Clinical changes of periodontal tissues such as gingival index, bleeding on probe, tooth mobility and swelling were observed daily. To evaluate different stages of liver fibrosis was used a high-frequency ultrasound examination.

Results. In groups C and BDL, gingival tissue had a normal aspect and smooth texture. Due to cholestatic injury, cyanotic aspect of periodontal tissue, necrotic ulcerations, swelling, malloclusion and bleeding on probe were greater in EP+BDL compared with EP.

In BDL and EP+BDL, the duct obstruction was associated with portal hypertension, hepato-splenomegaly and development of ascites.

Conclusions. Bile duct ligation and ligature-induced periodontitis techniques are easy to perform with a good survival rate. Further studies should be made to determine if liver fibrosis might be associated with periodontal disease.

A CASE REPORT OF PEDIATRIC SLEEP APNEA SYNDROME IN AN 8-YEARS-OLD PATIENT: EFFECTS OF AN ANTERIOR MANDIBULAR POSITIONING DEVICE AND RAPID PALATAL EXPANSION

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Introduction. Obstructive sleep apnea syndrome (OSAS) in children is characterized by recurrent events of partial or complete upper airway obstruction during sleep, resulting in disruption of normal gas exchange (intermittent hypoxia and hypercapnia) and sleep fragmentation.

In patients having OSAS associated with craniofacial anomalies, functional orthopedics are used to change the mandible posture forwards, to enlarge the upper airway and to increase the upper airspace, improving the respiratory function.

Material and methods. This case report describes the changes in dentoalveolar, maxillofacial and pharyngeal structures, after mandibular advancement-device treatment in a young female patient suffering from severe obstructive sleep apnea.

We present the case report of an eight years old girl, who has been diagnosed in 2015 with severe obstructive sleep apnea syndrome (AHI of 45.7 events/ hour). The patient underwent a tonsillectomy by an ENT surgery team and she had an indication for continuous positive airway pressure (CPAP) therapy. A functional appliance (mandible advancement) was indicated in this first treatment phase, as the child was in the late mixed dentition.

Two cephalometric lateral and anteroposterior radiographs were also performed before and after treatment.

Results. After tonsillectomy and 6 months later the apnea hypopnea index AHI had decrease at 13.4 events/hour and after wearing the mandibular advancement device for 12 months AHI decreased significantly from 13.4 to 7.4 events per hour of sleep. The mandibular position in relation to the skull base, the angle SNB, was increased on average of 3º, with an With appraisal of jaw disharmony from 14.65 mm to 8.82 mm and a restraining effect for the maxilla from 81° to 77º.

Conclusion. The management of OSAS in pediatric patients, requires a collaboration between a pediatrician, a pneumologist, a specialist in sleep disorders, an ENT physician, and an orthodontist, for an accurate diagnosis and a comprehensive treatment plan.

IN VITRO TESTING OF MEDICAL IMPLANTS MANUFACTURED BY SELECTIVE LASER MELTING AND NANO-STRUCTURES

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Introduction. In today's context of additive manufacturing techniques development, the present study had the objectives of exploring in vitro the biocompatibility of the selective laser melting (SLM) designed titanium implants, the influence of the nano-hydroxyapatite conditioning, and the identification of the mesenchymal stem cells line (MSC) collected from the oral cavity with the most promising proliferation and osteoblast differentiation capacity.

Material and methods. Eight titanium implants with a porosity of 600 μm were manufactured using a bioprinter. Half of them were conditioned with hydroxyapatite. Four adult MSC lines collected from the apical papilla, the dental pulp, the inter-radicular bone, and the tuberosity bone were isolated, characterized and cultured on the implants. Their evaluation was conducted over a period of 21 days using optical and fluorescent microscopy. Dye and fluorescent reagents were used in order to identify the proliferation (PKH26), viability (Alamar Blue), and osteoblast differentiation (Alizarin Red) of the MSC.

Results. The titanium scaffolds were found to be biocompatible. The inter-radicular bone stem cells presented a more intense proliferation than the other MSC lines, with a nodular architecture; as well as a superior osteoblast differentiation. No significant difference was identified between the results obtained by the cultivation of the MSC on the scaffolds conditioned with hydroxyapatite, in comparison with the non-treated ones, though the cell number of the treated implants was higher.

