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BASIC SCIENCES

Beneficial effects of two species of *thymus marshallianus* on *in vitro* and *in vivo* models

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Introduction. Diabetes mellitus (DM) is a chronic metabolic disorder that can associate with oxidative stress and behavioral changes. We aimed to evaluate the comparative effects of two species of Thymus Marshallianus (TM), wild flora (TMW) and culture (TMC) on both in vitro and in vivo models.

Materials and methods. In vitro studies were performed on HUVEC cell line, using TMW and TMC in two different dilutions (1/10000, 1/100000), under normoglycemic and hyperglycemic conditions. NF-kB, activated pNF-kB, HIF 1α and γH2AX were assessed by western blot and MDA levels by spectrofluorimetry. 36 Wistar rats were used for the in vivo study. The animals were divided in 4 groups (n=9/group): Control (Carboxymethylcellulose, CMC), DM, DM + TMW, DM+ TMC. TMW and TMC (200 mg/kg b.w.) were orally administered for 14 days. On the 15th day, one dose of STZ (30 mg/kg b.w.) was intraperitoneally administered. Subsequently, natural compounds were administrated for the next 14 days. On the 33rd day, Open Field Test and Elevated Plus Maze were performed. Oxidative stress biomarkers in serum, hippocampus and frontal lobe homogenates (MDA, GSH/GSSG) and NF-kB levels in hippocampus and frontal lobe samples were also assessed. Methyl CpG binding protein (MECP) 2 and histone deacetylase 1 (HDAC1) expressions in rats `brain were also analyzed by western blot.

Results. In vitro, TMW and TMC diminished MDA, NF-kB and γH2AX levels and increased pNF-kB and HIF 1α expressions. In vivo, TMW and TMC administration reduced blood glucose levels, improved the overall mobility and increased 5 times the entrances and time spent in the open arms in EPM. In frontal lobe, both extract diminished lipid peroxidation and enhanced the antioxidant capacity and HDAC1 expression. TMW administration increased NF-kB level and diminished MECP2 expression in hippocampus.

Conclusions. Both compounds exerted beneficial effect by increasing the antioxidant defense and improving the anxiety-like behavior.

Neuroprotective effects of memantine in combination with hypothermia in experimental hypoxic brain injury

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Introduction. Hypoxic encephalopathy (HE) is a major cause of perinatal mortality and subsequent severe neurological sequelae. Mild hypothermia is a standard therapy for HE, but there are significant cases when another neuroprotective therapy is necessary. Since neuronal death following HE occurs by a cascade of events triggered by activation of glutamate receptors, we used an experimental model of neonatal encephalopathy to examine whether the NMDA receptor antagonist memantine could exert neuroprotective effects, alone or in combination with hypothermia.

Aims. The main objective of this study was to test the possible protective effect of memantine and hypothermia in hypoxic-ischemic encephalopathy at newborn rats. We evaluated the oxidative stress parameters for lipid peroxidation and antioxidative defense.

Materials and methods. The experiment was performed on 20 newborn Wistar rats, subjected on the 7-th postnatal day to cerebral hypobaric hypoxia (9% O2 for 90 minutes). We administrate memantine (i.p., 5mg/kg) immediately after hypoxia. In order to test the effect of combined therapy of memantine with hypothermia, several animals were exposed after hypoxic injury to whole body hypothermia (with 4OC) for 3 h.

Results. In global hypoxic encephalopathy hypothermia exert neuroprotective effects, resulting in decreasing MDA levels and increasing antioxidant enzymes, memantine produce an increase lipid peroxidation, but the protective effect consists in stimulating antioxidant enzymes activity, at a dose of 5 mg/kg/dose.

Conclusion. The results of this study prove that mild hypothermia offers neuroprotection in hypoxic brain injuries, memantine treatment increase antioxidant defense, but when conjugated, the effect is not superior.

Keywords: neuroprotection, hypoxia, oxidative stress, memantine, hypothermia

Apoptosis induced by silver and gold nanoparticles on oral dysplastic keratinocytes - *in vitro* study

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Introduction. Oral squamous carcinoma incidence is increasing, especially in young people. Therefore, early detection and prevention, as well as development of safe, effective therapies are important. Nanotechnology has been previously used for the development of materials and medical devices for diagnosis and treatment, including for oral cancer. The current study aims to test the ability of silver and gold nanoparticles functionalized with Cornus mas (CM) or Sambucus Nigra (SN) plant extracts to induce apoptosis in displastic oral keratinocytes.

Materials and methods. Displastic oral keratinocytes (DOK) cultures were treated with silver nanoparticles functionalized with Cornus mas (AgCM), (AuCM), Sambucus Nigra (AgSN) or only extracts. Untreated cells were used as controls. Viability (MTS assay) was determined. Apoptosis was evaluated through FACS (annexin-PI staining), WB (p53, BCL2, Akt activation, ɣH2AX).

Results. Nanoparticles significantly decreased cell viability at doses higher than 20 µg/ml compared to natural extracts which did not show significant toxicity. AgSN and AgCM, respectively Au CM induced cell death through different mechanisms. AgSN and SN increased γH2AX, a marker of irreparable DNA double strand breaks. Ag and AuCM induced apoptotic levels of p53.

Conclusions. Although all nanoparticles led to apoptosis, the mechanism was strongly influenced by the type of the extract used for functionalization and less by the nanoparticle itself.

Acknowledgement. This work was supported through the National project PN-III-P4-ID- PCE-2016-0396 PCE, funded by Romanian Government.

3D imaging and anatomical study of the rat cochlea

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Background. The animal model for experimental studies regarding the inner ear, and more precisely the cochlea, is still the major information supplier. Though the new era of cultures of established cells lines is opening up new posibilities, the minute anatomy of the inner ear, tough access, the blood-perylimph barrier, and cells disposition and function makes the in vivo animal model the first option research. In order to reach the best approach a thorough anatomic representation is needed.

Methods. This descriptive anatomical study included both cochleas of two Sprague Dawley rats, adult males,.raised in the Experimental Animal Facility of University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca, born at Cantacuzino Institute, Bucharest. In order to determine the functionality of the ear, otomicroscopy and auditory brainstem response (ABR) measures were used. After sacrificing the animals, the whole temporal bone was dissected and underwent a micro-CT scan. A 3D model was obtained for each of the 4 cochleas using the ITK-SNAP Software.

Results. The otomicroscopy showed no signs of external or middle ear infection. The ABR measures using.tone burst stimuli of 3 single frequencies (1 ms), including 8 kHz, 16 kHz, and 32 kHz were in normal limits, implying a normal cochlear and auditory nerve function.

Conclusion. The 3D model of the cochleas obtained with the ITK-SNAP Software offered a detailed image of the disposition of the round and oval window. This project is intended to bring a further improvement in understanding the anatomical landmarks, which is paramount for a good surgical approach, reduced intervention time and limited trauma to the animal.

Effects of curcumin on blood pressure and ECG changes on induced myocardial infarction in rats

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Introduction. Curcumin has anti-inflammatory, anti-oxidative, anti-carcinogenic and cardiovascular protective effects. This study aimed to investigate the effects of pre-treatment with curcumin nanoparticles compared to conventional curcumin (low oral bioavailability) on blood pressure and ECG changes on isoproterenol(ISO)-induced myocardial infarction(MI) in rats.

Material and methods. Fifty-six Wistar-Bratislava white female rats, weighing between 250 and 300 grams were used. The rats were randomly divided into 8 groups of 7 rats/group. Curcumin and curcumin nanoparticles were given in three different doses (100 mg/kg body weight - bw, 150 mg/kg bw and 200 mg/kg bw) for 15 days by gavage. The MI was induced on day 13 using 100 mg/kg ISO administrated twice, with the second dose at 24h after the initial dose. The blood pressure and ECGs were recorded at the beginning of the experiment, 24 hours before ISO administration and 24 hours after the last dose of ISO.

Results. Curcumin and curcumin nanoparticles did not influence the blood pressure values before or after ISO administration ($P>0.10$). Curcumin in the dose of 200 mg/kg bw and curcumin nanoparticles in doses of 100 mg/kg bw ($P=0.0024$), 150 mg/kg bw ($P=0.0022$) and 200 mg/kg bw ($P=0.0022$) had significantly reduced the heart rate

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before and after ISO administration. Highest doses of curcumin nanoparticles prevented widening of the QRS complex (87 ms for 150 mg/kg bw and 82ms for 200mg/kg bw). Curcumin nanoparticles prevented QT interval prolongation (105 vs 96 ms, 103 vs 87 ms, 98 vs 82 ms) and ST-segment depression (-0.03 vs 0 mm, -0.02 vs 0.01 mm,.-0.01 vs 0.04 mm).induced by ISO, more than the conventional curcumin.

Conclusion. Curcumin and curcumin nanoparticles do not influence the blood pressure in ISO-induced MI in rats. Curcumin nanoparticles significantly reduce the heart rate and prevent widening the QRS complex, QT interval prolongation and ST-segment depression compared to conventional curcumin.

Choosing a speciality in medicine - undergraduate students' opinion

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Introduction. Choosing a specialty in medicine is a very important step for each medical graduate. The aim of this study was to assess the undergraduate students' options related with choosing the specialties in medicine after graduation.

Material and methods. A cross-sectional study, using an online survey in March and April 2017 was conducted for 2083 undergraduate eligible medical students from the Iuliu Haţieganu University of Medicine and Pharmacy Cluj-Napoca, Faculty of Medicine, Romanian section. The first part of the survey consisted of questions about motivational factors that would influence the career preferences, the second part asked the students' options for a specialty in medicine, while the third part had questions about career counselling methods.

Results. Four hundred sixty-three students, majority female (72.5% [68.43-76.57]) were the respondents. Most of the students (59.2% [54.72-63.68]) showed interest in the clinical specialties, while 28.7% [24.58-32.82] were more interested in a surgical specialty. Most of the medical students (75.2% [71.27-79.13]) said that they intend to sit to the residency exam in Romania. Among clinical specialties, the most preferred specialty was cardiology (9.9% [7.18-12.62]), followed by pediatrics (7.6% [5.19-10.01]). The most wanted surgical specialties were obstetrics and gynaecology (6.3% [4.09%-8.51]) followed by general surgery (4.1% [2.29-5.91]). The most important factors considered by respondents in choosing the specialty were the patient contact (76.24%), recognition of studies in the European Union (70.84), and opportunity to work in the private healthcare system (66.74%).

Conclusions. Most of the medical students who participated to our survey were interested in a clinical specialty. Patient contact was the most important reason why students would choose a certain specialty. Most wanted specialties are cardiology among clinical and obstetrics and gynecology among surgical specialties.

Is scientific medical literature evidence-based? A case study on randomized clinical trials

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Introduction. Informed decision-making requires physicians' abilities to identify and integrate scientific medical evidence. The dilemma is how a clinician could identify correct evidence given the doubtful integrity of published medical studies. This study aims to assess how the scientific literature related to the therapy of endometriosis fits the level in the hierarchy of evidence.

Material and methods. A search of the PubMed, PMC and Science-Direct databases conducted on March 3, 2018, by using as keywords *therapy & endometriosis & efficacy* was applied to extract medical articles written in English and published in the last ten years. Out of the retrieved article, those reporting a randomized clinical trial were evaluated to assess the extent to which they fit into the appropriate level of evidence (level 1, degree 1b).

Results. 2,235 were identified and after reading each abstract, 388 articles (17%) fit the searched keywords. Of the total number of 388 articles, 10.3% (n=40) were randomized clinical trials. Upon evaluating each randomised clinical trial, all 40 articles mentioned that the subjects had been randomized, but 75% of them failed to present who had decided and who had conducted the randomization, while in 55% of the trials, there was no mention of how randomization had been carried out. Only 42.5% of the articles specify the method used for the concealment of treatment. In 42.5% of the articles, no mention of where, when and how the treatment had been administered to the groups of patients was found in the full text. No mention of whether the patients and personnel involved had been "blinded" was observed in 52.5% of the evaluated studies. The number of individuals that completed the treatment was reported only in 10% of the trials, and 80% of evaluated articles were inefficient in reducing bias.

Conclusion. None of the 40 studies analyzed meet the randomized clinical trial criteria, so they cannot be fitted into the appropriate level of evidence.

The ability of a new Schiff base to modulate oxidative stress

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Introduction. Schiff bases (SBs) are chemical compounds displaying a significant pharmacological potential. SBs are able to modulate the activity of many enzymes involved in metabolism. SBs are found among antibacterial, anti-inflammatory and antioxidant drugs. The aim of the study was to assess the antioxidant ability of a new SB.

Material and methods. The SB was synthetized according to a previously described method. In vitro antioxidant activity was determined by DPPH bleaching assay, using BHT as positive control. The ability of the SB to modulate oxidative stress was assessed on HUVECs cultures. Cell viability was appreciated by colorimetric measurement in cell cultures exposed to different concentrations of SB. Three groups of cell cultures were made: (1) control cells treated only with medium; (2,3) cells treated with Schiff base in concentrations of 0.01 µg/ml and 0.001 µg/ml. After the treatment, MDA level was measured using spectrophotometry, while SOD1, COX2, NOS2 levels through Western Blotting.

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Results. DPPH bleaching assay showed that the new SB displayed a low IC50 value, similar to that of BHT. Schiff base did not lead to significant changes in cell viability for doses lower than 0.01 μg/ml. The high dose used (0.01 μg/ml) increased MDA level, while la lower dose (0.001 μg/ml) decreased it. Changes in the MDA level were not statistically significant. The lower dose was used for further testing. As compared with the control group, the new SB significantly decreased the expression of SOD1, COX2, NOS2.

Conclusion. The new Schiff base has excellent antioxidant ability in vitro. When tested on cell cultures the antioxidant effect is dose related. In the lower doses, the Schiff base has a moderate antioxidant activity on cell cultures.

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Social media usage among Romanian health care providers

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Aim. Our study aimed to evaluate physicians' perceptions, goals, and challenges in using social media as a professional tool.

Methods. Perceptions and attitudes toward social media as a communication tool of Romanian physicians were examined using a pre-validated 17-item questionnaire. The mail addresses of Romanian physicians (6220 address) from seven Romanian districts (Bacău, Bihor, Buzău, Cluj, Harghita, Hunedoara, and Satu-Mare) were collected in 2017 from the Romanian College of Physicians website. An invitation to the survey along with the survey was randomly sent in November 2017 to 2,000 doctors, respecting the proportions per county.

Results. Two hundred and seventy-one questionnaires were collected, six were excluded (one was returned blank, and 5 with missing data for age), and 265 were analyzed. The standard profile of respondents was female (68.68%, 95%CI [62.64–74.34]), from an urban area (86.42% [81.89–90.19]), who work only in a public funded healthcare facility (47.92% [41.89–53.96]). Most of the respondents (65.66% [59.62–71.31]) used Facebook, mostly from home (95.09%), for less than 1h/day (54.72%). The participant physicians search for medical information (79.25% [73.96–84.15]) on social media but not daily (27.55% [22.27–33.21]). Our respondents have not identified social media as a useful tool for the accomplishment of daily tasks, treatment of patients, or improvement of provided service. Most of the respondents do not interact with their patients via social media (68.3% [62.27–73.96]), but those who do it prefers Facebook (16.23% [12.08–21.13]). Most of the doctors that participated in our survey do not discuss with their patients the utilization of social media for searching health information (66.42% [60.38–72.07]).

Conclusions. Our study showed that Romanian physicians neither use social media to interact with their patients nor discuss with them about the healthcare information available online.

Allergic rhinitis to Ragweed pollen (Ambrosia Artemisifoliia) in Transylvania

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Introduction. Ragweed is a major source of allergens, especially in Central Europe and recently in western regions of Romania. In this study we evaluated the symptoms and associated factors in patients with allergic rhinitis (AR) to ragweed pollen in Transylvania. Secondly we evaluated the evolution of ragweed sensitization in time.

Material and methods. Patients with AR induced by ragweed pollen were evaluated in two allergology centers from North-West (NW) and Central part of Transylvania, between 2010-2011 and 2014-2015. Duration, presence and severity of the AR symptoms and the association with other allergic manifestations were noted.

Results. In the first period of evaluation, 455 patients from NW center and 706 from Central one with AR were included. The ragweed pollen as clinically relevant allergen was more frequently observed in NW center compared to the central one (16.2% vs 4.1%, p=0.03). Most of the patients were polysensitized in both centers. Patients with monosensitization to ragweed pollen presented more severe forms of rhinitis in NW part compared to polysensitized patients, while in the other groups there were no differences between mono and polysensitized patients. The total symptoms score was significantly higher in patients from Central part compared to NW part (p=0.0001). Bronchial asthma was associated to AR similary in both centers.

The second evaluation noted an increased number of patients with AR to ragweed pollen in both regions. The clinical pattern of AR to ragweed pollen was similar in both evaluations. Asthma association decreased over time in both regions.

Conclusions. AR to ragweed pollen was more frequently observed in NW part. The severe forms of rhinits was observed in Central part and in monosensitized patients in NW center. The prevalence of AR to ragweed pollen increased significantly in a period of three years in both regions.

The changes of inflammatory markers and irisine level in the first year of insulin therapy in type 2 diabetes patients

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Objective. To evaluate the changes of inflammatory markers and irisine plasma level in the first year after initiation of insulin therapy in type 2 diabetes patients (T2DM).

Material and method. Twenty-three T2DM patients who started insulin therapy for better glycemic control were enrolled in our study. The study was conducted during the first year of insulin therapy and included 4 visits: initial visit, after 3 months, after 6 months, and after one year of insulin-therapy. Anthropometric and metabolic parameters (basal glycaemia, HbA1c, lipid profile) were measured at each visit, while adiponectin, interleukin-1β and irisin at the beginning, after 6 months and after one year of insulin therapy.

Results. The mean age of the 23 patients was 62.30 ± 10.29 years, with a median duration of T2DM of 7 years (3-12 years). During the first year of insulin therapy the patients presented significant modification of HbA1c (10.23 ± 1.94% versus 7.63 ±

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0.78%, p<0.001) and basal glycaemia (248.17±61.84 mg/dl versus 151.89 ± 41.72 mg/dl, p<0.001), with significant increase in body weight and skeletal muscle mass, and no significant increase in body fat mass or percent of body fat. Adiponectin level was significantly lower after first year of insulin therapy: 7.06 mg/L (3.98;10.01) versus 4.81 mg/L (3.02;6.95), p=0.044; irisin level was significantly higher after one year of insulin therapy: 0.65 ng/ml (0.00;1.63) versus 1.37 ng/ml (0.57;1.70), p=0.004, with no significant change in circulating IL-1β levels: 5.45 pg/ml (3.54;7.22) versus 5.15 pg/ml (3.65;6.70), p=0.076.

Conclusion. One year after insulin therapy initiation, patients with T2DM showed a significant decrease in adiponectin levels, a significant increase in irisin levels and no significant changes in IL-1β levels.

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A plot twist in the analysis of students' sleeping habits and academic performance

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Introduction. Medical literature often suggests that a good quality sleep is a vital player in memory consolidation, both in young and older adults. In this study we aimed to point out the connection between students' sleeping habits and their academic performances.

Material and methods. A cross-sectional study was conducted during the academic years 2016-2018, including medical students from Iuliu Hatieganu University of Medicine and Pharmacy, by filling an online questionnaire. Descriptive and inferential statistics were calculated using Excel. The percentages and averages are taken from the 3 years in total.

Results. The study sample consisted of 1 351 students, with female predominance for a male to female sex ratio of 0.29. For the students to fall asleep, half of them (49.8%) go to bed before midnight, and only 65.6% fall asleep in half an hour. Wake up time was up to seven o'clock for 43% of students, even though 7.6% of them slept after two o'clock in the morning. Qualitatively, despite the fact that 30.63% of students participating in the 3-year study stated that they do not get satisfactory sleep, and that an average student will have 404.38 (±66.01 standard deviation) minutes per night, 33.11-52.84% of students claimed that they have medium to good academic performance respectively.

Conclusion. The students who completed the survey, within the reviewed academic years, had been to bed late, fallen asleep hard, slept less, and nevertheless had woken up early. Up to this point of the study, we found that the sleep quality does not significantly affect memory consolidation as students were able to score medium to good grades and not lower.

Platelet-to-lymphocyte ratio – a predictor of survival in ovarian cancer patients?

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Introduction. Ovarian cancer represents a major health problem due to its high incidence and.late-onset diagnosis with a 5-year survival rate below 25%, explained by the lack of effective screening methods and prognostic molecular factors. Several studies have evaluated the importance of platelet-to-lymphocyte ratio (PLR) as a prognostic factor of ovarian cancer patients.

The aim of this study was to assess whether PLR was correlated with 3-year survival rate in ovarian cancer patients. Secondary, it was intended to identify correlations between 3-year survival rate and the demographic, clinical and pathological characteristics of patients in order to individualize oncological treatment.

Materials and methods. 40 patients with ovarian carcinoma treated in IOCN by surgical resection, followed by 6 cycles of adjuvant chemotherapy (Taxol and Carboplatin) were included. All subjects underwent postoperative, respectively post-chemotherapy assessment of PLR. Demographic data, clinical and pathological features were also collected. Survival rate was assessed at 3 years. Data analysis was processed through Fisher's exact and Chi Square tests.

Results. There was no evidence of statistical significance of PLR values and 3-year survival rate. The majority of patients had an advanced-stage and a high-grade disease, but no differences were found significant for 3-year survival rate between patients residing urban or rural areas, tumor staging and grading.

Conclusion. Although both thrombocytosis and lymphopenia have poor prognosis regarding ovarian cancer patients, PLR evaluation is still a controversial predictive marker in patients with ovarian cancer.

Anti-inflammatory and antioxidant effects of mountain garlic (allium senescens ssp. montanum) extracts

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Introduction. Allium species have well documented anti-inflammatory and antioxidant effects..Aim of the study was to analyze these properties in the ethanolic plant extract of Allium senescens L. subsp. montanum (Fries) Holub, called mountain garlic.

Material and methods. Extracts of Allium montanum in three dilutions (100%, 50% and 25%, respectively) were orally administered to rats for seven days. Acute inflammation was induced with turpentine oil. Anti-inflammatory and antioxidant effects were assessed by measuring serum nitric oxide (NOx), total oxidative status (TOS), total antioxidant reactivity (TAR), oxidative stress index (OSI), malondialdehyde (MDA), and total thiols (SH). As control groups an NSAID (diclofenac), and the main alkaloid (allicin) were used.

Results. In subjects with induced acute inflammation, TOS and OSI were significantly decreased after the administration of A. montanum extracts, with the 25% dilution having the highest efficacy. Compared to diclofenac, the reduction of TOS and OSI was equal. Contrasting allicin, only the 25% dilution could prove a better effect. Considering NOx, all A. montanum extracts proved more antioxidant potential than

diclofenac, the 25% and 100% dilution also being more efficient, compared to allicin. All A. montanum extracts had a better effect on MDA reduction than allicin and diclofenac, and caused a higher increase in SH.

Conclusions. The results demonstrate in vivo antioxidant and anti-inflammatory properties of Allium senescens ssp. montanum. The efficacy was dose-dependent, with the 25% dilution being the most effective inhibitor. Further studies may be needed to widen the understanding of the antioxidant and anti-inflammatory potential of mountain garlic.

The effects of hypericum capitatum extract on experimental inflammation

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Introduction. Hypericum is a genus of flowering plants in the family Hypericaceae. It is a medicinal plant with demonstrated anti-viral, anti-depressive and anti-cancer properties.

Material and methods. In this study were used 7 groups (n=5) of Wistar rats with body weights with aprox. 250g. The rats were kept in cages under 12 h light/dark cycles, at a temperature of 22°C, with access to a standard diet and water ad libitum. The extract of H. Capitatum was tested. For 7 days, the extract was administered orally by gavage (1 mL/rat) in 3 different concentrations, respectively: 12.5 mg/kg bw, 25 mg/kg bw and 50 mg/kg bw. Tap water (1 mL/rat) was administrated for 7 days to the rats from C group and I group. The D-I group was treated by gavage for 7 days with diclofenac (10 mg/kg bw). Inflammation was induced with turpentine oil (6 mL/kg bw) administered intramuscularly, in the I, D-I, D1-I, D2-I, D3-I groups. One day after the inflammation induction, blood was withdrawn by retroorbital puncture and serum was stored until use. Total proteins, albumin, CRP, 3NT, SH, CAT, TBARS, TOS, TAC, OSI, NO, SOD, complete blood cell count were determined. All the animals were killed by cervical dislocation.

Results. Total proteins increased ($p<0.001$) due to the acute phase proteins. CRP was lowered by D3, D2 ($p<.0.001$), D1, R, D ($p<0.01$). D3 and D reduced TOS and OSI ($p<0.05$). 3NT was reduced by D1, D2 ($p<0.01$), R ($p<0.05$). SH was increased by D1, R ($p<0.01$) and D ($p<0.05$). CAT was also increased by D1 ($p<0.001$), R ($p<0.01$), D2, D ($p<0.05$). TBAR, NO and TAR were not influenced by the tested products. SOD was reduced by D1, D2, D3, D ($p<0.05$). PMN were not influenced significantly ($p>0.05$).

Conclusion. H. Capitatum extract had anti-inflammatory effect by reducing CRP. D3 was the most efficient. The extract reduced oxidative stress by lowering TOS, OSI and 3NT. D3 was the most efficient and it was comparable to diclofenac. The extract improved the antioxidant defense by increasing SH and CAT. D1 was the most efficient and comparable to diclofenac.

Minors' rights to confidentiality and derogations: ethical scenarios in every-day medical practice

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Confidentiality is one of the core duties in medical practice. It requires that a physician keeps a patient's personal information private unless the patient consents to release it. Patients under 18 years old are considered incompetent because of their age. They cannot make medical decisions without their parents' or their legal representative's consent. However, in some cases obtaining informed consent from the parents might conflict with the legal and ethical obligations of confidentiality towards the patient. Acting in the best interest of the minor, respecting their right to confidentiality, could be in conflict with the parents' interests: to be always informed about their children. Medical issues stemming from familial disputes or behaviors, such as a divorce or alcohol/drug consumption, are example of the reasons why minors could be protected, even against parents wishes. If their confidentiality is not protected, the trust in their physician would be tarnished and the professional relationship compromised, which would greatly affect the physician's credibility in front of the patient. By protecting the patient's privacy, the physician encourages them to seek medical care and to be truthful during health check-ups. Moreover, the introduction of new and revised pieces of legislation in Romania in the last few years has put the confidentiality of medical data at the heart of heated debates regarding medical malpractice or misconduct committed by some health professionals. In this paper, I am planning to focus on ethical and legal implications originating from the antagonism between the informed consent and the minor patient's right to confidentiality. The aim of the paper is to: 1) try to understand the „spirit" of the legal norms in force in Romania that regulate medical privacy; 2) delineate ethical principles in conflict and 3) present examples of conflicting interests of the minors and parents.

Medication errors - a cause for major cardiovascular events in Emergency Department

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Introduction. Cardiovascular diseases (CVD) represent the main cause of mortality worldwide. The drugs recommended for CVD are the most prescribed drugs and, as a consequence, the risk of medication errors is increased. Nowadays, medication errors are the most common type of medical errors. The objective of this study was to assess the major cardiovascular events due to medication errors in an Emergency Department (ED).

Material and methods. A retrospective observational study was conducted in 416 patients with major cardiovascular problems (acute coronary syndrome - SCA, ischemic/ hemorrhagic stroke, hypertensive crisis) in an ED from 1 July 2017- 31 August 2017.

Results. A total of 9086 patients were admitted in ED during July-August 2017. From this, 416 patients (4.57%) presented major cardiovascular events, 220 women (52.9%) and 196 men (47.1%). The mean age of analyzed patients was 67.68±14.2 years. The most common cardiovascular events were strokes (50%), hypertensive crisis (34.4%) and acute coronary syndrome (14.7%). In 99 out of 416 patients (23.8%), medication errors were identified. The main medication errors were lack of antiplatelet / anticoagulant therapy (43.43%), non-adherence to treatment (16.16%), inadequate antihypertensive therapy (7.07%), inappropriate treatment (e.g. association between two calcium channel blockers) (1.01%).

Conclusion. Medication errors are one of the major causes of major cardiovascular events. Many of the medication errors leading to visit in ED could be prevented. It is necessary to develop prevention strategies. Clinical pharmacologist can play an important role in this strategy.

Interobserver variability of various sonoelastographic techniques - an *in vitro* study

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Introduction. The aim of the study is to assess interobserver variability of various strain and shear wave sonoelastographic techniques in an experimental in vitro study. This study is part of a wider project, aiming at assessing the normal and pathologic uterine cervix through various elastographic techniques, using a silicone device as a stiffness reference.

Materials and methods. Three silicone types of devices, having different stiffness, were prepared, using standardized techniques. Out of each type, 5 devices were made. The devices were placed in 5 boxes and embedded in solid jelly, each box containing one device of each type.

The following sonoelastographic techniques were tested: strain ratio, acoustic radiation force impulse (ARFI), 2D shear wave elastography, with 3 dimensions of the region of interest (5 mm, 10 mm and 15 mm). The exams were performed by 2 individual observers, having experience in sonoelastography as follows: examiner 1 - 3 years, examiner 2 – 6 months.

Strain ratio and 2D shear wave ratio were considered for each sample as the means of 6 consecutive measurements. The stiffness value measured by ARFI was the result of the average of 6 consecutive measurements.

The final results of strain ratio, 2D shear wave ratio and stiffness determined by ARFI for each device were compared between examiners, using Paired Sample T-Test.

Results. Data analysis showed differences between the two observers. Statistical analysis revealed no significant difference between the results, with a good kappa coefficient.

Conclusion. The three elastographic techniques are reproducible, with no significant interobserver differences, regardless of experience in applying the technique.

ANA “Nuclear Rim” pattern influences progression of severity in primary biliary cholangitis

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Background. Anti mitochondrial antibodies (AMA) are diagnostic marker for PBC; 20% of PBC patients remain AMA negative. The patients are positive for antinuclear antibodies (ANA), with two different patterns, which are highly specific for PBC. These patterns in indirect immunofluorescence(IIF) technique are:“nuclear rim”pattern recognize autoantibodies of gp210 and nucleoporin p62 proteins, is associated with accelerated progression disease; “multiple nuclear dots ”pattern recognize sp100 and PML proteins. Our objective is to analyze the presence of ANA “nuclear rim” pattern in association with clinical progression of PBC, in the case of three male brothers, who have been diagnosed in different stages of disease according to EASL guidelines.

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Methods. We studied three male patients, in their fifth and sixth decade, to which we performed clinical examinantion, abdominal ultrasound, liver stiffness measurement, biochemical markers serum alkaline phosphatase (ALP) and gamma glutamyltranspeptidase (GGT). Liver biopsy was not necessary for diagnosis of PBC, although one of the patients was previously diagnosed before including him. AMA were performed by IIF-EUROIMMUN mosaic basic profile on sections of multi organ (liver, kidney, stomach) from rodents. PBC specific ANAs were performed by standard IIF on HEp2 cells line, at the screening serum dilution 1:40 for both autoantibodies.

Results. One patient was diagnosed with cirrhosis class B Child Pugh score-9 points and. ANA "nuclear rim" was positive in high dilution. Two patients were diagnosed with moderate fibrosis. All patients had elevated ALP, GGT and. AMA were positive at high titre even there is no correlation between the titer of AMA and progression of severity of the disease. All patients had "multiple nuclear dots" pattern.

Conclusion. ANA "nuclear rim" pattern can be predictive for accelerated progression and unfavorable course of PBC. We consider that a genetic study is important in this case in the near future.

Angiotensin gene polymorphism M235T and nonalcoholic fatty liver disease, dyslipidemia, carotid atheromatosis, increased body mass index in patients with systemic arterial hypertension

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Objectives. Uncontrolled systemic arterial hypertension (SAH) associated with dyslipidemia and increased body mass index (BMI), lead to ischemic coronary and cerebrovascular events. Carotid mean intimal thickness (CMIT) is greater in patients with NAFLD. Pathophysiological mechanisms responsible is activation of renin-angiotensin system (RAAS) and arterial stiffness. Met235Thr is a point mutation in the gene encoding angiotesinogen (AGT) and is associated with SAH, visceral obesity and hyperinsulinemia. RAAS is known to play a major role in pathophysiology of SAH and liver diseases. Increased BMI influenced the activity of RAAS and synthesis of adipocytes.

Our objective is to analyze the relationship between M235T polymorphism in patients with SAH and NAFLD, dyslipidemia, carotid atheromatosis and increased BMI.

Material and methods. We included 67 patients with SAH, to which we performed BMI, lipid profile, abdominal ultrasound and carotid arterial Doppler ultrasound. Alcohol consumption was excluded. The patient genotype was determined using PCR and restriction fragment length polymorphism. The statistical analysis was performed using EpiInfo7 statistic software.

Results. The group included 32 women and 35 men. The prevalence of carriers of M235T mutation was 77.6%; 37 patients were heterozygous. The carriers have 78% NAFLD, 71% carotid atherosclerosis and 57%, CMIT >1 mm, 86% LDL-hypercholesterolemia, 49% hypertriglyceridemia, 86% obesity and overweight. We found statistical significance between the presence of the mutation and GIM> 1 mm ($p<0.04$), carotid atherosclerosis ($p<0.01$), hypertriglyceridemia ($p<0.05$). The presence of NAFLD had a correlation trend, with no statistical significance ($p<0.09$).

Conclusions. In the case of patients with SAH, the M235T mutation of AGT mainly associates with carotid atheromatosis and the presence of hypertriglyceridemia, as an associated risk factor. More data is needed for association between NAFLD and M235T polymorphism.

Phenolic composition and antioxidant capacity of the medicinal mushrooms Trametes versicolor and Trametes gibbosa

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Introduction. Trametes versicolor sp. mushroom is considered a medicinal mushroom with important pharmacological properties. It is commonly used in the traditional Chinese medicine because of its known antioxidant and antiinflammatory activity, immune-enhancing activity, anticancer activity, antiviral effects, antimicrobial, prebiotic activity and anti-diabetic effect. Among the bioactive compounds with important biological activities, the polysaccharides fraction and the amino acids were intensively studied. However, few studies analysed Trametes versicolor phenolic compounds composition, known for their antioxidant properties.

Materials and methods. The phenolic compounds profile (high performance liquid chromatography HPLC-MS and Fourier-transform infrared spectroscopy FTIR), the antioxidant capacity (DPPH assay), total phenolic compounds and total flavonoids content (colorimetric assay) were determined for Trametes versicolor (TV) and Trametes gibbosa (TG) mushrooms. Various extracts of these mushrooms (water, methanol, and acetone) were analyzed.

Results. The phenolic compounds profile included 28 compounds, tentatively identified as phenolic acids, flavonols, flavones, coumarins, flavanols, isoflavonoids and biflavonoids. Comparing the two mushroom extracts, TG methanolic extract had the highest antioxidant activity (0.5 mM Trolox/1 ml extract), followed by TV water extract (0.4 mM Trolox/1 ml extract). Regarding the total polyphenols content, the highest concentration was obtained for both TV and TG water extract with values of 46 and 43 mg gallic acid equivalents /100 g fresh weight, respectively. The water extract of TV had the highest total flavonoids content (15 mg quercetin equivalents/100 g fresh weight), followed by TG methanolic extract (12 quercetin equivalents /100 g fresh weight).

Conclusions. The results obtained are confirming that Trametes species are valuable sources of bioactive compounds with important antioxidant properties.

Influence of a cocoa drink product on physical training in sedentary persons

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Background. Physical training can lead to fatigue and sympathetic reactions. Cocoa (CO) is known for its antifatigue and antioxidant effects. Objectives. This study aimed to evaluate the influence of a cocoa drink product (COP), on physical training, on sedentary people.

Material and methods. The physical training model chosen was pedaling on a cyclogerometer for 19 minutes a day for one week. 24 healthy volunteer subjects, men, were randomized divided into: control group (C = 8) without treatment; groups who received COP prior to treatment for one (CO1 = 8) and two weeks (CO2 = 8) respectively. Analyzed.indicators: fatigue state (FT) and heart rate (HR). Parameter determinations were performed 24 hours (T1) before the training starting; 15 minutes (T2) and 4 hours

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(T3) after physical exercise, on days 1 (T2-1/T3-1), 4 (T2-2/T3-2) and 7 (T2-3/T3-3). Statistical evaluation was based on the Student test.

Results. It was found that for C, compared to T1, the most significant increases were to: T2-1, T2-2/T3-2, T2-3/T3-3, for HR; and T2-2/T3-2, T2-3/T3-3, for FT. At CO1 and CO2 compared to C, the values were significantly low at: T2-1, T2-2/T3-2, T2-3/ T3-3, for HR; and T2-2/T3-2, T2-3/T3-3 for FT. The impact of COP on CO2 was more intense than CO1, differences being significant at T2-2 and T2-3/ T3-3, for HR and FT.

Conclusions. 1) Under the COP influence, HR and FT were significantly reduced to CO1 and CO2, compared to C, after the first 4 training days. 2) There were differences between C and CO1 / CO2 for the dynamic evolutions of HR and FT. 3) COP administration for 2 weeks compared to one week was more effective on HR and FT. 4) We suggest the use of COP, especially for 2 weeks, before a physical training on a cyclogerometer, for HR and FT modulation, in sedentary persons.

Keywords: cocoa, physical training, heart rate, fatigue

Influence of noise and music on acute physical stress in sedentary persons

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Background. Noise and physical exercise could be stress factors. Music (M) is know for its anti-stress effects. Objectives. This study aimed to evaluate the influence of noise (NS) and music (MS), on acute physical stress, in sedentary persons.

Methods. 24 voluntary healthy men subjects were randomized divided in: control group (C=8), without NS/MS; group that received NS (N=8), and group that received MS (M=8). Selected NS was the one of urban traffic and selected MS was instrumental. Subjects of N and M received noise/music during the stress. Stress was represented by an intense and short term physical effort, made with a cyclergometer. Assessments were done: 24 hours (T1) and 15 min (T2) before stress; 15 min (T3) and 120 min (T4) after stress. Analyzed indicators: anxiety (A) and heart rate (HR). Statistical analysis was made on the basis of Student test.

Results. In C and N, compared to T1, the most significant increases were at T2 and T3, for A and HR. In C and N compared to M, values were significantly increased for A and HR at T2 and T3. MS.impact was similar on A and HR, at T2, T3, T4. MS influence was more pronounced on A than on HR, but.differences were not significant. The MS effect on A and HR was the most intense immediate pre-stress.

Conclusions. 1) There were differences for the dynamic developments of A and HR, between C, N and M. 2) N incresed the stress effect of the physical effort, on both A and HR, immediately pre- and post-stress moments. 3) MS influence was similar for A and H, and significantly reduced A and HR immediately pre-/ post-stress moments. 4) We suggest MS use for A and HR modulation, in stress caused by cycling on the cyclergometer in sedentary people.

Keywords: stress, music, physical effort, cycle ergometer, anxiety, heart rate

Rhodiola Rosea influence on heart rate and salivary pH in physical stress

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Introduction. Rhodiola Rosea (RR) is one of the most important adaptogens.

Objective. The objective was to prove RR product (RRP) action on two parameters in stress induced by an intense physical effort.

Material and methods. Healthy volunteer 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 physical stress: an intense physical effort on cyclogergometer. Analyzed parameters: heart rate (HR) and salivary pH (SpH). Parameters evaluation was made: prior to P and RRP administration (T1); 15 min before (T2), 15 min (T3) and 4 hours (T4) after stress. Statistical evaluation was made on the basis of Student test.

Results. HR values were significantly higher at T2 and T3 for C and P compared to T1 and RR. SpH values were significantly lower at T3, T4, for C and P compared T1 and to RR. RR influence was more intense on HR than on SpH, but the differences were not significant. The RR effect on HR was the most intense immediate prestress and on SpH immediately poststress.

Conclusions. 1) Dynamic development was different for the three groups for both parameters. 2) RRP influenced the two parameters, pre-poststress. 3) RRP influence was more intense on HR than on SpH. 4) We suggest the RRP administration on the intense physical effort for.HR and SpH modulation.

Keywords: Rhodiola Rosea, physical streiss, heart rate, salivary pH

Brief analysis of the Citruses - Stress relationship, from the perspective of PubMed publications

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Background. Citruses (C) and Stress (S) represent subjects of research interest, but C-S relationship is modest investigated.

Aims. The purpose of the present paper is a brief analysis of the C-S relationship from the perspective of PubMed publications.

Material and methods. C-S relationship was analyzed in three types of investigations. A) Comparative analysis for the keywords combinations: C and Heart rate (C-HR), C and Pulse (C-P), C and Cortisol (C-Ct), C and Salivary Cortisol (C-SC), C and Inflammation (C-I), C and Leucocytes (C-L), C and Macrophages (C-M), C and Depression (C-D), C and Anxiety (C-A), C and Fatigue (C-F). B) Analysis for the filters: Species, Sex, Ages. C) Administration, Results.

Results. A) Total number of C-S publications was 910 for 59 years since 1959 to date. % of publications from C-S was 9.6% for C-HR, 13% for C-P, 25% for C-Ct, 0.3% for C-SC, 40% for C-I, 15.4% for C-L, 13.7% for C-M, 7.3 for C-A, 7.1% for C-D, 2.85 for C-F. B) For all keyword combinations most publications were with human subjects of both genres with age between 19-44 years. C) For all keyword combinations most publications were in favor of citrus; the way of administration was mentioned but the dose was not mentioned.

Conclusions. 1) Number of PubMed publications for C-S has an average of 15.4

publications per year; the number of publications for 2018 is 117. 2) Of C-S most of the publications were for C-I. 3) For most C-S studies, young human subjects of both genres were preferred and the results supported the benefits of C. 4) Studies on the C-S relationship, still moderate numerically, are still increasing in recent years covering the areas of interest.

Keywords: citrus, stress, cortisol, inflammation, anxiety, PubMed filters

Efficacy of unique dose chlorogenic acid (100 mg/kg/day) in carrageenan-induced rat paw oedema

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Introduction. Chlorogenic acid (CGA), a natural chemical compound found in green coffee, is a substance with antioxidant effects. The aim of this study was to evaluate the efficacy of a single dose of chlorogenic acid in rats with experimental inflammation, in comparison with a well-known anti-inflammatory medication (indomethacin).

Material and methods. The animals, randomly allocated in 3 groups, received physiological salt (0.5 ml/day) by oral gavage, for 7 days. On the 7th day, the rats were intraplantar injected with carrageenan and after one hour they received, by oral gavage, a single dose of either chlorogenic acid (100 mg/kg/day) or indomethacin (1 mg/kg/day). Measurements for paw's inflammation were done using a plethysmometer, at 2 hours and at 24 hours after carrageenan injection. The inflamed paws' tissues were taken for determination of oxidative stress parameters: malondialdehyde, glutathione, glutathione disulfide.

Results. Plethysmometry showed at 2 hours after carrageenan injection significant decreases of inflammation in all treated rats. At 24 hours, plethysmometry presented significant decreases of inflammation only in animals treated with indomethacin. In tegument, CGA and indomethacin had antioxidant effects.

Conclusions. Our study demonstrated the anti-oedematous and antioxidant effects of a single dose of chlorogenic acid (100 mg/kg/day) in experimental inflammation.