Conclusion. Inter-radicular bone MSC have the biggest capacity of proliferation and osteoblast differentiation on the SLM manufactured titanium implants. The in vitro biocompatibility of this technique makes it promising for further clinical applications.

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PRESSED CERAMIC VERSUS METAL-CERAMIC FULL CROWNS - A SPECTROPHOTOMETRIC COLOR MATCHING STUDY

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Objectives. To verify the color match of metal-ceramic and lithium disilicate pressed ceramic crowns, using spectrophotometric color measurement.

Material and methods. 147 teeth, in 59 consecutive patients, were restored either with metal ceramic (MC, n=119) or pressed-ceramic (PC, n=28) full crowns. The restorations had similar design metal or pressed ceramic core and layered glass ceramic. The shade of a reference natural tooth was recorded instrumentally, using a dental spectrophotometer (Vita Easyshade Advance 4.0) in "single tooth measurement", which provided the base color in VITA Classical (VC) and 3D Master (3D) codifications. For verifying the outcome of the restoration "verify restoration" mode was used, and color difference (ΔE*) values were recorded for both systems. Symbols which express the quality of color matching were also recorded (***=good, **=fair, *=poor) as well as differences in value (ΔL), chroma (ΔC) and hue (Δh). Data were analyzed for comparison with visual thresholds (perceptibility and acceptability) in dentistry (PT=1.2 and AT=2.7).

Results. Recorded color difference was significantly higher than PT and AT, for both types of restorations, regardless of the coding system ($p<0.05$). For MC crowns in 2.52% (VC) and 4.20% (3D), ΔE* was smaller than PT and in 78.15% (VC) and 76.47% (3D) was higher than AT. For PC crowns in 3.57% (VC) and 0% (3D), ΔE* was smaller than PT and in 71.42% (VC) and 67.85% (3D) of cases was higher than AT.

Conclusion. Within the limitations of the study, a better color match was achieved in the case of pressed ceramic crowns. In most of the situations the color difference between the restoration and the reference tooth exceeded the PT, but the matching was recorded as "fair" by the spectrophotometer. VitaEasyshade Advance 4.0 can record useful information regarding the nature and magnitude of the conflicting color parameters.

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LiSi - LITHIUM DISILICATE: THE MATERIAL THAT BRINGS RESISTANCE TO AESTHETIC RECONSTRUCTIONS

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Introduction. Everyday practice in dentistry has undergone a major change in the last 10 years by digitizing the services and production of dental prostheses in a struggle with resistance to the analog system.

Materials and methods. The present paper uses revolutionary material, lithium disilicate, the two being at the limit of professional challenge. The lithium disilicate is a glassy material in the form of ingots that are pressed under vacuum at high temperature by flapping.

Discussions. The digitization of dental laboratories and the emergence of specialized milling centers lead the production of prosthetic structures to standardization, leaving aside the individual factor of an oral rehabilitation in favor of accurate precision and quotas.

Results. The analog-hand made system proposes awareness and cognitive approach to the planning and execution of an individual and particular prosthetic piece and structure for each case.

Conclusions. The analog-hand made system is a system of choice in the production of dental art. The digital system is an integrated tool for performing high quality prosthetic works, being in competition with the analog system.

THE RELATIONSHIP BETWEEN THE STRUCTURAL AND FUNCTIONAL CHANGES OF TEMPOROMANDIBULAR JOINT (TMJ) AND THE MANDIBULAR KINEMATIC

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Introduction. The changes that may occur in dental arches, disturbing the occlusal contacts may cause in time remodeling in TMJ structures. The aim of the study was to evaluate different situations that characterize the connections between statical and dynamical occlusion and the pathology of the TMJ, muscles or parafunctions of dentomaxilary system (DMS).

The aim of this study was to correlate the possible connections between the statical and dynamical occlusion and the pathology of the TMJ, masticatory muscles and parafunctions.