The Influence of GSTT1/GSTM1 polymorphic variants on the occurrence and impact of psoriasis

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Introduction. Psoriasis is a chronic dermatological condition which, through its comorbidities, affects a multitude of organs and systems. Its chronic, relapsing character, coupled with the lack of curative treatment options, translates to a diminished quality of life in patients affected by this condition. The purpose of the present study is to shed light on how the variants of the antioxidant enzyme glutathione S transferase impact the occurrence of psoriasis, as well as its potential role in response to biological therapies.

Materials and methods. The study groups are comprised of 39 patients and 125 healthy controls. Peripheral venous blood was drawn and used to obtain genomic DNA, which was amplified through a PCR-Multiplex protocol, with the aim to detect the GSTT1 and GSTM1 isoformes.

Data regarding the patients' demographic parameters, condition history, prior treatment and response, as well as PASI and DLQI scores was gathered.

Results. The GSTT1 and GSTM1 null.alleles are correlated with the development of psoriasis (OR= 1.123, CI 95% 0.701-1.465, p=0.045 and OR=1.092, CI 95% 0.731-1.322, p=0.049, respectively). The present GSTM1 allele is correlated with the development of psoriasis (OR=0.981, CI 95% 0.799-1.322, p=0.039). In the Infliximab responder group, PASI is correlated with null GSTT1 (OR 1.899, CI 95% 1.564-2.201, p=0.048) as well as null GSTM1 (OR 1.566 CI 95% 1.023-1.877, p=0.049). The GSTT1 null allele is also correlated with DLQI in the same subgroup (OR=1.889, CI 95% 1.559-2.102, p=0.045). The combined GSTT1 GSTM1 null genotype is correlated with the development of psoriasis (OR=1.469, CI95% 1.103-1.89, p=0.048).

Conclusions. The GSTT1 and GSTM1 null genotypes seem to be a risk factor for the development of psoriasis, individually as well as combined, while the presence of the GSTM1 allele acts as a protective factor for the development of psoriasis. The null GSTT1 genotype is correlated with poorer PASI and DLQI scores in Infliximab responders.

Evaluation of optimization strategy for anti-TNF alpha treatment in patients with spondylartritis. Data from Registrul Român de boli Reumatice (RRBR) [Romanian Registry of Rheumatic Diseases]

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Introduction. The monthly cost of treatment with anti-TNF-alpha agents in patients with spondylarthritis (SpA) amounts to almost 1,000 euros. Optimizing the biological agent dose in patients with clinical rheumatic inflammatory disease is a therapeutic strategy used in recent years. Some studies and management recommendations suggest that SpA patients could get the same benefit at a lower dose of biological agent.

Objective. The purpose of our study is to evaluate the effectiveness of the strategy to optimize anti-TNF-alpha treatment in SpA patients evaluated in everyday clinical practice. The main objective is to identify the predictive factors of sustained remission.

Material and methods. An observational study was performed in which all SpA patients from. RRBR in whom anti-TNF-alpha treatment that has been optimized were included. Optimization dose is defined as administration of less than anti-TNF-alpha therapy dose or longer time intervals than those set out in the Summary of Product Characteristics. To qualify for treatment optimization, patients should be in clinical remission at 2 successive evaluations. Demographic, clinical and laboratory parameters were collected at initiation of biological therapy (TB) and at the time of optimization of treatment. We calculated the persistence of the biological treatment through the Kaplan-Meyer curves. For comparison of the mean values of the variables we applied nonparametric / parametric tests, statistical significance $p < 0.05$.

Results. Table 1. Parameters of disease activity in relapse patients and those who remain in remission.

Conclusion. Optimizing the dose of biological treatment in SpA patients is possible and allows for clinical remission to be maintained in almost half of patients. Our current data can not determine whether there is any factor that could be predictive of maintaining response after optimization at the start of treatment.

A retrospective study of invasive fungal infections in hospitalized patients in the "Prof. Dr. O. Fodor" Regional Institute of Gastroenterology and Hepatology of Cluj - Napoca

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Introduction. The aim of this study was to evaluate the distribution of fungal species isolated from bloodstream infections and the assessment of antifungal resistance.

Material and methods. A retrospective study was developed between January 2016-May 2017 regarding fungal bloodstream infections from hospitalized patients in the Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca. The fungal strains were grown in BacT/ALERT® system. Fungal identification was performed with VITEK®2 Compact automated system using YST ID cards. Antifungal susceptibility testing was performed with AST-YS07 VITEK®2 card, according to CLSI.

Results. Out of 1992 blood cultures, 512 were positive, 19 with fungal pathogens. The fungal strains were isolated from immunosuppressed patients with digestive malignancies on ICU (9 females, 10 males, average age: 59.1 years). Twelve (63%) of these patients died (6 males, 6 females).The positive range of blood cultures was 2.47 days. Candida glabrata was the most isolated species (n=10, 45%), Candida albicans (n=7, 30%), and one strain of the following species (5.26%): Candida tropicalis, Candida krusei, Candida parapsilosis, Candida pulcherrima, Saccharomyces cerevisiae. In 7 cases (36.84%) fungi were associated with one or more bacterial species. The association of two Candida species (C. albicans and C. glabrata) was found in 2 cases (10.52%). All Candida species were susceptible to caspofungin and micafungin. Only one C. glabrata strain was resistant to fluconazole (MIC≥32) (3 strains) and voriconazole (MIC=4). C. krusei was also resistant to fluconazole (intrinsic resistance). One strain of C. albicans and C. glabrata were intermediate to amphotericin B (MIC=2). C. krusei was resistant to 5-flucytosine (MIC=8).

Conclusion. Non-albicans Candida species were predominant, C. glabrata being the main involved species. No resistance to echinocandins was reported. Polimicrobial bloodstream infections, involving Candida species, are rare.

Retrospective study of polymicrobial bloodstream infections involving bacteria and Candida species in hospitalized patients from the "Prof. Dr. O. Fodor" Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca

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Introduction. Polymicrobial bloodstream infections (BSIs) are less common, but. more severe. This study aims to determine the etiology of BSIs in alarming antimicrobial resistance areas.

Material and methods. A retrospective study was developed between January 2016-May 2017 regarding BSIs in hospitalized patients. It was considered a total number

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of blood cultures (BCs), number of positive BCs, positive range of BCs, mono- and plurietiology of sepsis, involving bacteria and Candida species. BCs were processed using BacT/ALERT® system and bacterial and fungal identification with VITEK®2 Compact system.

Results. Out of 1992 BCs, 512 (25.7%) were positive, 245 (47.8%) with Gram–positive pathogens (GPp), 192 (37.5%) with Gram–negative pathogens (GNp), 13 (2.5%) with yeasts, and 62 (12.1%) had polymicrobial etiology. The mean time to positive BCs for GPp was 3.56 days, for GNp 1.9 days, and for yeasts 3.55 days. Average time to positive BCs for polymicrobial BSIs was 1.75 days [range: 0.5-5]. The most frequent combination of isolated microorganisms were grouped as follows: two bacterial species GPp+GNp (n=22, 35.5%), GNp+GNp (n=12, 19.4%), GPp+GPp (n=9, 14.5%), more than three bacterial species in 9 cases (14.5%). Bacteria (one or more species) and Candida spp. were responsible for 9 cases (14.5%). Species shown.responsible for polymicrobial BSIs are: C. albicans (n=6, 9.7%), C. glabrata (n=5, 8%), C. pulcherrima (n=1, 1.6%), K. pneumoniae (n=21, 33.9%), A. baumannii (n=14, 22.6%), E. coli (n=9, 14.5%), P. aeruginosa (n=8, 13%), P. mirabilis (n=5, 8%), Enterococcus spp. (n=23, 37%), coagulase–negative staphylococci (n=19, 30.6%), S. aureus (n=9, 14.5%) and anaerobes (n=6, 9.7%).

Conclusion. Our data showed a high percentage of polymicrobial BSIs, involving many bacterial species. The association of two bacterial species was the most common. The lowest positivity rate was observed at polymicrobial BSIs.

The prognostic value of some immunological markers in malignant melanoma

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Introduction. Malignant melanoma (MM) is the most aggressive type of skin cancer, with an ever increasing incidence among the Caucasian population and a mortality that accounts for 90% of all skin neoplasias. Over the decades, the relationship between cancer and the immune reactivity has been well-researched, being associated with increased levels of various serum markers of inflammation. This study aims to assess the various prognostic factors, both histopathological (mitotic index, tumor resection margins, tumor ulceration), as well as paraclinical (neutrophils/leukocytes ratio = NLR), for their subsequent use for early diagnosis, response rate to treatment and overall survival rate.

Materials and methods. 43 patients, aged between 25 and 83, diagnosed with MM and treated with adjuvant therapy with Interferon-α (IFN-α), at the "Prof. Ion Chiricuta" Institute of Oncology, Cluj-Napoca. Demographic, histopathological and laboratory data (NLR) was collected and evaluated before and after the first cycle of treatment with IFN-α. For the analysis of different correlations, Fisher's test, Chi-square test, Spearman test and non-parametric Mann Whitney test were used. The data was processed in GraphPad Prism.

Results. Following the statistical tests, a statistically significant correlation was found between the mitotic index and the tumor stage (p=0.01). With regards to the number of positive tumor nodes (greater than 1), it correlated with the mitotic index mentioned above (p=0.02), as well as with the resection margins (p=0.008) and the presence of tumor ulceration (p=0.003). Furthermore, a NLR preC1 value >0.5 (before the first cicle of IFN-α) is associated with a mitotic rate >3 mitosis/mm2 (p=0.005), thus with a poor prognosis.

Conclusion. In addition to histopathological prognostic factors known to have significant value in predicting the progression of MM, NLR preC1.(IFN-α) could be a prognostic marker in the evolution of this oncologic pathology.

Serum biomarkers for the assessment of inflammation in overweight or obese subjects

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Introduction. Accumulation of fat tissue may activate the inflammatory mechanisms and induce chronic inflammation in obese or overweight subjects. Our study aimed to identify the main circulating biomarkers used as pro-inflammatory or anti-inflammatory signals.

Material and methods. The search strategy was designed in MeSH and applied in PubMed on October 10, 2018. The keywords used in searching were (((”Overweight”[Mesh]) OR ”Pediatric Obesity”[Mesh] OR ”Obesity”[Mesh]) NOT (”Neoplasms”[Mesh]) AND ((”Inflammatory Biomarkers” OR ”Anti-inflammatory Biomarkers”) AND (”Inflammation”[Mesh]))). The search was restricted to humans, English language and a number of 35 full-text articles published over the last five years were retrieved and evaluated.

Results. The majority of studies on both adults and children determined the following markers: hsCRP (high-sensitivity C-Reactive Protein), quantified using ultrasensitive latex-enhanced Immunoturbidimetric Assay, interleukin-6 and tumor necrosis factor-α, measured by ELISA kits. Other molecules whose concentrations correlated to CRP and IL-6 blood levels, evaluated using ELISA assays are leptin, adiponectin (which decreases as the BMI value increases), MCP (monocyte chemo attractant protein)-1, matrix metalloproteinase (MMP)-9. Soluble CD14 and CD16 analyzed by ELISA assays showed low levels of CD14 (dim) and CD16+ cell counts positively correlated with BMI. Conflicting results regarding the serum levels of pentraxin-related protein (PTX3) and chemerin (retinoic acid receptor responder protein 2) and their local activity were reported.

Conclusion. C-reactive protein, interleukin-6, and tumor necrosis factor-α were the most frequently reported serum biomarkers. The most recent markers, such as serum levels of pentraxin-related protein (PTX3) and chemerin, need further investigations.

MEDICAL SCIENCES

SNPs in genetic association studies: single locus versus multilocus analyses

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Introduction. Due to the completion of human HapMap proje¬ct and the development of high-throughput genotyping methods, single nucleotide polymorphisms (SNPs) have been in the focus of recent studies on the genetic underpinnings of complex traits and diseases. However, the way in which the effect of these markers is tested differs from one research to another. Some genetic association studies analyze single SNPs, but considering their small individual contribution to polygenic phenotypes, the reliability of this approach has been recently questioned.

Objective. In this study, we will describe the advantages and shortcomings of modern genetic analyses: single SNPs versus haplotype versus diplotype vs MGPSs (multilocus genetic profile scores); we will illustrate them using data from studies in our laboratory, focused on SNPs and cognitive risk factors for neuropsychiatric disorders.

Methods. A sample of N=309 volunteers were genotyped for several SNPs for BDNF (Brain derived Neurotrophic Factor) and Catechol-O-methyltransferase (COMT) genes. The single locus and multilocus analyses were performed using Haploview and Plink v 1.07 software.

Results and discussion. The results indicated that the haplotype (a combination of marker alleles on a single chromosome, which have the tendency to be inherited as a unit) has a relatively greater effect and is thus more promising statistically than single locus analyses. To increase power even further, several studies have begun to examine the cumulative effect of multiple polymorphic loci on a specific signaling mechanism (multilocus genetic profile scores - MGPSs). These analyses allow us the inclusion of SNPs without a significant independent effect, which may nonetheless have an interactive effect on the phenotype.

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Effect of sleep apnea syndrome on glycemic variability in patients with type 2 diabetes

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Introduction. Acute glucose fluctuations around the mean glucose values (glycemic variability) activate oxidative stress and proinflammatory proteins, two of the molecular mechanisms underlying the development of chronic complications in type 2 diabetes. Sleep apnea syndrome (SAS), and particulary oxygen desaturation during sleep, has a deleterious effect on glycemic control in patients with diabetes. The objective of this research was to investigate the effect of SAS on glycemic variability in patients with type 2 diabetes.

Material and methods. Between November 2010 and May 2011, 18 patients with type 2 diabetes (10 with untreated SAS and 8 without SAS - control group) presenting for routine visit in an outpatient clinic were invited to perform a cardio-respiratory study (ApneaLinkTM, ResMed Corporation, Poway, Calif) concomitantly with a continuous glucose monitoring.

Results. Compared with controls, patients with SAS had significantly higher mean amplitude of glucose excursions (MAGE; 83.8 vs. 49.2 mg/dl, p=0.01), largest amplitude of glycemic excursions (LAGE; 181.1 vs. 114.1 mg/dl, p=0.04) and SD of interstitial glucose values around a mean glucose value measured over a 24 h period (SD24; 42.5 vs. 27.5 mg/dl, p=0.01) and measured during night (SDnight, 23.8 vs. 15.5 mg/dl, p=0.04). MAGE was associated with lowest (β=-0.604, p=0.005) and mean (β=-0.502; p=0.039) O2 saturation during sleep. SDnight was associated with oxygen desaturation index (β=0.564, p=0.030) and lowest O2 saturation during sleep (β=-0.810, p <0.001). All associations were independent of age, gender, HbA1c, diabetes duration and diabetes therapy. No association of LAGE and SD24 with sleep respiratory parameters was observed. None of the glycemic variability parameters were associated with the severity of SAS.

Conclusion. Higher levels of oxygen desaturation during sleep are associated with increased overall and nocturnal glycemic variability in patients with type 2 diabetes.

The importance of early diagnosis in amiotrophic lateral sclerosis

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Introduction. Amyotrophic lateral sclerosis (SLA), also known as Lou Gehrig's disease and Charcot's disease, is caused by the death of motor neurons in the cerebral cortex and the spinal cord. SLA is characterized by progressive motor deficiency, predominantly at the level of upper or lower limbs, or even hemiparetic debut.

Method. We present the case of a 62-year-old man, ex smoker 40 PA, who is admitted in the Pulmonary Service for breathlessness at moderate efforts, cough with mucopurulent expectoration, noisy snoring, apnea reported by the family, asthenia, fatigue, dysarthria. From the anamnesis and objective examination, it is raised the suspicion of an obstructive pulmonary syndrome and associated type II respiratory failure. Functional respiratory tests are performed that reveal severe mixed dysfunction, with FEV1 <1L. Additionally, nocturnal cardiorespiratory polygraphy is performed that detects the presence of an obstructive sleep apnea syndrome and the patient follows autoCPAP therapy at home associated with chronic medication. Later on, he is hospitalized in the Intensive Care Unit showing coma, type II respiratory failure, severe respiratory acidosis and he was intubated and then safely detubated, returning to our service with altered general condition, excessive sleepiness, bradilalia, dysarthria, hemiplegia at the left half of the body. Neurological consultation establishes the diagnosis of amyotrophic lateral sclerosis, and for this reason, due to the association of hypercapnic respiratory failure, non-invasive ventilation therapy was indicated, with BiPAP ST mode, with a partially favorable evolution in dynamics.

Conclusion. It is important to establish the early diagnosis of amyotrophic lateral sclerosis and to initiate non-invasive ventilation therapy at home, as well as the use of secretion management devices, because they increase both survival and quality of life and often the death of these patients often occurs due to respiratory failure.

Carfilzomib efficacy and safety in relapse / refractory multiple myeloma – single center experience

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Introduction. Relapsed and refractory myeloma (RRMM) is defined as progression of therapy in patients who achieve minor response or better, or who progress within 60 days of their last therapy. Treatment of RRMM and relapsed myeloma presents a therapeutic challenge, because of the heterogeneity of disease at relapse. Proteasome inhibition is highly effective treatment for multiple myeloma. Carfilzomib is a second generation proteasome inhibitor approved for the treatment of patients with multiple myeloma receiving at least a second line of therapy. Carfilzomib and dexamethasone significantly improve overall survival.

Material and methods. 23 RRMM patients were included. Data were collected from patient files retrospectively.The patients were treated between february and september 2018. It was analyzed the demographic characteristics of the patients, the stage of the disease at the beginning of Carfilzomib treatment, the overall survival, the response rate to the treatment, the adverse events.

Results. 12 cases (47% male, 52.17%female) were included in the study, patients received 3 or more courses of treatment. The median age of the study population was 64 years (range 40-82 years), and 65% of the patients were age 60 years or older. 67% of the study participants were diagnosed in ISS stage III, 33% in ISS stage II. Among the 23 of cases, 12 patients received two or more previous therapies. The overall response rate was 78%. The 6 month overall survival was 73%. Carfilzomib was well tolerated. The non-hematological AEs included nausea (8%), fatigue (16%), pneumonia (16%), upper respiratory tract infection (8%), one patient developed peripheral neuropathy. The most common hematological AEs included thrombocytopenia (43%), and anemia (16%).

Conclusion. In the setting of refractory and relapsed multiple myeloma, carfilzomib in a combination regimens yields effective results with a manageable toxicity.

Hyperimmunoglobulin E syndrome – rare in pediatric practice, but still a diagnostic to consider

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Introduction. Hyperimmunoglobulin E syndromes (HIES) are rare primary immunodeficiency diseases characterized by markedly elevated serum immunoglobulin (Ig) E, chronic eczema, infections, skeletal and connective tissue involvement. To date, information about pediatric HIES is limited.

Case report. An 8 year old boy presented for the evaluation of a chronic facial rash and recurrent hyper IgE levels. He had a history of respiratory and digestive allergies, recurrent upper and lower respiratory tract infections, hyperlaxity of joints, and scoliosis. His family history was negative for features suggestive of HIES. The patient's highest serum IgE level was 3200 U/L and he had eosinophilia to 14.2% (850 cells/μL). Other laboratory studies showed normal levels of serum IgG, IgA and IgM. The patient's NIH HIES clinical score for HIES was >40 which predicted that a STAT3 mutation was likely.

Conclusions. HIES could be misdiagnosed, including our case. Besides the extremely high level of IgE, noticing the proneness to the infectious disease, and the chronic eczema we could prompt further diagnostic work-up. We should raise awareness of this rare disease because early recognition is of clinical importance in prognosis and management.

Severe heart failure due to Galen malformations – case report

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Galen malformation is a rare brain vessel abnormality, in which there is an aneurismal dilatation and a direct communication between the arterial and cerebral venous system. It result from persistent shunting of primitive choroidal vessels into the median of the prosencephalic vein of Markowsky. Family cases have been reported. It seems to be a mutation of the gene RASA1, with dominant autosomal transmission. Although it is the most common arterio-venous malformation in the newborn, the anomaly is rare. Its true incidence is unknown. There is increased cerebral venous pressure that can lead to cerebral ischemic damages, hydrocephaly and congestive heart failure. The large volumes of blood under high pressure returning to the right heart may cause severe congestive heart failure. Larger arterio venous shunts correlate with severe hemodynamic effects and early onset of symptomes. The aim of this paper is to review the literature on the diagnosis, medical treatment and endovascular embolisation. We present a 37 weeks gestational age male new born , with severe congestive heart failure with onset on the first day of life. Serial echocardiography and head ultrasound were performed. Angio CT transcends the diagnosis. The treatment was supportive. Vasoactive amines were administered (Dopamine), cardiotonic (Dobutamine) and diuretics; drug closure of the patent ductus arteriosus was performed. Endovascular embolization with partial occlusion finally was done, which will be repeated after the age of 6 months.

Effects of weight loss on epicardial fat after laparoscopic sleeve gastrectomy - a 2D echocardiographic study

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Introduction. Obesity is a risk factor for cardiovascular disease and mortality. Epicardial fat (EF) is a visceral fat deposit, located between the heart and the pericardium, which shares many of the pathophysiological properties of other visceral fat deposits. EF> 5 mm has been proposed as a marker of cardiovascular risk. Significant weight loss after bariatric surgery has beneficial effects on cardiac function, particulary due to left ventricular (LV) hypertrophy regression. Less information exist in literature concerning evolution of epicardial fat after weight loss, or its importance to cardiovascular risk. We therefore evaluated the consequences of significant weight loss after laparoscopic sleeve gastrectomy (LSG) on LV morphology and function, but also on EF changes.

Material and methods. We performed a 2D echocardiographic study in obese patients before and after significant weight loss due to LSG surgery. Echocardiography was used to measure LV mass, LV systolic and dyastolic function, and EF. We measure EF in diastole on the right ventricular free wall in two locations, from both parasternal longitudinal and subcostal views.

Results. 40 patients (age 44.5 ± 12.7 yrs, body mass index 48.54 ± 6.9 kg/m2) underwent 2D-echocardiography before and a median 11.4 months after LSG surgery performed at the Municipal Hospital of Cluj-Napoca. The BMI declined by 13.3 ± 6.3 kg/m2 ($p < 0.001$). The LV mass decreased from 135.3 g ± 33.3 g to 119.0 g ± 32.7 g ($p = 0.001$), but the LV chamber volumes and systolic function remained unchanged. After LSG surgery, EF was reduced by 3.4 mm ± 1.1 mm ($p < 0.001$). There was a significant correlation for change in EF with change in LV mass ($R = 0.63$, $p = 0.02$).

Conclusion. Significant weight loss in obesity after LSG surgery is accompanied by a regression of LV mass, with no apparent change in cardiac volume or function. Along with LV mass changes, we found a significant reduction in EF.

Prognostic value of serum albumin on the intrahospital evolution of patients with unstable angina

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Introduction. Hypoalbuminemia is considered an independent prognostic factor for cardiovascular disease and it is associated with myocardial infarction, heart failure, atrial fibrillation and stroke. The aim of this study was to establish in which way the serum albumin level of the patients with unstable agina correlates with the evolution during hospitalization.

Method and materials. We enrolled 40 pacients with unstable angina admitted in Emergency County Hospital, Cardiology Department , Cluj-Napoca. They were diangnosed with unstable angina in conformity with the guidelines from the European Society of Cardiology and were evaluated during hospitalization. We considered as unfavorable evolution if the patient had developed frequent episodes of angina, signs of heart failure, heart rhythm disorders. The serum level of albumin was measured on the admission. We also studied the presence of traditional cardiovascular risk factors in the study group.

Results. Patients with unstable angina and low serum albumin under 3.4 mg/dl at admission (Se-62.5%, Sp-68.7%, 20 patients) had more frequently an unfavorable evolution during hospitalization (p=0.043, AUC=0.691, 95% CI (0.528;0.855), Ex(B)=0.193). Serum albumin level was inversly correlated with the risk of developing rhytm disorders (p=0,045, Ex(B)=0.217) and systolic dysfunction (ejection fraction < 50%) (p=0.026, Ex(B)=0.144, AUC=0.746).

We didn't find a correlation between albumin levels and traditional cardioavscular risk factors: age (p=0.107), sex (p=0.215), smoke (p=0.760), diabetes mellitus (p=0.454), LDL cholesterol (p=0.154), body mass index (p=0.793) and arterial hypertension (p=0.138).

Conclusion. Low serum albumin at admission can be used as a negative and independent prognostic factor in the clinical evolution of patients with unstable angina during hospitalization.

Cause of death among people living with HIV Infection: Cluj-Napoca AIDS Center Experience

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Introduction. Fifteen thousand nine people lived with HIV infection in Romania, on December 31st, 2017. This study aimed to evaluate the mortality patterns and causes of death among HIV-infected individuals in Romania.

Material and methods. A retrospective cohort study was conducted at the Cluj-Napoca AIDS Center. Our center had in evidence patients from five counties from the North-West of Romania (Cluj, Sălaj, Maramureş, Satu-Mare, and Bihor). All HIV-infected patients diagnosed from 1997 through 2017 were included. The medical charts were reviewed, and data regarding the causes of death were collected.

Results. Between 1997 and 2017, 704 HIV-infected patients were registered and followed up in the Cluj-Napoca AIDS Center. Five hundred and sixty-five patients were still in evidence, and 15 were lost from follow-up. A total of 124 deaths were registered during follow-up (17.61%, 95%CI: 14.92 to 20.59]). Mortality was in most of the cases related to an AIDS-defining illness (91/124) as compared to other causes of death

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(33/124). One hundred and eleven patients (89.51%) had Ly CD4 count under 200/mm3 and advanced immunodepression, eleven patients had Ly CD4 count between 200 and 500/mm3. In most of the cases (88/124, 70.96%) of deaths took place in the hospital.

Among those with deaths related to AIDS-defining illness, infection was the most common cause seen in 55/91 of cases (e.g., 10.99% bacterial sepsis, 19.78% tuberculosis, 13.19% pneumonia with Pneumocystis jirovecii, 6.59% cryptococcosis meningitis, 9.89% HIV-encephalopathy). The next common observed causes were malignancies (16.48%), cerebral toxoplasmosis (7.69%), Kaposi sarcoma (4.40%), wasting syndrome (9.89%), or progressive multifocal leukoencephalopathy (1.10%). The non-HIV related death were suicide, myocardial infarction, liver failure, renal failure, or accidents.

Conclusion. As expected, the main causes of death are HIV-related.

Diverticular disease: a systematic review

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Introduction. The diverticular disease (DD) of the colon is a widespread disease in developed countries, associated with significant economic burden in direct health care expenditures and in indirect costs to society (estimated at $4 billion dollars per year). Clinicians need to remain updated with new data on epidemiology and pathophysiology. The aim of this study was to undertake a systematic review on epidemiology and pathogenesis of DD.

Methods. A systematic literature search was performed on the PubMed database up to August 2018, using the following terms: ”colonic diverticulosis”, ”diverticular disease”, ”epidemiology”, ”pathophysiology”, according to the PRISMA methodology. We limited our research to articles published in English, conducted on human subjects, and with available abstracts. The following outcome parameters were assessed: incidence, prevalence, pathogenesis of diverticulosis and diverticular disease and risk factors for the development of acute diverticulitis and complicated diverticular disease. Reviews, case reports, conference presentations, letters to the editor, editorials, comments and opinions were not taken into consideration.

Results. Of the 108 articles identified in the PubMed/Medline database, 40 articles were eligible and included in the analysis. The prevalence of diverticulosis is largely age dependent, with a rate of less than 5% in people under 40 years of age, increasing up to 70% in people aged 80 years. Diverticular disease is commonly found in developed countries, slightly more frequently in USA than in Europe, and is a rare condition in Africa. The pathogenetic mechanism of diverticular disease is not fully understood, but are likely to be the result of interactions among age, diet, changes in the colonic wall structure, motility disorders and genetic factors. The majority of patients (80-85%) will remain asymptomatic during their lifetime. Symptoms occurrence is the latest subject up for debate. Different hypotheses have been elaborated, tackling subjects such as bacterial overgrowth and low-grade inflammation. Recent studies have associated specific host immune responses and the microbiome as contributors to diverticulitis. Diet, hereditary factors may raise an individual’s personal risk.

Conclusions. Diverticulosis is a multifactorial condition. Although a common condition, diverticular disease perturbs countless aspects of an individual’s life.

Analysis of the left atrial appendage function by intracardiac echocardiography in patients with atrial fibrillation

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Introduction. Intracardiac echocardiography (ICE) is frequently performed during catheter ablation procedures in order to guide the transseptal puncture and has been recently used to evaluate the morphology of the LAA. The objective of this study was to evaluate the feasibility of using ICE to delineate the LAA function during catheter ablation for atrial fibrillation.

Material and methods. We included 21 consecutive patients (age 62±9 years, 5 women, 6 paroxysmal AF) who underwent catheter ablation for AF. An 8-Fr phased-array ICE catheter was used to obtain images of the LAA, while in sinus rhythm. The LAA was visualized with the ICE probe placed sequentially in the left atrium (LA), with the ultrasound section plane parallel to the long axis of the left ventricle (LV), and in the coronary sinus (CS), with the ultrasound section plane perpendicular to the LV long axis. LAA emptying flow velocity, and LAA fractional area change (FAC) were used to evaluate LAA function.

Results. ICE imaging was possible in all cases. The LAA peak flow velocity was similar when the ICE catheter was placed in the LA and in the CS (64+/-7 cm/s and 62+/-5cm/s respectively, P=NS). The LAA FAC was significantly lower when the ICE catheter was placed in the CS when compared to an LA location (14+/-6% vs 36+/-14%; P<0.001). The LAA FAC measured from the LA correlated with the mitral annular plane systolic excursion while the LAA FAC measured from the CS did not. There were no procedural complications.

Conclusions. Imaging of LAA using an ICE probe positioned in the LA and CS was feasible in all cases. The LV longitudinal contraction appears to impact the LAA function along the same axis, while the LAA function in a plane perpendicular to the LV long axis appears to be independent of the LV contraction.

The right ventricular coronary venous system in patients undergoing cardiac resynchronization therapy: A high speed rotational venography study

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Introduction. Although the anatomy of the left ventricular (LV) coronary venous system has been well described, there are few anatomic and no angiographic descriptions of the right ventricular (RV) venous system.

Material and methods. To evaluate the anatomy of the RV venous system we analyzed rotational coronary venous angiograms (RCVA) obtained from 70 patients (age 64±12 years) undergoing cardiac resynchronization therapy (CRT).

Results. The RV veins were seen to fill during the injection of contrast through multiple connections with the left sided venous system in 54 (77%) patients. Anterior cardiac veins (ACV), which overlay the RV wall were observed in 45 (64%) patients, and had a diameter of 2.5 ± 0.9 mm. Multiple ACVs were seen in 28 patients. These veins were observed to empty directly into the venous sinus of right atrium (VSRA), into the right atrium (RA), or into the small cardiac vein (SCV) in 38, 7, and 1 patient

respectively. The right marginal vein (RMV) was visualized in 15 (21%) patients, had a diameter of 2.8 ± 1.4 mm, and ran a course along the right border of the RV, emptying directly into RA or into VSRA in 7 and 8 patients respectively. The one SCV seen had a diameter of 2.3 mm, ran along the RV base, drained 1 ACV and 1 RMV. VSRA present in 38 (54%) patients, coursed parallel to the right coronary sulcus, collecting blood from the ACV's and RMV's and drained into the RA; in 2 patients, 2 VSRA ostia were noted. VSRA lengths and diameters varied (32-80 mm, mean 44 ± 25 mm) and (2.9-6.7 mm, mean 3.4 ± 1.2 mm) respectively.

Conclusion. RCVA can be used to visualize the RV venous system, which shows considerable individual variability. The VSRA have anatomical features that would make direct cannulation of the RV coronary venous system technically feasible facilitating RV epicardial access. The connections between the anterior veins of the RV and LV are alternative pathways for lead advancement, when targeting the anterolateral LV wall for CRT.

Hyperammonemic crisis – metabolic disease or the consequence of valproic acid treatment?

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Introduction. Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome is caused by a disturbance in the urea cycle and the ornithine degradation pathway. Symptoms include neurocognitive impairment, ataxia, spasticity, seizures or hyperammonemic crisis (acute encephalopathy) with lethargy, nausea, and vomiting. Seizures treatment includes valproic acid, which might also produce a transitory hyperammonemia.

Case presentation. A 21-year-old woman presented in our Neurology Department with frequent episodes of nausea and vomiting, lethargy. The patient is known with encephalopathy, intellectual disability, ataxia, extrapyramidal syndrome, polymorphic epileptic seizures and spastic tetraparesis. Child development was normal until 4 years old. The first focal motor seizures with secondary generalization appeared at 5 years old, with prolonged refractory status epilepticus, without any neuroimaging modifications. Throughout the years the patient also presented atypical absence and myoclonic seizures. Treatment with valproate was initiated when she was 10 years old. She always presented hyperammonemia during her medical check-ups, with episodes of vomiting, somnolence and prolonged status epilepticus , induced by hyperprotheic meals or intercurrent infections. Gastrointestinal and central nervous system etiology were excluded. The clinical presentation and blood tests results were interpreted as side effects of the valproate treatment (seric concentration being above normal) with secondary hyperammonemia. The valproic acid dose was lowered and levetiracetam treatment was initiated with favorable outcome.

Results/Conclusions. The long-term, overdosed treatment with valproic acid along with the lack of a proper dietetic plan and the remission of the symptomatology after lowering the valproate dose, suggest a hyperammonemic etiology of the clinical picture; a genetic cause is not yet excluded (genetic testing was done, but the results are still awaited).

Differential susceptibility before birth: genetic moderators in the relation between maternal affect during pregnancy and infant stress reactivity and temperament

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Issues. Maternal stress during pregnancy has been consistently associated with atypical emotional responses in human infants, as well as emotional difficulties in children and adolescents.

Objectives. 1) Influence of maternal affect during pregnancy on infant stress reactivity and temperament. 2) Genetic moderators in the relation between maternal affect during pregnancy and infant stress reactivity and temperament.

Methods. 1) Participant recruitment. Inclusion criteria: an uncomplicated, singleton pregnancy less than 25 weeks gestational age; no current physical and mental health problems. Infant inclusion criteria will be full-term (≥37 weeks) delivery and 5-min Apgar score ≥7. 2) Assessment of maternal affect during pregnancy. Maternal affect will be assessed over three 7-day intervals chosen at the beginning of each of the last three months of pregnancy. Using a mobile phone app, participants will report levels of positive and negative affect and briefly describe the triggering events. 3) Assessment of stress reactivity in newborns. Infant behavioral and cortisol responses to stress will be assessed in the first postnatal day, during the routine vaccination for hepatitis B. Saliva cortisol will be measured and buccal epithelial cells from the saliva will allow us to extract infant DNA and genotype the functional polymorphisms. 4) Assessment of temperament in 6-month old infants. The Pre-Locomotor Version of the Laboratory Temperament Assessment Battery will be used to assess several dimensions of temperament.

Resources and budget. This research and all the analyses will be carried out in the Cognitive Neuroscience Laboratory, Department of Psychology, Babeș-Bolyai University.

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Particularities of acute liver failure in neonates and infants

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Introduction. Acute liver failure (ALF) is a devastating syndrome in neonates and infants, with a very high mortality. The Paediatric Acute Liver Failure Study Group (PALFSG) defined the diagnosis of ALF in neonates and infants as the presence of biochemical evidence of acute hepatic injury and INR >1.5 with encephalopathy or INR>2 without encephalopathy. The aetiology is represented mainly by metabolic disorders, infections, vascular causes and less often by toxins or autoimmune disorders. The aim of our study was to evaluate the causes of ALF in this population.

Material and methods. We have analysed retrospectively the aetiology of the ALF in all neonates and infants (0-12 months) hospitalized in our hospital between January 2012 and September 2018.

Results. During the last 7 years, 34 infants (0-12 months) were admitted in our hospital with ALF. Viral and bacterial infections were the most important causes of ALF:

23 patients (67.64%). Cytomegalovirus, Epstein-Barr virus, Herpesvirus, Parvovirus or HBV were involved. Also, systemic sepsis with Gram-negative bacteria was another important cause of ALF (11 patients, 32.35%) in infants, with a high mortality: 6 patients (54.55%). The third group was represented by the metabolic disorders (7 patients, 20.58%). There were two infants with galactosemia and mitochondrial disorder respectively, and one with neonatal haemochromatosis, tyrosinemia, and hereditary fructose intolerance. In two cases the aetiology of ALF remained unidentified.

Conclusions. In neonates and infants, the aetiology of ALF is different from the older children and is associated with a high mortality despite the intensive care therapy. A high index of suspicion is necessary to establish the aetiology. In these cases, emergency therapies that include specially adapted diets or administration of antivirals/antibiotics may be lifesaving. The emergency liver transplantation may be an option, but it is difficult to be performed at this age, especially in neonates.

A newborn with subcutaneous fat necrosis

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Introduction. Subcutaneous fat necrosis of the newborn (SCFN) is an uncommon panniculitis, with unknown pathogenesis. This disorder presents with erythematous-violaceous subcutaneous nodules which develop on the face, posterior trunk, buttocks or proximal extremities, in the first weeks of life.

Case-report. We report a male, 12 days old, who was referred to our hospital with generalized lymphadenopathy. The boy was delivered full term by caesarean section for maternal causes (myopia, gestational diabetes) and fetal cause (macrosomia). Soon after birth, he was admitted to the Neonatal Intensive Care Unit for perinatal hypoxia and hypoglycemia. On the seventh day of life, he presented erythematous painful nodule in the left supraclavicular area with progressive growth and multiple new similar lesions in the right supraclavicular area, bilateral axillar and inguinal areas. Laboratory investigations showed elevated inflammatory markers indicating severe bacterial infection, high lactate dehydrogenase, calcium, phosphorus and triglycerides. Soft tissue ultrasound described multiple well-circumscribed hypoechoic areas encapsulated by a hyperechoic border, revealing the image of locules. We defined the case as subcutaneous fat necrosis of the newborn associated with infection of these nodules. Antibiotic and anti-inflammatory treatment was started with favorable outcome. At 3 months follow-up, the panniculitis was in complete remission, with persistence of elevated calcium, phosphorus and triglycerides which required further monitoring.

Conclusions. Being a rare disease, difficulties in timely diagnosis can be encountered as many illnesses mimic the subcutaneous fat necrosis of the newborn, including malignancies of lymph nodes. Although this kind of panniculitis is self-limited, it requires long-term monitoring for potential complications regarding hypercalcemia.

An infant with sepsis and infected urachal cyst – case report

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Introduction. The urachus is a cloacal/primitive structure that connects the umbilical cord to the bladder during the development of the baby. It allows urine drainage through the umbilical cord and it closes before birth. The incidence of these anomalies is 1 to 5,000-8,000 live births and most of the cases (over 70%) remain asymptomatic, only occasionally manifested as sepsis secondary to superinfection.

Case report. We report the case of a two-month-old girl who was hospitalized in a regional hospital with psychomotor agitation, non-coercive weep, refusal to eat, fever (38.3°C). The diagnosis of sepsis has been established based on clinical and laboratory data, but the origin of the infection was not elucidated, all cultures being sterile. She received antibiotics, medication for fever and rehydration infusion with persistence of the symptoms. She was referred to us with the diagnosis of prolonged febrile illness. At the admission, physical examination was normal and the laboratory parameters revealed an important inflammatory syndrome, leukocytosis with neutrophilia and increased C-reactive protein (CRP). The abdominal ultrasound reveals an infected urachal cyst. We administered a combination of third generation cephalosporin and aminoglycoside and the evolution was favorable. Few days later she has been transferred in a department of infantile surgery for the removal of the cyst.

Conclusion. We presented an infant with urachal cyst infection manifesting by a systemic infection treated with antibiotics and surgical excision. Urachal cyst is a rare cause of sepsis in infants/children and sometimes a strong clinical suspicion is necessary in order to establish the diagnosis.

Cerebral oxygen saturation in preterm newborns under 33 weeks - useful marker of neonatal transition

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Introduction. The value of brain oxygen saturation (rSO2) measured with the NIRS device may be a prognosis element for the premature neonate.

Objective. To establish a correlation between cerebral oxygen saturation and neonatal morbidity.

Material and methods. We conducted a descriptive study of 28 neonates under 33 weeks of gestation hospitalized in the Department of Neonatology of the Gynecology Hospital 1 in 2017. The monitoring was performed with the NIRS device during the first 72 hours of at birth. All the children enrolled in the study have consented to their legal representative through this study.

Results. The maximum value of 88.56% rSO2 corresponded to 93% on peripheral pulsometry. The mean blood pressure (TAM) ranged from 28.3 to 52.5 mmHg. and the minimum value corresponded to a value of 46.6% rSO2. Lower values 68 of rSO2 have frequently been associated with circulatory disorders requiring the establishment of inotropic support. In the cerebral hemorrhage, rSO2 did not significantly correlate ($p = 0.99$). The variation in cerebral saturation was significantly correlated with the number of early morbidity in the neonatal period (over 60% variation was associated with over 4 morbidity) ($r = -0.6$).

Conclusions. The value of brain oxygen saturation is a useful element in the evaluation and monitoring of premature neonatal haemodynamics.

The value of brain oxygen saturation is correlates with the number of early morbidity.

Reclassify the type of diabetes mellitus-clinical case

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Introduction. Diabetes is grossly classified in two types, however, the heterogeneity of the characteristics of patients with type 2 diabetes often places us in the difficulty of a refined diagnosis. Moreover, in the choice of therapy, the focus should be on the risk of complications that are most likely to occur.

Materials and methods. This is the case for a 60-year-old patient diagnosed with type 2 diabetes at age 55 without a family history of diabetes, hypertensive grandmother and daughter with hypercholesterolemia, menopause at 47 yrs. Diabetes has been accidentally discovered, treated to date with biguanid and sulphonylurea. Upon admission, elevated basal blood glucose (240mg/dl), influenced general condition, polyuria, polydipsia, alternating diarrhea with constipation, accentuated after biguanide administration, periorbital xantheasm, TA = 126/77 mmHg, AV = 65/min, balanced respiratory and cardiovascular, BMI = 20.02 kg/m2.

Results. A1c=9.35%, hypercholesterolemia (LDLcol= 179.2mg/dl). Thyroid function screening confirmed autoimmune thyroiditis (ATPO=192.4u/ml). Stage diagnoses have been established: LADA? (Latent Autoimmune Diabetes in Adults), Hashimoto's thyroiditis, familial hypercholesterolaemia. To confirm the type of diabetes, dosages of C-peptide, antibodies GAD-65, IA-2, Zn8, IgG anti-insulin were performed, results completed after 3 weeks.

Conclusions. Basal insulin therapy with glargine (0.3 ug/kg body weight) was initiated and then added GlucophageXR® progressively titrated for digestive tolerance testing, then combined with the DPP4 inhibitor (Janumet®50/1000mg) with regressive basal insulin titration. After discharge, Toujeo® was reduced to 6ui/24h, basal blood glucose maintained at 95-130mg/dl. 3 weeks after discharge, autoimmune diabetes was infirmed, but severe insulin deficiency was confirmed (unstimulated C-peptide=0.144 nmol/L, VN = 0.300-2.376). Final diagnosis: Type 2 diabetes with severe insulin deficiency.

Intravenous administration of levodopa + carbidopa in advanced Parkinson's disease. Associated comorbidities and their impact on the quality of life. Case presentation

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Introduction. Parkinson's disease is a progressive neurological disorder, which in advanced stages can significantly affect the quality of the patient's life. At this stage the treatment should be adapted. Levodopa intravenous administration provides a consistent blood and cerebral dopamine level leading to a significant decrease in dyskinesias and off-time periods, and furthermore avoids gastric barrier activity.