Material and method. 83 subjects, 38.6% males and 61.4% females were included in the study. Initially we noted the presence of parafunction of DMS. We correlated the anamnestic data with the clinical results obtained after the examination. The clinical examinations addressed the TMJ, the path and the amplitude of the maximal opening of the mouth, the jaw muscles and static and dynamic occlusion. The data was analized using MedCalc Software version 17.4 program, with statistical significance at $p<0.05$.

Results. The results showed an increased frequency of interferences in the protrusive movement (77%) especially in females. 71.1% of laterotrusive contacts were found in women, significantly higher than in males ($p=0.004$). As well, there is an evidence of an association between premature contacts in protrusive movement and unilateral clicking (48.8%) ($p=0.05$), sometimes accompanied with pain in TMJ. The synusoidal trajectory of the mouth opening is associated with protrusive interferences in 63.2% of cases ($p=0.03$).

Conclusions. The presence of dental malocclusion, bruxism and other parafunctions in the initiation of the TMJ disorders is still a controversial issue. The studies performed until now, including the present one, showed that these factors could be considering favoring factors rather than determinant ones in producing of TMJ dysfunction, along with other associated pathologies.

SYSTEMIC COMPLICATIONS OF DENTAL MALOCCLUSION

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Introduction. Pathologic dental occlusion can alter the state and dynamic activity of temporomandibular joint, creating an imbalance in tonicity of masticatory muscles. This imbalance triggers a series of compensatory mechanisms in the spinal muscles, the spine being the main structure involved in posture. A frequent association has been reported between bruxism and sleep disorders such as snoring, respiratory breaks during sleep or obstructive apnea, the latter being frequently encountered and with a high risk for general health.

Materials and method. A 23 years old patient was subjected to complex occlusal static and dynamic analysis. Postural examination was carried out with the photographic method using the PostureScreen Mobile application. This application is in fact the digitalization of a validated posture evaluation technique: the photographic method using a vertical marker or the lead wire method. Two photographs were taken: front and profile. Sleep quality evaluation was performed using a polygraph method from Phillips Respironics Sleep Test.

Results. Dental occlusion examination revealed the presence of centric relation interferences on the left side. On the dynamic examination passive interferences were noticed on both sides during laterality movement. Left lateral movement was dysfunctional. Interferences were also observed during propulsion. Patient confirmed bruxism episodes.

Frontal postural analysis showed left deviation of shoulders and hips. Hips were tilted towards left. Lateral postural examination highlighted shoulders and hips shifted backwards.

Polygraph sleep test confirmed the presence of obstructive sleep apnea episodes and snoring. Desaturation periods were also encountered.

Conclusions. Changes in spine axis were correlated with centric relation interferences and nonfunctional lateral movement on the same side. Most of obstructive apnea episodes were of periphery origin, bruxism being probably one of determining factors.

ANALYSIS OF THE SEALER-ROOT DENTIN INTERFACE USING SCANNING ELECTRON MICROSCOPY

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Introduction. There is a great variety of materials used in endodontic practice and the newly developed bioceramic-based root canal sealers have improved physicochemical properties. An important advantage is the ability to form hydroxyapatite (during adhesion) and bond to dental tissues (dentin). The current study aimed to evaluate the apical sealing ability of two bioceramic-based root canal filling materials (the conventional Total Fill BC sealer and an experimental material developed in collaboration with "Raluca Ripan" Institute for Research in Chemistry, Cluj-Napoca) using scanning electron microscopy (SEM).

Material and methods. The study included 40 monoradicular teeth that underwent preparation, filling and sealing. Mechanical preparation of the teeth was carried out using the ProTaper® rotary system (Dentsply Maillefer). For 20 teeth continuous irrigation with 2% sodium hypochlorite (5 ml per sample) was performed and rinsed with 1 ml of 17% EDTA for 3 minutes. The mechanical and antiseptic preparation of the other 20 teeth involved the use of low-power laser therapy with HELBO TheraLite Laser. The teeth embedded in resin blocks were sectioned into 1 mm slices and the slices obtained were further analyzed using SEM.

Results. The images obtained by SEM allowed the identification and measurement of void spaces at the dentin wall / root canal filling material interface and thus the determination of the extent of apex sealing. Samples treated with the bioceramic-based experimental sealer and stored in saliva showed a better adhesion to the dentin wall.