Material and methods. We present the case of a 70-year-old patient known for 10 years with Parkinson's disease. At the moment of presentation, the patient was in the 4th Hoehn and Yahr stage, the „off" periods during: 10h/day with 75% of the dyskinesia during the day.

Results. Given the status of Parkinson's disease, the existence of debilitating motor complications with considerable impairment of quality of life, enteral administration of Levodopa was indicated. Under duodopa therapy the patient showed a favorable evolution,

with the abolition of off periods and the marked decrease of dyskinesia, stiffness and bradykinesia. The patient was monitored periodically with ambulatory levodopa dose changes, and after 3 years accused memory and concentration disorders (MMSE - 20), swallowing disorder with significant weight loss, and cerebral computer scan examination reveals an extraaxial tumor formation at the right paramedian preponderant cistern, with an important mass effect on the adjacent cerebral trunk and the IVth ventricle with the significance of clivus meningioma. Neurosurgical intervention is indicated but the patient refuses and death occurs after 6 months.

Conclusion. The particularities of the case reside in very good tolerance of Duodopa therapy with the considerable improvement in motor status and patient quality of life, after which the evolution of the case was influenced by the appearance of clivus meningeoma with mass effect indicating surgical therapy.

The relationship between insulin resistance, visceral fat thickness and subclinical atherosclerosis in patients with non-alcoholic steatohepatitis (NASH)

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Introduction. Abdominal obesity and insulin resistance (IR) are the most important pathogenetic factors in non alcoholic steatohepatitis (NASH) and atherosclerosis.

Aim. NASH presents a independent cardiovascular risk and the purpose of our study is to evaluate visceral fat thickness (VFT) and to investigate the relationship between VFT, insulin resistance and subclinical atherosclerosis measured by carotid intima-media thickness (c-IMT) in pacients with NASH.

Materials and methods. 50 patients with NASH and 30 healthy controls, age and gender matched, were recruited. Lipid profile, liver biochemical markers, fasting plasma glucose (FPG), insulin level, insulin resistance index (HOMA-IR), VFT and c-IMT were assayed.

Results. Patients with NASH had an altered lipid profile and liver biochemical markers; HOMA-IR, VFT and c-IMT were significantly higher compared to controls. HOMA-IR was positively correlated with VFT, transaminase levels and c-IMT. Multiple linear regression analysis showed that NASH, HOMA-IR and age were independently factors associated with higher c-IMT.

Conclusions. Pacients with NASH showed a marked increase in the prevalence of subclinical atherosclerosis compared to the general population. Abdominal obesity plays a central role in the development of IR, NASH and atherosclerosis. Ultrasound measurement of VFT is proving to be a very good independent predictor of NASH and also, a simple and non-invasive ultrasound method for assessing abdominal obesity.

Keywords: non-alcoholic steatohepatitis, insulin resistance, visceral fat thickness, carotid intima- media thickness, subclinical atherosclerosis

Granulocitic sarcoma - a rare form of acute myeloid leukemia

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Introduction. Granulocytic sarcoma (GS) is an extramedullary tumor, consisting of immature granulocytes and representing 1-2% of all cases of acute myeloid leukemia (AML), 6.5% having gastrointestinal tract localizations. The delay in the diagnosis of GS is a rising issue, firstly, because of the difficult symptoms, given by the various presentations and secondly, as a result of the diagnosis, run by the pathologist. Therefore, delayed induction therapy may jeopardize the outcome.

Case presentations. The issue is outlined by these two cases of GS, in young patients, at the Oncology Institute „Prof. Dr.Ion Chiricuţă „, Cluj-Napoca. The symptomatology of the first case, in May 2017, was digestive, for which paraclinical investigations were recommended: magnetic resonance imaging (MRN), suggestive of cholangiocarcinoma, ERCP (Endoscopic Retrograde Cholangiopancreatography) and histopathological examination (HPE), with ambiguous results. A repeated biopsy further recommended performing an osteomedullary aspiration and led to the diagnosis of an AML M1, with the unusual hepatic SG debut and to the initiation of chemotherapy, in March 2018. The patient has atypical karyotype: 47, XY, + 22; FLT3, NPM1-negative. The second case, debuted in May 2015, with superficial adenopathies, respiratory and digestive tract symptoms. Further investigations were needed: computed tomography (CT), biopsy and HPE, suggestive of Burkitt NHL. Through an osteomedullary aspiration was given the diagnosis of AML M4, subsequently chemotreated, in August 2015, with recurrence as blastic meningitis.

Conclusion. The efficient diagnosis and treatment of GS, which most often evolves to an AML is of utter importance. A multidisciplinary approach could be the key, when the pathologists can eliminate the diagnostic bias and facilitate the management of GS.

Floppy infant, severe hypercalcemia and genetic link

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Introduction. The presence of CYP24A1 mutations explains the increased sensitivity to vitamin D in patients with idiopathic infantile hypercalcemia and is a genetic risk factor for the development of symptomatic hypercalcemia that may be triggered by vitamin D prophylaxis in otherwise apparently healthy infants.

Case report. We present a case of a 4-month old girl who was initially hospitalized for severe hypotonia, lethargy and failure to thrive. The patient's history revealed recurrent vomiting. On the clinical examination we also noted a high forehead, a high arched palate and short metacarpal bones. Blood tests showed hypercalcemia, low PTH and phosphate and high vitamin D levels. Renal ultrasound showed medullary nephrocalcinosis. Correlating the clinical examination with the blood work vitamin D intoxication, hyperparathyroidism and Jansen's metaphyseal dysplasia were considered and ruled out. Genetic testing was performed and a compound heterozygote state was identified (mutations p.E143del and p.R396W) confirming the diagnosis of idiopathic infantile hypercalcemia. Both mutations have been formerly identified as loss-of-function mutations in the vitamin D-24-hydroxylase gene. Rehydration and furosemide therapy was applied and resulted in the normalization of calcium values and clinical improvement. On the long term the patient followed a low calcium diet and vitamin D supplementation was discontinued.

Conclusion. Clinical symptoms, such as failure to thrive, vomiting, increased thirst, anorexia or hypotonia should always bring in discussion the possibility of hypercalcemia in order to diagnose and treat idiopathic infantile hypercalcemia early and also to prevent long-term complications.

Chronic myeloid leukemia associated with hypothyroidism and QT prolongation syndrome

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Introduction. Chronic myeloid leukemia (CML) represents a myeloid proliferation accompanied by Philadelphia chromosome. The most modern treatment of this disease is represented by second generation tirosinkynase inhibitors. Sometimes because of adverse effects of these medication, the doses should be decreased or stopped.

Material and method. We present the case of a 54 years old female patient, diagnosed in February 2011 with CL, chronic phase, high risk Sokan and Hasford scores. The patient started Nilotinib treatment, 2x300 mg/day. After a month, the patient had major molecular response after 6 months of treatment and no side effects. After 3 years and 9 months of treatment, a prolongation of QTc (Bazett) interval was diagnosed, 462 msec. We stopped Nilotinib treatment, monitorised QTc interval and when QTc was normal, we reintroduced Nilotinib, 450 mgx2/day because Nilotinib has the QT prolongation potential. Meanwhile, we searched for other QT prolongation causes (diselectrolitemia, other drugs or food with action on P450 citocrome which metabolise Nilotinib). Finally, thyroid function was investigated and the patient was diagnosed with hypothyroidism and treated with Euthyrox.

Results. We introduced Nilotinib full dose after normalization of thyroid function and the patient achieved complete molecular response.

Conclusion. For Nilotinib treated CML patients, in case of Qt prolongation syndrome, hematologists should investigate other causes of QT prolongation. For each patient Nilotinib doses should be adapted.

Henoch–Schönlein purpura – neurological involvement

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Introduction. Central nervous system involvement in HSP (Henoch-Schonlein purpura) is very rare. CNS (central nervous system) vasculitis in HSP may occur as oedema, ischemic lesions and haemorrhage. The most frequent clinical signs and symptoms are seizures, headache, focal neurological deficit and altered consciousness.

Material and methods. 25 year old male patient, with a history of HSP secondary to tonsillitis (9 years old) complicated with intraparenchymal haemorrhage, surgically treated, is admitted for motor partial seizures secondary generalised. Physical and neurological examination, reveal no pathological signs. Laboratory studies are within normal range. Cerebral MRI reveals postoperative frontal-temporal-parietal-occipital left sequelae, bilateral ischemic lacunar lesions in the head and body of the caudate nucleus, supracentrimetric and with hemosiderin deposits on the right, pencil-like on the left and an ischemic sequelae lesion adjoining the frontal horn of the LLV. The EEG exams reveals frontal-temporal-parietal dysrhythmia.

Results. Treatment with Levetiracetam and Diazepam is administered, with favorable outcome.

Conclusion. The particularity of this case is the very rare occurrence of neurological involvement in HSP and delayed onset of seizures, more than 10 years after the surgery.

The predictive value of immunological markers in breast cancer patients

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Introduction. Breast cancer is the main cause of death among women. Several markers as Ki67, HER2, or estrogen (ER) and progesterone (PR) receptors have a prognostic value for being used for molecular classification of breast cancer. The aim of the study was to assess the values of these molecule as predictive markers for chemotherapy in patients with breast cancer receiving neoadjuvant chemotherapy in order to individualize the oncological treatment.

Materials and methods. We performed a longitudinal retrospective,analytical and observational study,from 2010 to 2015, involving 39 patients with breast cancer, treated in IOCN. The stage of disease was divided into 7 subgroups. The patients received 4 cycles of neoadjuvant chemotherapy(Farmorubicin+ Cyclophosfamide, EC) associated with Herceptin(antibody anti HER2) followed by surgery. Correlations between demographic characteristics of patients, stage of disease, response to treatment and expression of Ki67, HER2, ER, PR were made after surgery. Data analysis was processed through Fisher's test, Chi Square test and non-parametric test Kruskal-Wallis.

Results. The response of treatment was complete, partial or stationary and most of the patients had responded partially to treatment (57%). The response to treatement was influenced by the stage of disease. The ER and PR were poorly represented in most of patients(values between 0-25). The proliferative marker, Ki67, presented medium values, most of patients having values between 26-75%. The only marker which correlated statistically significant with the response of treatment was progesterone receptor (p=0.02).

Conclusion. Our study confirm that the response to treatment in breast patients depends on the stage of the disease. For the first time, in our study the expression of PR on tumor tissue correlated statistically significant with the response to treatemet. This result confers to PR a predictive value for treatment, the results have to be confirm on largest number of patients.

Psycho-social analysis regarding patients with chronic kidney disease

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The present research approach an analysis regarding patients with chronic kidney disease. Chronic kidney disease (CKD) represents a life-threatening pathology. Moreover, people suffering from this condition experience high levels of both physical and mental stress and must deal with a lot of changes in their personal life and lifestyle choices. The purpose of this study is a better understanding of the factors which have the biggest impact on the quality of life in people diagnosed with CKD. The research method consist in application of a questionnaire completed by a group which includes 39 randomly chosen patients suffering from CKD who undergo haemodialysis. They completed an adapted questionnaire by Kidney Disease Quality of Life - Short Form which includes 39 preformulated questions structured by our domain of interests. The results emphasizing a difference between similar studies regarding the prevalence of different diseases such as Chronic glomerulonephritis and Chronic pyelonephritis. This phenomenon could be explained by the lower median age of our group. When asked to self-assess their health status, most of our respondents considered it stationary compared to how they felt 12 months before. Their most limited daily activities proved to be those that require an

intense physical effort. The disease sometimes has an influence on the social activities of the patients creating difficulties such as having a job or going to school. In this study group the level of social support is high, coming from their family and friends, but also from the medical staff. Since the quality of sleep in the studied population proved not to be significantly affected by CKD, this represents an advantage for both physical and mental wellbeing. The study conclusion pointed a better understanding of what CKD means is very important for improving the healthcare system and social support.

The administration of nebulization medication to preschool children

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Introduction. The administration of drugs on inhalation route has numerous advantages in respiratory disorders. Out of the 3 standardized techniques of administration, nebulization is preferred in preschoolers. Acute bronchiolitis, laryngitis, and pneumonia represent the majority of respiratory diseases in the emergency department. Asthma is the most frequent chronic disease in children that requires inhaled therapy both during exacerbation and on long term.

Matherial and methods. We analyzed a group of 51 patients treated with nebulized medication in an opened prospective observational study. Parents filled a questionnaire by under physician supervision. We recorded demographic data, the number of episodes treated, the diagnosis and the drugs recommended, the technique of administration, the acceptance level by the child and parents satisfaction on therapeutic efficacy. An informed consent was obtained. Statistics include the mean values, standard deviation, and coefficient of correlation (r2).

Results. Out of the 51 patients, 24 were girls, with a mean age 2.53 ± 0.73 yrs. Diseases treated were: acute bronchiolitis (48pts), laryngitis (14pts), asthma (3pts), pneumonia (2pts) and tracheobronchitis (1 pt). The drugs used for nebulization were: normal (29pts) or hypertonic saline 3% (18pts); adrenaline (20pts); salbutamol (37pts); fluticasone propionate (26pts) and dexamethasone (11pts). Only 4 parents declared that the therapy is not accepted by the preschooler, while 42 of them accept the nebulization well. The level of satisfaction regarding results of the inhaled treatment was poor in 2 parents, 4 did not report it, and the majority (38 pts, 80.8%) were satisfied on the results. There was no correlation between patients age and the acceptance of treatment (r2=0.018), or with the satisfaction level of the parents (r2=0,047).

Conclusion. Nebulized medication is used mainly for acute bronchiolitis. Patients acceptance and the efficacy reported by the parents are good.

Epitopic incompatibility in pediatric renal transplantation (R-Tx)

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Introduction. Epitopic incompatibility appears to be a better predictor of the de novo appearance of donor-specific antibodies (dnDSA) post-Tx than HLA antigen matching in adults. We evaluated the HLA Matchmaker® software (version 2.1) in our pediatric cohort to predict the appearance of dnDSA post-Tx.

Material and methods. We included 70 pediatric patients (26 girls, 10 living donors, mean age 11.2 ± 3.9 years) after a first R-Tx (January 2010 - August 2016), without prior immunization, having complete HLA typing (A, B, C, DRB1 and DQB1) and dnDSA follow-up for at least one year.

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Results. The mean of HLA and epitope incompatibilities were 4.7 ± 1.3 and 15.5 ± 6.1, respectively, with a correlation coefficient r2 between these two variables of 0.34 ($p<0.001$). The epitopic load was 12.8 ± 5.0 in living donors vs 15.9 ± 6.2 in deceased donors (p=NS), 12.6±6.1 in pre-emptive R-Tx (n = 14) vs 16.3 ± 5.9 for non-preemptive R-Tx (p=0.04). Seven patients (10%) developed dnDSA during the 3.5 ± 1.2 years post-Tx. The epitope load was 13.7 ± 5.5 for those who developed dnDSA vs 15.7 ± 6.1 for the others (p=NS).

Conclusions. In our single-center series of pediatric R-Tx with good HLA matching and lower epitopic load than previously published series, eplet incompatibilities do not predict the development of dnDSA. The question of the HLA matching requirement and the daily interest of the HLA Matchmaker® software to help select the grafts remains open.

From hypothalamic–pituitary–adrenal (HPA) axis to microbiota-gut-brain axis (MGBA): Development in infancy and implications for health

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Recent studies have revealed that, besides an important role in digestion-metabolism-immunity, the gut microbiota has a significant effect on the brain development: in regulation of emotions, stress response, or even in higher cognitive functions. The bidirectional communication of these systems defines the "microbiota-gut-brain-axis", and is not fully understood. In the HPA axis, the glucocorticoid receptors (GR) are crucial players; the loss of GR function impairs the regulation of this axis, and mutant animals for the GR gene (NR3C1) show an impaired behavioral response to stress. In addition, cytosine methylation of the GR gene represents a possible mechanism by which trauma exposure could influence HPA axis functioning.

Recent studies aim to uncover important mechanisms in this field. One corresponds to genetic association studies on genes involved in HPA axis functioning. In our research, we have adapted protocols for studying polymorphic regions in GR gene (N363S, BclI, ER22/23EK) and in the corticotropin-releasing hormone receptor 1 - CRHR1 gene (rs242938). In the light of recent articles showing stress-related changes in NR3C1 DNA methylation, it is also important to consider the epigenetic regulation of the promoter of GR gene – another trend in recent work, which has been linked with childhood experiences and stress response; increased methylation is hypothesized to be a consequence of childhood maltreatment, and alters GR gene expression in the brain. Finally, new studies have shown that in mice, different gut microbiota significantly regulate the activity of HPA axis, and future studies could show links of HPA axis and gut microbiota, influencing the host's brain functions, including behaviour. One supportive argument is that both systems (HPA, MGBA) show a rapid and profound development during the first year of life.

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The role of TLR4 – IL17 axis in the immune and inflammatory responses involved in non-alcoholic steatohepatitis, component of metabolic syndrome

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Introduction. Non-alcoholic steatohepatitis (NASH) is a major public health problem. NASH is the hepatic manifestation of the metabolic syndrome(MS). Chronic inflammation in the liver is essential for progression of simple hepatic steatosis to steatohepatitis. Immune and inflammatory pathways play a crucial role in the hepatic inflammation. This is why it is important to elucidate connections between immune mechanisms, Toll-Like receptor cytokine signaling, in perspective of finding new treatments.

Material and methods. The research is a prospective and longitudinal study on 100 patients with NASH and MS. We will determine IL17-F genotype (7488 A/G,–737 C/T), IL17-A(–197 G/A), TLR4 (D299G, T399I), plasma level of IL17 and TLR4 and blood testing for MS elements (cholesterol, triglycerides, glucose, abdominal circumference, blood pressure). Diagnosis of NASH will be made with abdominal ultrasound and histological exam of liver samples. The study group will be compared with a (witness) control group of 100 healthy volunteers to which we will determine the same IL17F/A and TLR4 genotypes and plasma level of IL17 and TLR4.

Results. The primary outcome is to determine the role of genetic/biochemical markers in the modulation of hepatic fibrosis in patients with NASH and metabolic syndrome. To achieve the proposed objective, levels of IL17 and TLR4 will be assessed quantitatively and genotypes for genetic variations located in the IL17 and TLR4 genes will be determined.

Conclusion. One possible mechanisms responsible for activating the immune system is the activation of the IL17 axis. The other one is activation of TLRs. Elucidation of mechanisms underlying the progression of hepatic steatosis towards steatohepatitis is essential for development of useful diagnosis and treatment for medical practice.

Ultrasonographic findings at the level of foot and ankle in rheumatoid arthritis patients

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Introduction. In rheumatoid arthritis (RA) patients, the foot is involved from the early stages of the disease and results in pain and deformities that have impact on the functionality and quality of life. The disease activity measuring tools do not take into account the foot and ankle joints. The aim of this study is to evaluate by ultrasonography the foot and ankle joints and tendons in symptomatic and asymptomatic patients with RA.

Material and methods. We included in the study patients with RA, symptomatic and asymptomatic at the level of foot and ankle. After the physical examination, disease activity was established using CDAI and DAS28-CRP score. The limitation of physical activity was established using RAPID3 questionnaire and the quality of life was assessed

by applying RAQoL questionnaire. Ultrasonography (US) of the foot and ankle of this patients was performed searching for synovitis, Power Doppler (PD) signal, erosions, osteophytes and thenosynovitis.

Results. 30 patients, 60 feet respectively were examined. Mean age was 60.1 ± 11.2, mean body mass index was 26 ± 5.6 kg/m2. 63.3% of the patients were symptomatic. Dividing the patients in two groups – group 1 for asymptomatic and group 2 for symptomatic patients at the level of the foot and ankle – there were statistically significant higher DAS28-CRP, RAPID3 and lower RAQoL scores in group 2. Most frequent US finding at ankle were: tibiotalar synovitis in anterior approach (58.3%), talo-vanicular synovitis (66.7%). Tenosynovitis was identified rarely. At the level of the foot the most frequent findings were first, second and third MTF synovitis. Erosions were identified at the level of fifth MTF (40% anterior, 51.7% lateral and 38.3% plantar).

Conclusion. Symptomatic patients at the level of the foot and ankle have a higher disease activity level and a poorer quality of life. Patients with RA develop synovitis at the level of the ankle and foot frequently and erosions al the level of fifth MTF joint.

The prevalence and clinical profile of permanent atrial fibrillation at a tertiary care hospital

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Background. Atrial fibrillation (AF) is the most common cardiac arrhythmia with an increasing prevalence and incidence worldwide. Permanent AF occurs in approximately 50% of patients, and paroxysmal and persistent AF in 25% each.

Objectives. To determine the prevalence of permanent AF in a tertiary care hospital and to identify the clinical profile of permanent AF in hospitalized patients.

Material and method. A total of 511 patients with AF, average age 70+/- 10.9 years, 50.8% female, were enrolled between July 2017- December 2017 from Cardiology Department. Patients with documented AF were classified into three subgroups: paroxysmal, persistent or permanent according to the latest ESC guidelines for AF. Only patients with permanent AF were included in this study. ECG was done in all cases. 2 D echo study was performed in all the cases to find out etiology of AF. Statistical analyses of the collected data were performed.

Results. During the study period, 311 (60.86%) of patients were admitted with permanent AF. Maximum numbers of patients were in the age group of 60-80 years (29.37%). Hypertension was the most common underlying cardiovascular condition (53.7%), followed by coronary artery disease (34.2%), heart failure (31.7%) and diabetes (17.7%). Majority of patients presented with more than one symptom. The commonest presenting complaint was dyspneea (42.1%) followed by palpitation (21%). The echocardiographic findings of left atrial enlargement, left ventricular hypertrophy and depressed left ventricular function were more common in permanent AF.

Conclusion. Nowadays, hypertension, coronary artery disease , and diabetes are becoming the most common predisposing factors for permanent AF and require prevention and control.

The role of intracardiac echocardiography in atrial fibrillation ablation

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Introduction. Atrial fibrillation (AF) is the most common arrhythmia worldwide. Radiofrequency ablation is an effective therapy for AF. The addition of imagistic techniques such as three dimensional electroanatomic mappyng systems (Carto System) and intracardiac echocardiography can improve the clinical outcome.

Material and method. We are going to present a case of a 52-year-old woman who was referred to our institution with repeated episodes of paroxysmal AF with no response to antiarrhythmic therapy. Radiofrequency catheter ablation was performed using Carto 3D Navx for electroanatomical mapping and intracardiac echocardiography. Both these techniques helped in guiding the transeptal puncture and in an appropiate contact between ablation catheter and antral walls. Complete isolation of all four pulmonary veins was realised.

Conclusion. Intracardiac echocardiography may contribute to a safe and effective atrial fibrillation ablation.

Smoking during pregnancy

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Background. Smoking during pregnancy is one of the main causes of prenatal morbidity. Women smoking while they are pregnant have an increased risk of developing serious adverse health events and they also put their child at considerable risk. This paper aims to assess the demographic factors and to evaluate smoking behaviour in a group of pregnant women.

Material and methods. 43 pregnant women, current smokers with pregnancy in evolution were enrolled. A questionnaire conceived by a pulmonologist that assessed multiple risks factors during pregnancy was applied to all Demographic factors, maternal prenatal smoking behavior and prenatal complications in infant were assessed.

Results. The majority of patients were from the urban area, married, employed and had a high school degree. When finding out that they are pregnant they either reduced the number of cigarettes (57%) or stopped smoking (16%). Nevertheless a significant percentage (27%) continued smoking during pregnancy. One baby was born prematurely and 3 had congenital malformations (hemangiomas, pigmented nevi and hydroceles).

Conclusion. Tobacco dependence among pregnant women is a real public health problem and active anti-smoking counselling is required. Smoking cessation advices should be given to pregnant women on a regular basis, by every physician that attends them during pregnancy, emphasizing the risk that is includes not only her, but also her baby.

Non invasive ventilation in amyotrophic lateral sclerosis patients with bulbar involvement: case series

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Introduction. Amyotrophic lateral sclerosis (ALS) is a progressive neurological disease of unknown etiology that can affect respiratory muscle strength. Respiratory failure it's a common and often lethal complication of ALS. Non invasive ventilation (NIV) is a well established treatment as it prolongs survival and increases the quality of life in these patients. However, in patients with bulbar involvement NIV is not very well tolerated, and these patients need tracheostomy ventilation in specialized care centers that are not available in our country. If respiratory complications appear these patients end up in the intensive care unit department, are intubated and often die. There are no official recommendations for NIV in patients with respiratory failure and bulbar involvement. However some authors recommend it as long as the patient wants and tolerates it. This paper presents the cases of five patients with ALS and bulbar involvement and their outcomes after receiving NIV for type II respiratory failure. All patients were diagnosed with ALS, they had bulbar dysfunction when presenting in our department. They have never had respiratory complications and they were all hospitalized for acute-on-chronic type II respiratory failure. 2 of them had gastrostomy tube. NIV in pressure controlled mode was started in all of them with clinical and gas improvement. All patients were discharged with permanent NIV at home. Four patients died in the following 3 months and only one survives.

Conclusions. Considering that there are no other alternatives for these patients in our country a trial of NIV should always be considered, however if severe bulbar dysfunction is present tracheostomy ventilation is necessary.

Angiogenesis in a group of patients with chronic obstructive pulmonary disease

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Background. Angiogenesis represents a complex process of vascular remodelling and repair. Vascular endothelial growth factor (VEGF) is a molecule with angiogenic potential, with implications in vascular remodelling, permeability and angiogenesis. The complete understanding of the angiogenic and angiostatic mechanisms in chronic obstructive diseases could facilitate a better therapeutic management of the illness.

Material and methods. The study took place in Cluj-Napoca, during 1 year period of time, and was conducted on COPD patients and healthy subjects (case-control study). The assessment of the study group consisted of: functional testing, arterial blood gas analysis, serum VEGF levels (ELISA assay), inflammatory serum markers.

Results. VEGF serum levels in control group were bellow the limit of detection, with much higher values in the study group. Positive correlations were found between VEGF serum levels and inflammatory markers, respiratory failure severity, exercise and functional capacity - $p<0.05$.

Conclusions. The results of our study strongly suggest that angiogenesis plays a major role in patients with pulmonary obstructive disease, and could serve as a targeted therapy.

Clinical evolution of a patient with amyotrophic lateral sclerosis

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Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder with progression to death in 3 to 5 years, witch affects both the upper and lower motor neurons. The average age of onset of the disease is between 47-52 years (familial ALS) and 58-63 years (sporadic ALS in 80% of cases).

We present a case of 54 years old woman who upon presentation had language disorder (dysarthria) and difficulty chewing and swallowing. In 2014 the patient presented slurred and nasal speech, difficulty in swallowing and fasciculations. She was diagnosed with cerebral microangiopathy. After two years she had progressive symptomatology and muscle atrophy in the upper right limb. Based on the El Escorial criteria we established the diagnoses of possible ALS and we initiated the treatment with Riluzole. In March 2018 new signs appeared: tetraparesis, piramidal signs, global hypotonia and global muscle atrophy.

Electromyography reveal chronic neurogenic tract with acute denervation of bulbar, left mentalis and trapezius muscles.

At the present time the patient can communicate in writing and eat semi-liquid food. Based on clinical and paraclinical criteria we changed the diagnosis to definite ALS. We communicate the prognosis and the options of palliative treatment to the patient and the family.

The particularities of this case are: our patient survived more than the average (four years until now), muscle strength is not significant affected, she can perform daily living activities and she doesn't present difficulty breathing (at spirometry the vital capacity is normal).

SURGICAL SPECIALTIES

Ocular toxocariasis combined with glaucoma and retinal detachment. An insidious case presentation of a 3-year-old male

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Introduction. Toxocariasis is a zoonotic disease caused by the second stage larva of Toxocara canis. Clinically, two syndromes are described: visceral larva migrans (VLM) and ocular larva migrans (OLM). OML may presents as peripheral inflammatory mass, posterior pole granuloma and chronic endophthalmitis. We report a histologically confirmed case of OML in a 3-year-old male with poor prognosis.

Case presentation. A previously healthy 3-year-old boy presented with right eye leukocoria and exotropia for 3 months prior to admission in 2012. No history of trauma or foreign body to the right eye, no previous history of eye diseases. The echographic findings were: a solid, high-reflective vitreous mass with moderate echogenic echoes, with membranes extending towards the posterior pole and a traction retinal detachment. Posterior Pars Plana Vitrectomy was performed, and the histological examination of the vitreous piece revealed larvae of Toxocara canis. On the second admission in 2014, he was diagnosed with subluxated crystalline and secondary glaucoma. Surgical removal of the right crystalline was performed. One month later, his right eye was injected, corneal oedema, pupil mildly dilated and non-reactive. In 2016, due to the intense pain and despite of the pharmaceutical treatment, trabeculectomy was performed to reduce glaucoma. The persistence of pain and secondary glaucoma, combined with hemophthalmia, photophobia and disorganization of the retinal inner layers with total vision loss proposed the right eye evisceration.

Conclusion. The diagnosis of OML requires funduscopic findings, serology and histology of the vitreous. OLM may cause increase in morbidity if diagnosis is not established, leading to delay or fail to initiate prompt treatment.

Particularities. Serological diagnosis of OLM is more challenging than serodiagnosis of VLM, because the levels of antibodies in the serum are usually low or undetectable and eosinophilia is often absent.

Tanathophoric dysplasia type I – case report

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Introduction. Tanathophoric dysplasia is the most common form of osteo-chondrodysplasia, with an incidence of 1 in 30000 pregnancies and is usually lethal in the perinatal period. This condition is autosomal dominant, but it is usually the result of a de novo mutation of the FGFR3 gene. It is normally suspected in the second trimester due to the aspect of the long bones, cranium and thorax.

Case report. We report the case of a 23-year-old woman G1 P0 who was referred to our service for second trimester scan.

We report that the patient had done the first trimester scan that showed a combined risk of 1/10000.

Our exam revealed a 23 weeks male fetus with anomalies of the lower extremities (short femur, short tibia and short fibula, all under the 5th percentile), anomalies of the upper extremities (short humerus, short ulna and short radius, all under the 5th percentile); short ribs, narrow thorax and hypoplastic lungs; head anomalies (enlarged head circumference, cloverleaf skull, calcification of head bones).

We arose the suspicion of tanathophoric dysplasia type I and we performed an

amniocentesis which revealed a mutation of gene FGFR3 on chromosome 4p16.

The patient had a medical interruption of pregnancy at 23 weeks and 5 days. She delivered a male fetus of 298 g who was sent for X-rays and pathology exam.

The couple was referred to the genetics department for counselling. Because this condition is the result of a de novo mutation, the risk for the couple to have another pregnancy with the same problem is not increased.

US probe pressure on the maternal abdominal wall and the effect on fetal MCA Doppler ultrasonography

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Introduction and objective. The aim of the study was to evaluate the effect on middle cerebral artery (MCA) resistivity index (RI), pulsatility index (PI), and peak systolic velocity (PSV) of increased pressure exerted on the maternal abdominal wall during routine ultrasound.

Materials and methods. A prospective study was conducted, in which we included 40 pregnant women between 24+0 and 41+3 gestational weeks (GW), with singleton pregnancies, without any associated pathologies, undergoing routine US examination. We recorded the flow velocity waveforms in the MCA, and we measured the RI, PI, PSV and the applied pressure on to the maternal abdominal wall, needed for a proper evaluation of MCA. We then, repeated the same measurements at another two different higher pressure levels, and at the same time having a proper image of the targeted vessel.

Results. We found significant differences for the PI and RI levels with increase in abdominal pressure (median PI 1.46, 1.58 and 1.92 respectively; median RI 0.74, 0.78, and 0.85 respectively, $p<0.05$), for both PI and RI. At the same time, we found no significant differences for PSV in the studied group in relationship with increase in abdominal pressure (median PSV 39.56, 40.10 and 39.70 respectively, $p>0.05$).

Conclusion. In conclusion, the applied abdominal pressure by the examiner's hand, during routine US scan in pregnancy, can modify the MCA Doppler parameters, thus influencing the diagnostic accuracy in a series of pregnancy associated pathologies, such as chronic fetal distress (CFD), intrauterine growth restriction (IUGR), fetal anemia.

New prognostic factor in the first trimester pregnancy with potentially reserved evolution prognosis

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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%). Prenatal monitoring aims are increasing the effectiveness of screening methods and improving diagnostic methods for first-trimester pregnancies whose evolution potential may be reserved.

Material and method. The paper is a prospective case-control analysis that took place at the „Dominic Stanca" Clinic of Obstetrics and Gynecology in Cluj-Napoca

between 2015-2017 and includes two groups of patients: 81 patients with first trimester pregnancies in evolution and 89 of patients with a potentially reserved evolution, both groups having amenorrhea between 6-11 weeks. Endovaginal ultrasounds were performed to evaluate the distance between the yolk sac and the embryo (DYSE), and venous blood was harvested for serum dosing of Human Placental Like Growth Factor.

Results. Significant statistical differences were observed between the serum level of the serologic parameter observed in the two groups, respectively a significantly lower serum level in the risk pregnancies group compared with the physiological ones ($p < 0.001$).

Conclusion. The identification of low serum levels of serological parameter followed in this study can be considered as early prediction screening of potentially reserved evolution of pregnancies.

Pregnancy smoking and fetal development

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Introduction. Smoking remains a major health concern, especially for pregnant women, being the cause of an elevated maternal and fetal morbidity. Biological changes associated with smoking are determined by a decrease of biological placental functions that induce an insufficient development of the placental mass. Chemical substances from pregnancy smoke have a direct impact over the placenta, altering the proliferation and the differentiation of the trophoblast by altering the mechanical properties of villous vascularization with reduced blood flow in feto-placental circulation.

Material and methods. Prospective study done between July 2017 and March 2018 in Dominic Stanca Clinic, Cluj-Napoca. We included 40 non-smoking pregnant patients and 49 smoking pregnant patients who were subdivided into 2 groups (IIa- patients with medical counselling during pregnancy and IIb- patients without medical counselling during pregnancy). All patients had to answer a survey about socio-demographic data, and clinical parameters of the mother and the new-born. New-born babies from both groups were measured and we marked the cranial perimeter, abdominal perimeter, weight and APGAR score. We calculated descriptive statistical elements and the date was presented using centralized indicators for localization and distribution.

Results. We identified significant differences regarding the birth weight, the cranial perimeter and abdominal perimeter in new-borns from the two groups. The APGAR score at 1 minute was not different but at 5 minutes, the APGAR score of new-borns from smoking mothers was lower than that of new-borns from non-smoking mothers.

Conclusions. Low level of education and lack of counselling during pregnancy are associated with a rise in cigarette consumption during pregnancy. The fetal outcome was influenced by cigarette consumption.

Keywords: fetal outcome, smoking, pregnancy

CD133 expression in colon cancer. An immunohistochemical analysis of 72 cases

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CD133 is a transmembrane protein of 120 kDa expressed in various digestive and non-digestive cancers. However, its precise role remains unknown. In colon cancer, various studies found CD133 expression a negative prognostic marker and highlighted a correlation between CD133 expression at tumoral level and advanced stages of the disease, poor differentiated tumors, high number of lymph nodes involved or the presence of distant metastases. The aim of this study was to analyse CD133 expression in colon cancer samples and to evaluate the correlation between CD133 expression in colon cancer tissue and the clinical and pathological characteristics of the patients.

Material and methods. Patients that underwent surgery for colon cancer between January 2017 and January 2018 in number III, General Surgery Clinic from Cluj – Napoca were included in the study. CD133 expression at tumoral level was recorded as grades: 0 - negative (if no CD133 expression was found), grade 1 (if <50% of the cells expressed CD133) and grade 2 (if 50% or more tumoral cells expressed CD133).

Results. A number of 72 patients were included in this study (54.2% females, 45.8% males). The majority of the patients presented with tumors located in the sigmoid colon, 50%, followed by tumors located in the ascending colon, 41.6%. CD133 expression was confirmed at tumoral level, 70.8% of the cases had CD133 expression (44.4% had grade 2 CD133 expression while 26.4% had grade 1 CD133 expression while 29.1% of the samples had no CD133 expression (grade 0). The relation between CD133 expression at tumoral level and the clinical and pathological characteristics of the patients did not found, however, any significant correlation.

Conclusions. CD133 expression was confirmed in colon cancer tissue but its role as a predictive factor was not observed.

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The role of surgical treatment in polycystic ovary syndrome related infertility

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Introduction. Polycystic Ovary Syndrome (PCOS) is one of the most frequent endocrine pathologies that affects women within their reproductive years. Infertility is one of the common problems for these patients that rises numerous therapeutic challenges. Due to the underlying clinical and biological polymorphism of PCOS that characterize these patients unable to conceive, it is difficult to establish a unique therapeutic algorithm.

The place of surgical treatment with these patients was thoroughly debated in the last 30 years, in the latter decades being an adjuvant or last resort treatment for these cases. Surgery was the first treatment for women with PCOS when the syndrome was first described but after 2000 it was considered outdated. In the last decade tough, new evidence suggested that surgery could be an option for infertile idiopathic cases with PCOS. Our research is trying to answer this very uncertainty and evaluate the place of the surgical treatment for these patients.

Material and methods. Initially we included in our research 389 patients with idiopathic PCOS and infertility. We evaluated medical treatments alone or associations (methformin, clomiphene citrate, letrozole) and surgical approach as initial treatment or associated with medical agents for over more than 6 years.

Results. 112 patients with idiopathic PCOS and infertility were subjected to surgical treatment (alone or in association), with 27 obtaining a pregnancy. This percentage places surgery as a prime option for these cases. In addition, detailed analysis of our patients profile allowed us to pinpoint a subgroup of women with idiopathic PCOS and infertility that have the best response to surgery and these are non-obese patients.

Conclusion. Our research suggest that surgery is a prime therapeutic option for idiopathic PCOS infertile non-obese women.

Klatskin tumors' survival by intervention type and Bismuth-Corlette anatomic classification

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Introduction. The Klatskin tumor is a malignant disease representing 3% of all digestive tumors. Around 10% of patients could benefit by surgical treatment and those with palliative procedures survive 6 to 8 months. We aimed to evaluate the survival of patients with Klatskin tumors by the type of intervention and tumor extension.

Material and methods. A cohort study with retrospective data collection was done. All patients treated for a Klatskin tumor at the Third Surgery Clinic, "Prof. Dr. Octavian Fodor" Regional Institute of Gastroenterology and Hepatology from January 2012 to December 2016 were eligible for the study. The medical charts were reviewed, and all patients with data regarding the Bismuth-Corlette classification and the type of intervention were included in the study.

Results. Forty-eight patients aged between 39 and 79 years, male/female ratio of 1.5 were evaluated. Most cases were observed on patients older than 60 years (36 cases), males being affected from the age of 30 while females from the age of 50. The type IV Bismuth (involvement of the common hepatic duct (CHD) and extending past the confluence involving right and left hepatic ducts) was observed on 20 cases (43%) while the type II Bismuth (involvement of the CHD and extending just to the confluence) was seen on two cases (4%). Patients with type IIIb Klatskin tumor survived significantly longer, followed by those with type IIIa tumors (Log-rank: $p=0.019$). In most of the cases, the intervention was resection (19 patients) followed by drainage (12 ultrasound-guided percutaneous drainages, and 11 surgical drainages). Patients with resection survived significantly longer while, as expected, those with endoscopic palliative drainage survived less ($p<0.001$).

Conclusion. A better survival was observed among patients with type IIIb Klatskin tumor as compared to other Bismuth types. As expected, the surgical resection assured the best survival.

The use of pulsed short waves (Diapulse) to promote bone consolidation *in vivo*

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Introduction. Pulsed short waves (PSW) are high frequency pulsed electromagnetic fields provided by Diapulse machine. This therapy can facilitate bone consolidation process by increasing osteogenic markers and promote bone matrix mineralization "in vitro". The aim of this study was to evaluate PSW effects, "in vivo", on a rat fracture model.

Materials and methods. Medical titanium nails (Ti90Al6V4) were implanted after an open femoral diaphysis fracture was performed, on 20 rats. Beginning with the first postoperative day, ten animals (n=10) were exposed to pulsed short waves (PSW group), 10 minutes/day at 400 pps, at a mean power of 25.35W and at a total energy of 15.21 kJ, daily for two weeks. The bone consolidation was assessed, in both groups (control group = CG and PSW group), at two and eight weeks.

Results. At two weeks, histological images in optical microscopy, showed in the PSW group, a more advanced fibro-cartilaginous stage of soft callus formation without inflammatory infiltrate, less chondrocytes and new collagen fibers synthesis. Furthermore, μCT scan revealed a higher bone volume in the total tissue volume from the callus in PSW group (p=0.047). Serum levels of alkaline phosphatases (p=0.026) and osteocalcin (p=0.006) were statistically significant higher in the PSW group compared to the CG. Mechanical strength assessed by the tree-point bending test showed significantly higher values in the PSW group (p=0.03). At eight weeks, histological images in PSW group, revealed a regular appearance with woven bone completely formed and dense trabeculae, in contrast to CG, where it was present a medullar cavity with less bone marrow and presence of less defined woven bone trabeculae of hard callus stage development. μCT showed higher bone volume/tissue volume ratio (61.34% ± 2.61 vs. CG 55.23% ± 3.8, p=0.01) in PSW group.

Conclusion. Pulsed short waves applied immediately postoperative, can enhance fracture healing process mainly in its early period.

Rats as experimental models for vocal fold studies – personal experience

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Purpose of the study. Identifying the possibility of using Sprague Dawley rats as experimental models for vocal fold healing.

Objectives. Determining the morphological parameters of the rat larynx. Identifying instruments and adapting them for this experimental model.

Introduction. There is a growing publication tendency regarding the use of rat models for evaluating vocal fold scaring and healing, using diverse bioactive agents. The contribution of emerging countries for the literature is minimal. These difficulties are partially related to the existing infrastructure, the excessive logistics necessary to perform simple tasks and the sub financing of research. In some of the published literature the methodology is scarcely discussed and reproducing the results can be quite challenging.

Methods. The study was conducted at the University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca and Experimetal Animal Facility of the Iuliu Hatieganu University of Medicine and Pharmacy of Cluj Napoca. Three male Sprague Dawley rats were included in the study. Mean weight was 380 g. Endoscopic endolaryngeal images were obtained after sedation of the animals (8/80mg/kg Xylazine/Ketamine and 0.05 mg/kg atropine). The animals were euthanized, Micro-CT images were obtained and processed.

Results. Endoscopic images were analyzed. Anthropometric analysis was performed using the 3D images. After identification of the dimensions of the working space provided by the rat larynx, instruments were selected and adapted for the purpose.

Conclusion. Sprague Dawley rats can be considered candidates for experimental vocal fold studies. They respond well to sedation if appropriate protocol is used. Best suited rigid endoscope would be 1.9 mm, 30 degree, given the position of vocal folds, but a 0 degree 2.7 mm would suffice in appropriate sedation. 23 Gauge needle is appropriate to create lesion, given the 1 mm size of the vocal folds.

FUNDAMENTAL RESEARCH

Synthesis and antimicrobial activity evaluation of some new thiazolyl-oxadiazoles

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Introduction. The development of new antimicrobial drugs is a key concern, as the emergence of multi-drug resistance among bacterial and fungal pathogens has become a worldwide health threat. Due to the promising antimicrobial activity of compounds bearing the thiazole and/or the oxadiazole rings in their scaffold, we decided to synthesized a series of new 2-(thiazol-5-yl)-1,3,4-oxadiazoles.