Conclusions. Storage media can influence the adhesion of the root canal filling material to dentin walls. Low-power laser therapy by means of HELBO TheraLite laser (modified technique, without developer) improves adhesion of the root canal filling material to dentin walls through a more efficient smear layer removal using laser compared to the action of conventional root canal irrigants.

TRANSLUCENT ZIRCONIA: A REVIEW OF THE LITERATURE

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Introduction. Since the introduction of CAD/CAM system, zirconia ceramic has been successfully used for dental restorations due to its good biocompatibility and high mechanical strength. However, due to the material's opaque-whitish appearance, zirconia ceramic would look unnatural for aesthetic restorations. Recently, translucent zirconia has been developed, with improved optical properties.

Objectiv. The purpose of this review was to assess the available literature regarding mechanical, chemical and optical properties of recently marketed translucent zirconia ceramics.

Material and methods. The literature search was done in the PubMed and ResearchGate database using relevant keywords (zirconia, color, translucency, optical proprieties) for the interval 2012-2017 and was limited to articles in English.

Results. The electronic search identified 64 titles, of which 54 were chosen for evaluation. Of these 34 discussed the interaction of light with zirconia, 7 studies reported the effects of extrinsic factors on the optical proprieties of zirconia, 4 reported the grain size effects on the optical properties, 4 reported the ability of masking colored substrates and 5 reported the mechanical properties of translucent zirconia.

Conclusion. Translucent zirconia is a new innovation in the process of creating aesthetic restorations. In terms of optical properties, the new zirconia is significantly more translucent than conventional zirconia, but compared to feldspathic or lithium disilicate ceramic, its translucency is generally lower. However, translucent zirconia has lower mechanical strength (from 1000+ to 650 MPa) than conventional zirconia.

FINISHING DENTAL PREPARATIONS WITH ULTRASONIC INSTRUMENTS IN ORDER TO PREVENT MICROLEAKAGE

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Introduction. In this study was followed the improvement of the bonding quality by ensuring a good adhesion of the luting resin cement at the dental finished surface through different techniques and prevention of microleakage by ensuring a good marginal adaptation of the fixed prosthetics.

Progresses in minimal invasive dental preparations were possible due to evolution of prosthetic materials and luting resin-cements. Regarding dental surface, there is a classic method of finishing using high speed rotary instruments and a modern sonic finishing method.

Material and method. Finishing dental preparations has the purpose of allowing a good mechanical adaptation of the fixed prosthetics as well as microscopic roughness. Studies show differences regarding surface roughness and thickness of resulted smear layer, between classical finishing with high speed rotary tungsten and fine diamond burs, compared with sonic oscillating instruments.

According to these observations, the resulted smear layer after dental preparations is not entirely removed by acidic etching before cementation. The evaluation of finished dental surfaces with sonic oscillating instruments show a reduced thickness of the smear layer and a more receptive for bonding due to higher surface tension.

In this study were compared ten cases of fixed prosthetics finished with classical rotary diamond burs with ten cases of modern sonic finishing. Cementation was conducted with the same luting resin cement in all cases.

Results. After 3 years of clinical observation one case with marginal microleakage in patients whose dental preparations were finished classic with rotary fine diamond burs was found, and no microleakage in the second group whose preparations were finished with diamonds sonic oscillating instruments.

Conclusions. Marginal microleakage was absent when sonic finishing method was conducted. The gingival margins were protected and optimal results were achieved at precise limits of the preparations.

MANAGEMENT OF FACIAL SKIN TUMOURS BASED ON ULTRASONOGRAPHIC EVALUATION

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Introduction. Our paper presents the ultrasonographic evaluation for diagnosis and planning as well as the surgical management of facial cutaneous tumors.

Material and methods. A 84 years-old patient presented herself with two cutaneous lesions, in the left and right infraorbital regions. They appeared simultaneously and symmetrically. Ultrasound evaluation was carried out before surgery.

Results. Clinical and dermoscopy evaluation pointed towards a basal cell carcinoma. Ultrasound showed tumors with a high degree of vascularization and a 3 and 4 mm sonographic index respectively. Histology results after complete resection revealed squamous cell carcinomas.