Material and methods. The chemical structures of the 8 new compounds obtained were investigated by physicochemical characterization including: 1H-NMR, MS and elemental analysis. Antimicrobial activity was investigated against 5 Gram-positive bacterial strains, 2 Gram-negative bacterial strains and 2 fungal strains.

Results. The structures of all new compounds were verified and confirmed. In the preliminary in vitro qualitative screening of the antimicrobial activity, the newly synthesized compounds showed modest biological activity.

Conclusion. In spite of their structural resemblances with other active molecules, the newly synthesized molecules seem to have limited antimicrobial effect. The structure-activity relationships provided by this work can be used to generate future molecules with improved antimicrobial effect.

Synthesis, characterization and anticancer activity of several new thiazole aurones

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Introduction. Aurones represent a less studied class of flavonoids, but recent data from literature reveals their anticancer, antioxidant, antimicrobial and enzyme inhibitory potential. Continuing our research on the study of synthetic analogues of natural compounds, we have proposed the synthesis, spectral characterization and evaluation of the antiproliferative activity of several new thiazole aurones.

Material and methods. Thiazole aurones were synthesized through the oxidative cyclization, with mercury (II) acetate in pyridine, of some previously synthesized thiazole ortho-hydroxychalcones. The structural analysis of these compounds was performed by spectral methods: 1H NMR, 13C NMR, MS and IR. The anticancer potential of the thiazole aurones was determined in a panel of nine cancer cell lines including sensitive and drug resistant phenotypes. The resazurin reduction assay was performed to assess the cytotoxicity of these compounds and doxorubicin was used as standard.

Results. A new series of thiazole aurones was synthesized with 70-80% yields by the oxidative cyclization of the corresponding thiazole ortho-hydroxychalcones with

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mercury (II) acetate in pyridine. The spectral analysis, 1H NMR, 13C NMR, MS and IR, confirmed the structures of the newly synthesized compounds. The anticancer potential of the thiazole aurones was evaluated and some of the tested compounds proved to be good antiproliferative agents.

Conclusion. New thiazole aurones were synthesized from the corresponding thiazole ortho-hydroxychalcones. The structures of the synthesized compounds were confirmed on the basis of spectral analysis. Some of the synthesized thiazole aurones showed good cytotoxic activity on the tested tumour cell lines.

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Magnetic nanoparticles with high heating power for in vitro apoptosis of cancer cells

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Introduction. Magnetic hyperthermia is a therapeutic approach using magnetic nanoparticles (MNPs) to heat cancerous cells above normal physiological conditions by converting externally supplied magnetic energy into thermal energy. Among the intrinsic MNPs characteristics, crystallinity influences the heating efficiency of MNPs.

Materials and methods. By means of a polyol method, using chloride magnetic precursors, sodium acetate and polyethylene-glycol, polyhedral iron oxide NMPs were synthesized at high temperature and high pressure conditions. The MNPs were systematically investigated by means of X-ray diffraction, transmission electron microscopy, vibration sample magnetometry and magnetic hyperthermia. Their cytotoxicity has been investigated on the cell line T47D-KBluc by means of the Alamar Blue test at an incubation time of 4 h.

Results. The specific absorption rate (SAR) of highly crystalline ferromagnetic MNPs increases and saturates to 2000 W/gFe, as the external alternating magnetic field amplitude (AMF) is varied between 5 and 65 kA/m (f = 355 kHz). The SAR values decreased one order of magnitude in highly viscous media. Toxicity assays revealed almost no toxicity for MNPs at concentrations of 0.05 mg/ml and 0.1 mg/ml. A very small level of toxicity is recorded upon increasing the concentration at 0.2 mg/ml. The MNPs penetrated the cells through endocytosis, in a time dependent manner and escaped the endosomes forming aggregates more or less compact in contact to cytosol. Biodegradation of the MNPs inside cells was not observed. Preliminary results show that free cells keep their integrity upon exposure to AMF of different amplitudes.

Conclusion. Polyhedral iron oxide MNPs are promising candidates for in vitro destruction of cancer cells though magnetic hyperthermia therapy.

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Electrochemical surface plasmon resonance aptasensor for Ampicillin detection

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Introduction. Ampicillin (AMP) is a broad spectrum antibiotic, which due to its widespread use has led to the development of antibiotic resistant bacteria. A number of analytical methods have been reported for the determination of AMP, all of them with certain limitations.

Electrochemical surface plasmon resonance (EC-SPR) technique combines an optical method, surface plasmon resonance (SPR), which is sensitive to various processes taking place on a metal film, with electrochemistry, using the gold film of the SPR chip as the working electrode.

In this work, an EC-SPR method was developed for AMP determination, using an aptamer-modified SPR chip.

Materials and methods. The gold chip was functionalized through potential-assisted immobilization, with a thiol terminated anti-AMP aptamer, as a specific ligand and with mercaptohexanol to cover the unoccupied binding sites on the gold surface. All surface binding processes, as well as the specific recognition of the analyte were monitored by the changes in the SPR and signal and through electrochemical techniques.

Results. Using the optimized method, different concentrations of ampicillin were detected in real time, monitoring the SPR response, in the range of 2.5 - 1000 μmol•L-1 and the method was successfully applied for analyses of spiked river water.

Conclusions. A novel EC-SPR aptasensor was developed for the selective detection of AMP, proving the complementarity of different analytical methods .and the utility of their combination.

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Dopamine detection using electrodes modified by diazonium salts

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Introduction. Dopamine plays an important role in the control and regulation of the main neuronal functions, being involved in psychological and neurological pathologies and it can be considered as biomarker in the emergence and monitoring of the progression of neurodegenerative diseases. Thus, the detection of dopamine quickly, at low cost and without the need for separation in case of determinations made on complex matrices, is of great interest to the medical field. Dopamine is a phenolic compound having the property of being electroactive and it can be detected using electrochemical sensors. In this work, the electrochemical signal of dopamine was evaluated using carbon based electrodes modified with diazonium salts, containing the carboxyl, methoxy or phenol moiety.

Materials and methods. The glassy carbone electrode (GCE) and screen-printed electrode (SPE), used as working electrodes, were modified by electrochemical reduction of diazonium salts, containing the carboxyl, methoxy or phenol moiety, Ag/AgCl electrode was used as reference and Pt as auxiliary electrode. The influence of the electrode modification on the dopamine signal was evaluated by cyclic voltammetry.

Results. The modification of the electrodes with diazonium salts, containing

the carboxyl, methoxy or phenol moiety was optimized. The organic film grafted at the surface of the electrode was characterized using different redox probe. The thickness of the organic film and the moiety present in the film plays a role in the oxidation/reduction of dopamine.

Conclusions. The electrochemical signal of dopamine can be improved using electrodes modified with diazonium salts containing the carboxyl moiety.

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Pivot based molecular imprinting for the chiral separation of atenolol

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Introduction. Molecularly imprinted polymers became popular analytical tools, mainly employed with the purpose of concentration, separation, chiral discrimination and analysis of various biomolecules. However, there is still a gap of knowledge when it comes to imprinting highly polar compounds. In the present work we focused on the imprinting of atenolol for studying the favorable kosmotropic effect of a ternary metal complex by selecting the appropriate metal ion, functional monomer, molar ratio and porogenic solvent to be tested.

Material and methods. Two distinct approaches, non-covalent and metal ion-mediated molecular imprinting, have been undertaken, obtaining MIPs both in bulk and monolithic forms. The influence of various components of the polymerization mixture on the efficiency of separation has been studied. The characterisation of our polymer, in terms of morphology, was achieved by SEM studies and in terms of performance as chiral stationary phases in HPLC.

Results. The superiority of metal ion-mediated molecular imprinting, doubled by the beneficial effects of the ionic liquid on the imprinting efficiency has been unequivocally demonstrated ($\alpha = 1.60$). The most promising MIP in terms of enantioselectivity has been obtained by the polymerization mixture consisting of S-ATNL:Co(II):4-VPy, EDMA as cross-linker and [BMIM]BF4 in DMF/DMSO as porogenic solvent.

Conclusion. Concerning this study, we proved that in terms of selectivity, the performance was way better when a ternary complex was involved comparing to the non-covalent imprinting, but still, finding the ideal polymerization mixture is not a very straightforward process.

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A signal-off assay-based DNA-sensor for detection of profenofos pesticide

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Introduction. Herein, we propose an electrochemical DNA-based sensor for the sensitive detection of an organophosphorus pesticide, namely profenofos. The sensor is based on a competitive assay where the graphite-based screen-printed electrodes (GSPEs) were electrochemically modified with polyaniline (PANI) film and gold nanoparticles (AuNPs) by cyclic voltammetry (CV), which were further functionalized with thiol-tethered DNA oligonucleotide sequence complementary to the DNA aptamer [1].

Material and methods. PANI was electropolymerized by CV (−0.4V→+0.8V; 0.05V/s; 10 scans) from 2.5 mM ANI in 50 mM HClO4; AuNPs were electrodeposited by CV (−0.2V→+1.2V; 0.1V/s; 15 scans) at PANI/GSPE from 0.5mM HAuCl4 in 0.5M H2SO4.

Results. Different profenofos solutions containing a fixed amount of biotinylated aptamer by DNA-based arrays were analysed. Streptavidin-alkaline phosphatase conjugate was then added to trace the affinity reaction and catalyse the hydrolysis of 1-naphthyl phosphate to 1-naphthol which was electrochemically triggered. A decrease of the signal was obtained when the pesticide concentration was increased, making the sensor work as signal off competitive assay. A dose response curve was obtained between 0.10-10 μM with a LOD of 0.27 μM.

Conclusion. Affinity-based biosensing can contribute to pesticide detection as a valid and innovative analytical approach. The obtained results showed that the sensor could be applied for application in real samples analysis, since it involved low amounts of reagents and easy-to-prepare portable aptasensors.

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Click chemistry on azide functionalized graphene

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Introduction. Chemical functionalization of graphene oxide represents a major challenge in chemical engineering in order to extend the properties of the material and to generate versatile platforms with a broad range of applications. Click chemistry reaction represents an important strategy for the covalent linking of different compounds on the substrate bearing the complementary azide or alkyne groups. The mild reaction conditions allow the preservation of the properties of biomolecules, the orientation towards green chemistry enabling a new range of biomedical applications.

Material and methods. The azide group was introduced in the graphene oxide backbone by chemical functionalization and the resulting product was thoroughly characterized by FTIR spectroscopy, scanning electron microscopy, electrochemical impedance spectroscopy and cyclic voltammetry after clicking ethynylferrocene.

Results and discussion. The spectra registered on G-N3 depicted the presence of an absorption peak at 2122 cm-1, corresponding to the stretching vibrations of the azide group chemically bound to GO, confirming the functionalization of GO with the

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azide groups. As expected, the current intensity of the oxidation signal proportionally increased with the scan rate (I(μA)=-0.92v+0.13, R2=0.99), confirming the adsorption of ethynylferrocene on the graphene layer and its successful immobilization via click chemistry.

Conclusion. The new method of graphene functionalization allowed the detection of one electroactive molecule, providing a novel way of controlled immobilization of different (bio)molecules, useful in the development of electrochemical sensors or targeted delivery systems.

Quantification of human interleukin 6 in serum using an inovative magnetoimmunosensor

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Introduction. A magnetoimmunsensor for the selective and sensitive detection of Interleukin 6 (IL6) is described. IL6 is a polypeptide cytokine with an important role in the immune system Detecting differences in its production play an important role in many diseases such as: lupus erythematosus, acute infections, rheumatoid arthritis. IL6 is also overexpressed in cancers like gastric cancer and can be considered a biochemical biomarker.

Materials and methods. The covalent immobilization of anti-interleukin 6 antibody(anti-IL6 AB) was made through an amidic bond formed with the carboxyl functionalities provided at the surface of protein G functionalized magnetic beads, assuring a sandwich-type immunoassay with electrochemical label free detection. A blocking step with bovine serum albumin was performed in order to minimize the nonspecific adsorption of the protein on the remaining active sites after the anti-IL6 AB immobilization. All the analytes used in the study were of analytical grade. This immunosensor was characterized using electrochemical impedance spectroscopy and Raman spectroscopy.

Results. A linear calibration plot between the charge transfer resistance and the logarithmic concentration of IL6 was achieved in the 1 pgmL-1 to 1 μgmL-1 range. A limit of quantification of 1 pgmL-1 and a detection limit of 0.3 pgmL-1 were obtained. The sensor showed good selectivity against some potential interferences. The Raman characterization confirmed the modifications described before (1).

Conclusions. A simple, relatively fast magnetoimmunosensor was developed for the selective and highly sensitive quantification of IL6 in human serum. The promising results obtained using serum spiked with IL6 proves its possible clinical applicability.

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Liquid chromatography/electrospray tandem mass spectrometry method for the determination of Dapagliflozin in human Plasma. Application to a pharmacokinetic study

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Introduction. The incidence of type two diabetes resistant to biguanides, the most frequently used agents for treatment of this disorder is increasing. The discovery of new treatments for these patients needs immediate attention, as consequence new classes of compounds like SGLT2 inhibitors are tested.

Material and methods. A high performance liquid chromatography-tandem mass spectrometry method (LC-(ESI)/MS/MS) was developed and validated to determine Dapagliflozine in human plasma. Following the solid phase extraction of 0.200 mL of plasma, a baseline separation was achieved on Gemini-NX C18 110A, 3 µm, 50x3 mm column using isocratic mobile phase consisting of methanol: acetonitrile: water: ammonia solution 25 % (70:10:20:0.1 v/v/v/v) at the flow rate of 0.300 mL/min. The retention times are 1.3 and 1.3 for Dapagliflozin and Dapagliflozin D5 respectively.

Results. Detection of analytes and internal standards were achieved by tandem mass spectrometry with electrospray ionization (ESI) interface in negative ion mode. The method linearity was attained in the range of 1.01 to 352.50 ng/mL. The within batch accuracy for three precision and accuracy batches ranged from 0.27% to 2.99%. The matrix effect observed in this method is very small and has no impact on the samples analyzed. Two open label, balanced, randomized, two-period, single-dose, crossover bioequivalence studies comparing Dapagliflozin tablets 10 mg manufactured by Sun Pharmaceutical Industries Limited, India with Farxiga® (Dapagliflozin) tablets 10 mg manufactured by Bristol-Myers Squibb Company for AstraZeneca Pharmaceuticals in healthy adult volunteers under fed and fasted conditions were analyzed using this method.

Conclusion. The validated LC-MS/MS method was successfully applied for the evaluation of pharmacokinetic and bioequivalence parameters after oral administration of Dapagliflozin 10 mg tablets to healthy volunteers. The investigated products can be interchangeable.

Overcoming plasmodium's drug defense mechanisms: role of lipids in malaria pigment formation

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Introduction. Malaria is an infectious disease caused by parasites of the genus Plasmodium, responsible for nearly half a million deaths only in 2016. The sequestration of toxic heme into a crystallized polymer, known as malaria pigment, is an essential process for the survival of the parasite. Even though the exact mechanism of hemozoin biosynthesis under physiological conditions is still under debate, it is hypothesized that the formation of malaria pigment takes place in the presence of a biological material. The major objective of this study is to understand the link between Plasmodium lipid metabolism and hemozoin formation to propose a possible strategy for new antimalarial drugs.

Material and methods. As experimental model, micro-emulsions of neutral lipids in citrate buffer identical in composition with the neutral lipid droplets present in the digestive vacuole of the parasite were employed. In order to mimic the phospholipid

bilayer, liposomes were made of dioleoyl phosphatidylcholine.

Results. The kinetics of β-hematin formation have shown that hemozoin-associated neutral lipids or phospholipids are capable of mediating β-hematin formation at adequate rates under physiologically relevant conditions. Scanning electron microscopic imaging taken from the water-lipid interface confirmed the presence of crystals enveloped in the neutral lipids. Hemozoin content after 48 hours was higher when Plasmodium falciparum was cultivated on a lipid-supplemented medium.

Conclusion. This method showed potential application to monitor β-hematin formation in vitro and the effects of antimalarial drugs that exploit this process as their target.

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Synthesis, molecular docking studies and antifungal activity evaluation of new 1,3,4 oxadiazolines

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Introduction. Candida species represent the most common fungal pathogens that affect humans and the mortality associated with invasive mycosis increased in the last decade. Prolonged use of azoles as antifungal agents has resulted in the emergence of drug resistance among certain fungal strains. One of the strategies for developing new clases of antifungal agents is the merger of two or more biologically active azole scaffolds, in order to obtain compounds with improved activity. To this end, we chose two biologically important azole scaffolds: thiazole and 1,3,4-oxadiazole and fused them into hybrids molecules that are supposed to possess a broad spectrum of biological activities, including antifungal activity.

Material and methods. A new series of thiazolyl-methylen-1,3,4-oxadiazolines derivatives were synthesized and were characterized by NMR, MS and elemental analysis techniques. These compounds were screened for their antifungal activity against the Candida albicans ATCC 90028 strain and compared with a standard. Molecular docking studies were performed to investigate the interaction modes between the compounds and the active site of lanosterol 14-α-demethylase, the target enzyme for anticandidal azoles. Theoretical ADME predictions were also calculated for the compounds.

Results. Results of the antifungal study indicated that some of the compounds showed better anticandidal activity than the standard. Molecular docking studies showed that these compounds interact with lanosterol 14α-demethylase in a different manner compared with classical antifungal azoles. ADME predictions support the druggability of these compounds.

Conclusions. A series of new oxadiazoline derivatives were synthesized and evaluated for antifungal activity. The preliminary results showed a promising antifungal activity for some of the tested compounds.

Interaction studies between gold nanoparticles, propranolol enantiomers and L-Cysteine

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Introduction. Gold nanoparticles (AuNPs) are important components for biomedical application, offering unique optoelectronic and catalytic properties. As such, they continue to attract considerable interest in electrocatalysis and in the design of chemo- and biosensors. Cysteine can be used to control the size and shape AuNps; during the process it can form complexes with gold ions. By adding L-cysteine to the HAuCl4 solution used for gold deposition (AuNps – L-Cys), the number of nucleation sites is increased and also the kinetics parameters are improved without major changes in the purity of deposits. The present study aimed to investigate the interaction between AuNPs, the enantiomers of propranolol L-Cys using differential pulse voltammetry, electrochemical impedance spectroscopy and computational modelling.

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

Results. There are considerable differences in the peak potential and current intensity of the two enantiomers explained by the fact that R-(+)-Propranolol adsorbs stronger on the L-Cys AuNPs surface than S-(-)-Propranolol. Computational modelling showed that the propranolol enantiomers adsorbs differently on the AuNPs – L-Cys surface.

Conclusion. We have seen that the enantiomers adsorption on the electrode surface modified with gold nanoparticles it's non-chiral. R-(+)-Propranolol adsorbs stronger on L-Cys Au Nps surface and can forme more hydrogen bonds.

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Influence of the co-exposure to ruthenium (III) on the subacute toxicity of silver ions in rats

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Introduction. Ruthenium is one of the rare earth elements, often used in technology, without having enough knowledge regarding its toxic effects. Silver on the other hand is well known for its antiseptic, antibacterial and immunonostimulant properties, being used for these reasons in medicine. The combination of ruthenium with silver compounds may represent an alternative for platinum based anti-cancer drugs which are known to display a high toxicity.

Material and methods. The present study investigated the co-exposure to ruthenium (III) on the subacute toxicity of silver ions in rats after daily administration of low doses for 28 days by oral gavage. Three groups of Wistar rats were used for this aim

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(n=6): M - the negative control group, Ag - the treated group with $AgNO_3$ (9 mg/kg) and Ag^+Ru – the treated group with $AgNO_3$ (9 mg Ag^+/kg) and $RuCl_3$ (2,25 mg Ru^{3+}/kg). The subacute toxicity was investigated by: 1) the evaluation of several specific biochemical and hematological parameters after 14 and 28 days of exposure, 2) the evaluation of specific oxidative stress biomarkers from liver and kidney, 3) histopathological investigation of liver and kidney tissue samples after 28 days of exposure, and 4) silver and ruthenium concentration determination in urine, liver and kidney parenchyma after 14 and 28 days of exposure.

Results. The obtained results show that subacute exposure to low doses of silver ions slowly changes some of the oxidative stress biomarkers (MDA, GSH and GSH/GSSG ratio) without affecting the other investigated parameters. The co-exposure to low doses of ruthenium (III) mitigated the oxidative stress caused by silver ions.

Conclusion. This is the first *in-vivo* study investigating the toxic effect of co-exposure in low doses of silver and ruthenium ions, and the obtained results may justify further research on this subject mainly on some possible competitive mechanism investigation.

Extraction optimization for the determination of phenolics from five *Galium* species (*Galium verum*, *Galium erectum*, *Galium rivale*, *Galium pseudoaristatum*, and *Galium purpureum*) from Romania and their antioxidant and tyrosinase inhibitory properties

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Introduction. *Galium* species are used in Romanian traditional medicine as diuretics, choleretics, against diarrhea and in the treatment of some stomach complaints, gout and epilepsy. In this study, five species of *Galium* (*G. verum*, *G. erectum*, G. rivale, *G. pseudoaritatum*, and *G. purpureum*) were investigated in terms of chemical composition, antioxidant and tyrosinase inhibitory proprieties.

Materials and methods. In the current study, liquid phase and microwave extraction procedures combined with HPLC-PDA detection were applied to identify phenolic multi-

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component pattern of the five *Galium species*. Also, the antioxidant capacity of the extracts was evaluated using microtiter assays (DPPH and ABTS scavenging capacity assays, FRAP assay, correlated with total phenolic and flavonoid content). Moreover, the tyrosinase inhibitory potential was evaluated for all considered species.