Conclusion. Ultrasound proved to be helpful as means of preoperative evaluation of skin tumors, providing valuable information about their extension in surface and depth. This emphasizes the importance of multi-disciplinary approach to such tumors.

IN VITRO EVALUATION OF SEALING MATERIALS ADHESION TO ENAMEL

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Introduction. Sealing the pits and fissures of posterior teeth represents a local and specific method of caries prevention.

The aim of this study is to evaluate the adhesion of two materials used in sealing pits and fissures: Pitt and Fisure and Fissurit, by using the scanning electronic microscope (SEM).

Material and methods. The study was carried out on 20 premolars, which were extracted during orthodontic treatments in young patients. The selected teeth presented no carious lesions and no erosions on the enamel surface. The teeth were divided into two groups, one for the sealant Pit and Fisure and one for the sealant Fissurit.

The realization of this study respected all the stages of the posterior teeth sealing. The extracted and sealed teeth were held in artificial saliva for 14 days, at 37°C, for aging. After this period of time, the teeth were rinsed with water and then immersed in 3% Methylene Blue substance for 24 hours. All the teeth were embedded in acrylic resin and then left untouched for one day. Afterwards, the teeth were sliced in 1mm strips with the sample slicing machine.

The equipment used for this study was: The Scanning Electronic Microscope INSPECTS IN CO (SEM)-FEI Company, IsoMet1000- biomaterials sample slicing machine, Stereomicroscope STEMI 2000C.

Results. The study reveals a higher degree of detachment on a restricted area (x1000 magnification factor) for the Pitt and Fisure sealant (50%). The Fissurit sealant shows an extremely reduced detachment- 2% - at the same magnification factor of the SEM.

Conclusions. The better adhesion of the Fissurit material is due to the homogeneity of the material and the very small dimensions of the inorganic substances (2-3 μm).

Thereby, oral hygiene, periodic inspections, the use of an adequate technique and an adequate sealing material lead to an efficient caries prevention.

STUDY ON THE ANTIBACTERIAL ACTION OF NATURAL REVEALING AGENTS

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Introduction. Dentists have to deal regularly with oral infections which untreated may cause systemic infections. Antimicrobial chemical treatment is nowadays widely used in the prophylaxis and treatment of inflammation-induced plaque with the risk of resistance development. The aim of this study was to evaluate the antimicrobial activity for four experimental revealing agents based on natural compounds. This study is part of a project aiming to obtain photosensitizing agents for the photodynamic therapy of oral cavity disorders generated by the oral biofilm.

Material and methods. The microorganisms used in this study were Staphylococcus aureus for Gram positive bacteria and Escherichia coli for Gram negative bacteria. The revealing agents tested are gels mixed with various essential oils, divided in 5 groups: 1 – Curcuma longa (curcumin); 2 - Origanum vulgare (oregano) essential oil; 3 - Thieves (a mixture of essential oils); 4 - Boswellia Carteri (incense) essential oil and 5-Methylene blue. In this regard, the antimicrobial effect of new revealing agents was compared to commonly used products, such as methylene blue.

Results. Most revealing agents that were included in this study showed antimicrobial activity for both the Escherichia coli strain and Staphylococcus aureus strain. The weakest antibacterial activity was recorded in group 1 represented by curcumin (Curcuma longa) gel for both the Gram negative and the Gram positive strain.

Conclusion. Dental plaque is the first phase in the development of dental diseases. Elimination of pathogenic microorganisms on tooth surface is fundamental in preventing and controlling dental diseases, so using different revealing agents based on natural compounds can play an important role in removing plaque.

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IN VITRO TESTING OF THE REMINERALIZATION POTENTIAL OF DIFFERENT COMMERCIAL PRODUCTS

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The aim was to compare the remineralization properties of three products: Elmex geleé (group A), Tooth mousse (group B) and artificial saliva (group C) on enamel and dentine of extracted teeth.

Material and methods. a 3 mm window was prepared using standard diamond-coated turbine burs) which were previously demineralized for 30 seconds. The remineralization potential was compared using DIAGNOdent device.

Results. The lowest difference between the scores after demineralization and after treatment were found in group C, followed by group B and the highest one were found in group A, the group treated with Elmexgeleé. The score before any intervention and the Diagnodent score after the treatment shows a good correlation of 49.05% with R2=0.2406 for group A. Unexpectedly, the scores after the treatment minus the scores after demineralization were not correlated (6.16%) with the scores in the window before any treatment.

Conclusion. Remineralization on extracted teeth was significantly more effective for Elmex gelee. A larger study would be necessary, because most values recorded are not placed close to the median line (the values are too scattered due to the small number of samples).

EVALUATION OF THE EFFECT OF GREEN TEA EXTRACT ON CHANGING COLOR OF THE FILLINGS OF CARBAMIDE PEROXIDE BLEACHED TEETH

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Objectives. The aim of this study was to obtain an experimental green tea extract, which does not contain any preservatives and additives and does not have any secondary effects.

The objective of this study was the evaluation of color change of fillings for carbamide peroxide bleached teeth.

Material and methods. A number of 18 extracted molars were taken into this study with their roots mounted in self-cure acrylic prisms until the enamel-cementum junction. Their coronal part remained free.

The 18 molars were divided in two groups of 9: group A exposed at 16% carbamide peroxide gel and group B exposed at 16% carbamide peroxide gel and green tea extract. Specimens were prepared with a medium depth cavity, filled with nanohybrid composite resin, then stored for 24 hours in artificial saliva. Then, teeth and fillings color was recorded using VitaEasyShade device. After that, group A was exposed at 16% carbamide peroxide gel and group B was exposed at 16% carbamide peroxide gel and green tea extract. Surfaces of all specimens were examined for color change using VitaEasyShade device.

Results. At the end of the bleaching process, no significant differences were found in the two colors pre and post bleaching. 77.7% did not change the color. However, within group B, where carbamide peroxide and green tea extract was used, the fillings kept their color in a larger proportion than in group A.

Conclusion. The green tea extract has a low protective effect on the color changes of carbamide peroxide bleaching gel.

ASSESSMENT OF IN VITRO CYTOTOXICITY OF A COMMERCIAL ACRYLIC RESIN MODIFIED WITH GRAPHENE WITH SILVER NANOPARTICLES

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Introduction. Acrylic resins are the most common materials used for the manufacturing of removable dentures, and have been used for a very long time because of their many advantages. Local side effects such as irritation, inflammation or hypersensitivity reactions of the oral tissues are most probably due to the cytotoxic effects of the residual monomer.

Materials and methods. In our study we measured the cytotoxicity of a commercial acrylic resin used for denture bases, Castavaria (Vertex Dental), after the addition of graphenes with silver nanoparticles using fibroblast stem cells.

Results. The results showed that the viability of the cells exposed to modified acrylic samples was slightly reduced when compared with the acrylic samples used as control.

Conclusion. The material we tested was proved to be biocompatible, the tests showed comparable viability when compared with the material used as control.

COMPARATIVE STUDY OF THE RECONSTRUCTIONS QUALITY USING DIFFERENT CAD CAM SYSTEMS

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Introduction. The study intended to determine whether the quality of the prosthodontics restorations may be influenced by the CAD/CAM system or by each component of the systems. We wanted to determine if we can configure new systems more performant from the components of the standard systems.

Material and methods. We took into consideration 5 different laboratory scanners and 5 different CAD CAM machines. We used 5 mono brand systems and after we combined each scanner with different machines, thus obtaining 25 systems. We scanned 1 model and milled in this combinations 75 PMMA restorations.

Results. The scanning time and the volume of the files and the milling time are very different for each system. We measured the precision by calculating the occlusal and axial internal space. 3 systems did not perform in the mean average limits. We found that combining the components the values were better then for the standard systems.

Conclusions. Each system and each component of the systems had a big influence upon the quality of the restorations. The impact factors involved are: the precision of the scanner, of the milling machine, the material used for the restoration, the spacing set in CAD phase, the total convergence angle, the type of marginal preparations, the modifications between the system components.

GIOMERS – A REVIEW OF LITERATURE

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Introduction. Out of the multitude of dental materials available for direct restorations, the most utilized at present are the composite resins. However, to combine the conservative preparation necessary for the composites, the excellent esthetic results, good mechanical qualities and surface finishing properties with the protective properties due to fluoride releasing from the glass - ionomers, lead to a new generation of dental materials: the giomers.

Objective. The purpose is to review the available literature about the giomers, regarding mechanical, surface finishing, fluoride releasing and esthetic properties.

Materials and method. The search was carried out using the databases of ScienceDirect and PubMed, with the following keywords: giomer properties, fluoride releasing restorative materials and esthetic properties of composite resins. A total of 37 articles published in 2004 – 2017 were selected. The selection criteria for the articles were the English language and topics a addressing the properties of the glass - ionomers, composite resins and giomer materials as well as their clinical implications.

Results. Out of the 37 selected articles, 22 referred to giomer restoration materials: 7 studies reported about the properties of the materials (4 clinical studies), 7 studies reported about fluoride release and caries prevention (2 clinical studies), 2 studies referred to the bleaching effect on giomer restorations, 6 studies discussed the adhesion quality of giomers (1 clinical study).

Conclusions. Giomers prove to be incorporating the mechanical and esthetic properties of the composite resins and the preventative effects of the fluoride specific to glass-ionomers. They were also effective in sealing the cervical carious lesions where adhesion is problematic for composites and esthetics is not perfectly achieved by using glass-ionomer cements.

IN VITRO ASSESSMENT OF DIFFERENT NATURAL COMPOUNDS WITH DENTAL-PERIODONTAL REPARATIVE ABILITY

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Introduction. Our purpose it was to identify from the studied compounds, the substances with the better tissue tolerance for obtaining a material with reparative properties for the dento-periodontal tissues.

Material and methods. A cell line of stabilized and characterized mesenchymal stem cells, obtained from human palatal subepithelial connective tissue was cultured and after 24 hours was treated with the following natural substances: two different types of shell clams, propolis extract, raw propolis powder, Cordyceps mycelium, chitosan and extract from the plant Croton Lechleri Muell. The cytotoxic and viability tests and Scanning Electronic Microscopy (SEM) characterizations of the substances were performed.

Results. The cells rest viable expressing different levels of proliferation in the presence of all the evaluated natural compounds. Best results have been observed for the propolis extract, propolis powder and chitosan. The ultrastructural characterization revealed types of morphology that encourage cells connections and development, some of materials seemed to provide a structural support for cell proliferation.

Conclusion. The studied materials are well tolerated by the stem cells. The fact was also confirmed by the electronic microscopic images which revealed a good interaction between cells and the selected compounds, some of them serving as a scaffold for cellular multiplication and display.

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IN VIVO TESTING OF THE TITANIUM SCAFFOLDS MANUFACTURED BY SELECTIVE LASER MELTING TECHNIQUE (SLM)

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Introduction. Selective Laser Melting is an additive manufacturing method by which a laser melts and solidifies a titanium powder and layer by layer builds solid structures with tridimensional guided architecture. The objective of our study was to determine the ability of the animal organism to integrate the titanium scaffolds with different sizes of the matrix holes, manufactured by SLM. On the surface of some scaffolds, nanohydroxiapatite was added which gave us the opportunity to observe the influence of the nanohydroxiapatite in the osteointegration process as well.

Materials and methods. Six male, adult, Californian White rabbits where included in the study. Three of them recieved femoral implants with the size of the matrix of 0.8 mm and the other 3 with the size of the matrix of 1 mm. Each subject received 2 implants, one with the surface conditioned with nanohydroxiapatite and one without any treatment on the surface. The evaluation was made at 2, 4 and 6 months after the implantation by histology and scanning electron microscopy (SEM).

Results. The scaffolds with nanohydroxiapatite on the surface had a superior osteointegration than the ones with unmodified surface. The presence of the nanohydroxiapatite accelerated the process of bone developement and helped forming a more resistant structure. The scaffolds with the size of the matrix of 1 mm had a better interaction at the bone-implant interface.

Conclusion. The presence of nanohydroxiapatite on the surface of the implant and a larger size of the matrix bring benefits in the process of osteointegration and bone development of the scaffolds manufactured by SLM.

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