Results. The chromatographic fingerprint showed that among investigated compounds, rutin was found as the main compound in *G. verum* extracts (3623.91 ± 96.81 µg/g d.w.), while chlorogenic acid was the dominant compound found in the other four species. Antioxidant capacity assays showed an important antioxidant potential for all investigated species, especially for *G. purpureum* (6.31±0.71 mgTE/g extract, 16.74±0.82 mgTE/g extract, and 45.22±1.10 mgTE/g extract, for DPPH, ABTS, and FRAP assays, respectively). These results can be ascribed at least partially to the determined polyphenolic compounds. Concerning the enzyme inhibitory assay, *G. erectum* extract presented the highest inhibitory potential against tyrosinase (13.78±3.43 mgKAE/g extract, with a high percent of inhibition of 70.98%), an enzyme involved in ocular diseases, hyperpigmentation, and other skin disorders.

Conclusions. Further studies are needed to elucidate the specific compounds responsible for the tested biological activities, as well as the different mechanisms of action involved.

Chemical composition of different species of Salvia from Romania (*Salvia transsylvanica*, *Salvia glutinosa*, *Salvia officinalis*) and their biological activities

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Introduction. Sage species are used in Romanian traditional medicine for coughs, rheumatism and inflammatory diseases, as well as antidiabetic remedies. In this study, *Salvia glutinosa* and the endemic *Salvia transsylvanica* were compared with the well-known *Salvia officinalis* in terms of chemical composition and biological activities.

Material and methods. In the current study, an HPLC method was applied for determination of 22 phenolic compounds in dry extracts of *S. glutinosa*, *S. transsylvanica*, and *S. officinalis*. The antioxidant capacity and enzyme inhibitory potential of the extracts were evaluated using microtiter assays, and the antimicrobial potential was tested using the microdiluation assay for eight bacterial and fungal strains. These extracts were further tested on three different cancer cell lines (A549, HepG2 and MCF-7) at increasing concentrations (1.56-200 µg/mL) for 24h/48h to assess a possible cytotoxic activity.

Results. The HPLC fingerprint revealed that among investigated compounds, the dominant compounds of *Salvia* species are rutin (1357.9 - 4070.2 µg g-1) and catechin (1112.6 - 1911.1 µg g-1). In the antioxidant measurements, generally *S. officinalis* exhibited high antioxidant capacity for all assays, the highest values being obtained for the CUPRAC test: 400.01 mgTE/g extract for *S. officinalis*. Concerning the enzyme inhibitory assays, S. officinalis extract presented the highest inhibitory potential on butyrylcholinesterase (2.40 mgGALAE/g extract) followed by *S. transsylvanica* (1.43 mgGALAE/g extract). Additionally, both *S. officinalis* and *S. transsylvanica* extracts exhibited an important inhibitory potential against alpha-glucosidase (27.01 mmolACAE/g extract, and 25.62 mmolACAE/g extract, respectively). From the three extracts tested, the S. officinalis extract exhibited the most potent cytotoxic effect. Interestingly, when testing on the estrogenic responsive cell line MCF-7, an increase in the viability was observed for

intermediary doses which we hypothesize to be related to the estrogen-like compounds present in *Salvia* species.

Conclusion. Other studies are needed to elucidate the different mechanisms of biological activity, as well as the specific responsible compounds.

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Development and validation of a UPLC-MS/MS method for the determination of selected protein oxidation biomarkers

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Introduction. Protein oxidation by reactive oxygen species (ROS) has been shown to be the cause of protein misfolding and loss of enzyme function. Aromatic amino acids such as p-tyrosine (p-Tyr) and phenylalanine (Phe) are readily oxidized by ROS, leading to the formation of dityrosine (Dityr) and o- and m-tyrosine (o-Tyr and m-Tyr). These oxidation products have been used as biomarkers of protein oxidation, but their low concentrations in samples compared to the non-oxidized amino acids raise analytical challenges.

Material and methods. The separation of analytes was performed using an Acquity CSHTM C18 chromatographic column and a mixture of 0.05% formic acid in water and methanol as the mobile phase, with a gradient elution at a flow rate of 0.4 mL/min. The total run time was 6 minutes. D4-p-tyrosine was used as internal standard. Detection of the analytes and internal standard was performed by MS/MS, using ESI+ ionization mode and MRM.

Results. Analyte separation and peak shape were adequate for quantitation. The calibration curves were linear for all analytes (Phe, p-Tyr, o-Tyr, m-Tyr, Dityr) over the chosen concentration ranges. Intra- and inter-day assay precisions were satisfactory (<5% CV) and the inaccuracy for each analyte was within the recommended limits (±15%, ±20% at LLOQ).

Conclusion. A fast and sensitive UPLC-MS/MS method for the quantitation of Phe, Tyr and their oxidation products was developed and validated. The method could be applied to assess protein oxidation in different biological matrices, after further validation using matrix-matched calibration curves and QC samples. SSRIs have been shown to modulate lipid peroxidation and antioxidant defenses, but little is known about their influence on protein oxidation. Quantifying these protein oxidation biomarkers after SSRI exposure/treatment using the elaborated method could reveal new aspects regarding their redox modulating potential.

PHARMACEUTICAL SPECIALTIES

European pharmaceutical initiatives in environmental protection

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Introduction. At the international level, there is an increased interest for establishing specific regulations and programmes in order to protect the environment from the risks of contamination with active pharmaceutical ingredients. At the national level, the involvement of both the State and pharmaceutical enterprises is important. The aim of this paper is to identify and analyse European initiatives involving pharmaceutical enterprises in the field of environmental protection.

Material and methods. Initiatives from five European States (Finland, France, Spain, Hungary and Romania) were researched using the comparative method. The legal framework, the role of each type of pharmaceutical enterprise and the source of funding for specific activities were used as elements of comparison.

Results. In Finland, by law, expired medicines are collected by community pharmacies or local points designated by municipalities, which fund the activity of waste disposal. Hungarian legislation states that manufacturers have the obligation of organizing and funding the pharmaceutical waste disposal, with the participation of community pharmacies in collecting expired medicines. In France and in Spain, the most important pharmaceutical organisations created Cyclamed, respectively Sigre, which are non-profit associations responsible for proper medicines disposal, on the expense of the pharmaceutical industry. Romanian legislation establishes that any community pharmacy should accept and collect expired medicines brought by patients, for further disposal, on its own expense. The Romanian College of Pharmacists adopted a procedure that should be applied for this purpose.

Conclusion. Each country has a policy for proper disposal of medicines, but the level of involvement of each stakeholder is different, from regulating, to collecting or funding. The involvement of all types of pharmaceutical enterprises in these activities is needed in order to improve the whole process in Romania.

EGCG liposomes optimization through the use of experimental design

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Introduction. Liposomes are drug carriers used in targeted therapies, consisting of the main components of the cellular membrane like phospholipids and cholesterol. They encapsulate both hydrophillic as well as lipophilic drugs, in their aqueous core and lipophilic membrane, respectively. The main objective of this study was to optimize the formulation of liposomes with epigallocatechin gallate (EGCG), a catechin extracted from green tea, by using the design of experiments approach.

Material and methods. For the development of the liposomes, the influence of the independent variables, namely phospholipids concentration, phospholipids to cholesterol molar ratio and the concentration of EGCG, on the physio-chemical characteristics of the liposomes was studied, using an experimental design consisting of 14 formulations. The liposomes characterisation consisted in determination of the liposomal size, Zeta potential and EGCG concentration, and of the encapsulation efficiency (EE).

Results. Results showed that EGCG concentration was between 36.7 and 249.8 µg/ml, liposomal size between 157.36 and 202.83 nm, EE between 26.71 and 76.7% and Zeta potential between -80.23 and -38.56 mV. The use of statistical analysis showed that all the results were well predicated by the suggested model. Also, by analysing the

influence of the formulation factors on liposomal characterisation, we concluded that the use of a lower phospholipid:cholesterol molar ratio lead to a higher EE and the utilisation of a higher EGCG concentrations lead to smaller liposomal size. The results of the optimized formulation were as follows: EGCG concentration of 221.93 µg/ml, vesicle size of 175.23 nm and EE of 69.16%.

Conclusion. This study is the starting point in the development of a new pharmaceutical formulation with potential application in the treatment of parodontosis and showed that EGCG encapsulation in liposomes can successfully be optimized by using a D-optimal experimental design.

Electrospun amorphous solid dispersion of meloxicam. Influence of polymeric carrier matrix on pharmaceutical properties and downstream processing to orodispersible tablets

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Introduction. The development of amorphous solid dispersions (ASD) is an efficient strategy to overcome the solubility issues of BCS class II molecules. The objective of this work was to develop ASD with meloxicam through electrospinning, investigating the effect of the polymeric matrix on the pharmaceutical properties of the fibers.

Materials and methods. Electrospun fibers were prepared with PVP (±HPBCD) and Eudragit E (EE) considering two co-solvent systems (DMF:THF=1:1; ethanol) at room temperature (22±2°C) and a voltage between 25-30kV. The fibers were characterized in terms of: content uniformity, crystallinity, diameter, dissolution/absorption studies. For tablet preparation the EE based fibers were triturated in the presence of fillers, further on the disintegrant and lubricant was added and compressed using Ø10 punches.

Results. The API – EE interaction enabled the solubilization of API in ethanol leading to an improved production rate (6 ml/h) compared to the DMF:THF system (3 ml/h). The recovery of API content was close to 100%, excepting the PVP/ethanol system as the API was found in a suspended form. XRPD showed that meloxicam was amorphous. The fiber diameter was mainly influenced by the solvent volatility, obtaining lower diameter fibers for DMF:THF system. Microflux studies showed that under acidic conditions the API release and absorption is not influenced by the polymer, whereas at pH 6.4 the flux through the membrane for EE fibers was slightly reduced. EE fibers presented good fracturability enabling the development of ODTs (4.5 sec disintegration time, 0.37% friability, 46 N), moreover Raman mapping showed that API was still in amorphous state.

Conclusion. Developing EE based electrospun fibers enabled an increased productivity, moreover it presented appropriate processing ability for tablet production. In vivo animal studies will be considered to elucidate the effect of EE over the API absorption.

ESTICOST: factors associated with eating disorders among medical students

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Introduction. Eating disorders are frequent in young adults, including medical university students [1]. The objective of this study was to evaluate the prevalence of eating disorders and their associated factors among medical university students.

Material and methods. Cross-sectional studies were carried out among students from the University of Medicine and Pharmacy Cluj-Napoca, during the first three academic years of ESTICOST (a multiannual survey on the lifestyle and behaviors of students): 2015-2016=E1, 2016-2017=E2 and 2017-2018=E3. Data, anonymously collected by using questionnaires, included socioeconomic and behavioral characteristics. The SCOFF questionnaire was used for screening eating disorders.

Results. A total of 1350 questionnaires were included: 222 for E1 (16.4%), 582 for E2 (43.1%) and 546 for E3 (40.5%). Most students were attending General Medicine (69.3%) and Pharmacy (26.4%) studies. The mean age was 21.5 (SD 1.9, range 18-28) for E1, 21.2 (SD 3.2, range 18-45) for E2 and 22.2 (SD 2.9, range 18-42) for E3. The sex ratio (female/male) was 4.6 for E1, 3.4 for E2 and 3.1 for E3. The mean BMI was 21.3 (SD 3.3, range 14.2-35.9) for E1, 21.5 (SD 3.2, range 15.1-38.4) for E2 and 22.1 (SD 3.6, range 14.9-40.4) for E3. From all students included, 13.4% were underweight and 15% overweight at the time of survey participation. A total of 25.7% students from E1, 24.1% from E2 and 23.4% from E3 had positive SCOFF score. We found differences between the observed and expected frequencies of the SCOFF score associated with factors like: academic year, self-estimated academic level, studies attended, presence of financial difficulties and BMI score.

Conclusions. The awareness of eating disorders should be risen and programs to prevent and manage eating disorders among medical students should be implemented.

Effects of Lycium barbarum polysaccharides on inflammation and oxidative stress markers in a pressure overload-induced heart failure model

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Introduction. Heart failure (HF) prevalence is still high, with 1-2% in the general population and more than 10% in the elderly, despite modern treatments. L. barbarum polysaccharides (LBPs) are widely used for their antiinflammatory and antioxidant properties. Thus, our aim was to evaluate the effects of LBPs on inflammation and oxidative stress markers in a pressure overload-induced HF model.

Materials and method. Four week-old rats were included in the study (n=38). Pressure overload HF was surgically induced by abdominal aorta banding (AAB) (n=28) and the rest were sham rats (n=10). At 24 weeks after the surgery, AAB rats (n=16) received LBP 60% standardized extract: n=9, 200 mg/kg bw/day and n=7, 100 mg/kg, respectively. The other AAB rats (n=12) were considered controls. After 12 weeks of treatment, rats were sacrificed, organs and plasma were sampled for further analysis.

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Results. At 24 weeks after the surgery AAB rats presented with reduced ejection fraction (EF) (mean 36.5 ± 5.2%) and high left ventricular diastolic and systolic diameters (mean 11.2 ± 1.2 mm and mean 9.88 ± 1.33 mm, respectively), thus being diagnosed with HFrEF. At 36 weeks after the surgery, in the LBP treated group, the decline of the cardiac function was not as important as for the controls (EF mean 34.8 ± 2.2% compared to 32.1 ± 1.3%). For LBP treated AAB rats MDA plasma levels were significantly lower in the LBP group compared to controls (mean 3.13 ± 0.47 nmol/ml, compared to mean 6.03 ± 1.37 nmol/ml, $p<0.001$). Inflammation markers, IL-6 and TNF-α plasma levels were significantly lower in the LBP group compared to controls (mean 77.62 ± 53.8 pg/ml, compared to mean 517 ± 506 pg/ml, $p<0.034$), respectively (mean 14.21 ± 12.5 pg/ml, compared to mean 44.57 ± 16.5 pg/ml, $p<0.026$).

Conclusion. Treatment with LBP 60% standardized extract reduced inflammation and oxidative stress markers and the decline of the systolic function in a pressure overload-induced HF animal model.

Effect of food on the pharmacokinetics of Gliclazide 60 mg modified release tablets in healthy Caucasian volunteers

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Introduction. Gliclazide is a sulphonylurea used as a second-line treatment for Type 2 diabetes patients. Modified release pharmaceutical formulations ensure a better glycaemia control and a high compliance to treatment. Food intake may induce physiological changes, with potential influence on drug pharmacokinetics. The objective of the research was to evaluate the food effect on glicazide disposition in clinical trials conducted on healthy Caucasian volunteers who were given a new modified release oral formulation of Gliclazide 60 mg developed by Ranbaxy Laboratories Limited, now Sun Pharmaceutical Industries, India.

Materials and methods. The studies were open-label, randomized, single-dose, two-period crossover studies. During each study, venous blood samples were taken before and after dosing up to 96 hours. Individual plasma profiles were determined and non-compartmental method was used for the assessment of food effect on the pharmacokinetic (PK) profile of gliclazide. The statistical significance of differences for the main PK parameters was evaluated by ANOVA test, for $p<0.05$ statistical significance was decided. The relative profiles of absorption of gliclazide were obtained by mathematical deconvolution. All calculation were performed by Pheonix WinNonlin® PK version 6.3.

Results. High-fat, high-calorie meal decreased gliclazide exposure. The mean maximum plasma concentration decreased with 14% and the mean total area under the plasma concentration-time profile registered a 17% decrease. The elimination half-lives were comparable and the time to maximum plasma concentration was shorten under fed condition. Safety evaluation showed that overall gliclazide was well tolerated under both fasted and fed condition.

Conclusions. The statistical analysis revealed the lack of food effect on the new modified release tablets of Gliclazide 60 mg. Therefore, gliclazide can be safely administered to patients regardless of food intake.

The pharmacokinetics of a new formulation with Dapagliflozin under fasting conditions

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Introduction. Dapagliflozin is a selective and highly potent sodium-glucose linked transporters-2 inhibitor which improves the glycemic control in patients diagnosed with type 2 diabetes mellitus by reducing the renal glucose reabsorption and increasing the glucose renal excretion, through an independent insulin process. It has been developed a new test formulation with dapagliflozin and assessed its pharmacokinetics in comparison with an authorized reference product under fasting condition.

Material and methods. The single-dose study was design as crossover, open, balanced, randomized, with two treatments, two periods and two sequences. It was conducted on 48 healthy volunteers under fasting conditions out of which 38 subjects completed the study. 46 blood samples were taken during each period. For determination of dapagliflozin concentrations 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 AUC0-t, AUC0-∞, Cmax, Tmax. Kel and T1/2.

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

Results. Ratios of least square means for ln- transformed pharmacokinetic parameters for dapagliflozin using 90% Confidence Interval were calculated. The results obtained for ln Cmax was 105.17% (96.07% – 115.12%), for ln AUC0-t was 103.15% (101.04% – 105.30%) and for ln AUC0-∞ 102.09% (99.90% - 104.33%).

Conclusion. Based on these results, the two formulations containing 10 mg of dapagliflozin were determined to be bioequivalent in healthy, adult, human subjects under fasting condition as the 90% confidence intervals for the ratio of test and reference product averages of the pharmacokinetic parameters were within 80.00-125.00% acceptance range.

Preliminary phytochemical analysis and antioxidant activity of *Taraxacum officinale* (L.) Weber/ Asteraceae

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Introduction. The purpose of this study was to complete the current knowledge about the chemical composition of T. officinale (L) Weber indigenous species, the influences of the harvesting area, in order to establish some correlations with the therapeutic properties.

Materials and methods. The vegetable material (Taraxaci herba, radix) was collected from various Romanian counties. The polyphenols were analysed by chromatographic and spectophotometric methods. The total polyphenolic content (TPC) was assesed by Folin-Ciocalteu method, expressed as galic acid equivalents (GAE); the total flavonoid content (TFC) was determined with the reaction with AlCl3, expressed as rutin equivalents (RE) and for caffeic acid derivates content the results were expressed as caffeic acid equivalents (CAE). The evaluation of antioxidant activity was carried out with the DPPH• radical scavenging method. The polyphenolic compounds were analysed

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by HPLC assay.

Results. The TPC values for the analysed samples were between 10.7-28.1 mg GAE/g dry material for herba and between 0.7-4.2 mg GAE/g dry material for radix. The antioxidant capacity expressed as IC50 was in accordance with the levels of total polyphenols. The differences between the TPC values are linked to the different areas where the plant samples were harvested. The HPLC analysis revealed caffeic acid, clorogenic acid, cichoric acid, p-coumaric acid, ferulic acid, hyperoside and rutin among other compounds.

Conclusion. T. officinale is a source of valuable polyphenols, especially flavonoids and caffeic acid derivatives with good antioxidant activity. The climatic environment could influence the TPC, which could explain the differences between the analysed samples. For a better pharmacological evaluation it is important to know the quality of the raw material.

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Development of bioactive compounds-loaded chitosan films using a QbD approach

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Introduction. In the present study, a Quality by Design (QbD) approach was applied in order to develop and optimise a bioactive compounds-loaded chitosan film formulation, intended for further use as an aid in the acceleration of diabetic wound healing.

Materials and methods. Chitosan was chosen as film forming polymer, polyethylene glycol (PEG) was used as plasticiser, while polyvinyl alcohol (PVA) was added to improve the bioadhesive properties of the films. A concentrated alcoholic extract consisting of a mixture of Plantago lanceolata, Arnica montana, Tagetes patula, Symphytum offcinale, Calendula officinalis and Geum urbanum was added in the formulation in order to enrich the film with bioactive compounds. Risk assessment strategy was applied to identify the critical formulation variables, which were further introduced as factors of a 3 level Box Behnken design of experiments (DoE). The studied outputs of the DoE were critical quality attributes of the films. Solutions consisting of chitosan, PEG, PVA and herbal extract, all in various proportions according to the DoE specifications, were prepared and casted onto polypropylene plates. The films were obtained after drying at 40°C for 24h.

Results. Following experimental data analysis, the Design Space was established and an optimal formulation was prepared. This formulation registered a film thickness of 0.092 mm, solubility in water of 44.8% and a high swelling degree of 2157%, values within the specifications of the quality target product profile. The antimicrobial effects of the optimised formulation and of a placebo formulation without bioactive compounds were determined by the disk diffusion method, against common wound pathogens. The formulations proved to have a good antimicrobial activity.

Conclusion. Taking into consideration the promising results obtained, we conclude that in our study, the QbD approach was successfully applied in order to ensure a good understanding of the manufacturing process, as well as to optimise the formulation of chitosan films.

A comparison of pregnancy prevention programmes in the EU with a focus on valproate and related substances

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Background. A pregnancy prevention programme (PPP) is comprised of a set of interventions aimed at minimizing exposure to medicines with known or potential effects, during pregnancy. Appropriate access control to medicines is accomplished through a combination of different educational tools. PPPs may be imposed by regulatory authorities to minimize the risk of pregnancy exposure and consequent congenital malformations. The present study aims to compare the PPP imposed for valproate, with the similar risk minimization interventions in place for other medicinal products.

Methods. PPPs were assessed for valproate and other drugs that had a PPP in place, using data primarily gathered from the EU publicly available information from the European Public Assessment Reports (EPAR) via the European Medicines Agency (EMA) website. Secondly, relevant other sources were assessed (Heads of Medicines Agencies (HMA) website, referral assessment reports, etc.

Results. In 2017 a new referral procedure was triggered for valproate, and recently concluded in amendments to product information, a PPP and a direct healthcare professional communication. Among the PPPs assessed (valproate compared to thalidomide, retinoids), educational materials uniformly targeted prescribers/patients, and were represented by brochures, checklists/guides, patient cards. All PPPs included patient counselling on pregnancy prevention as well as precautions for male patients.

Conclusions. The PPP for valproate and related substances generally followed the design of other similar programmes in place, enclosing common elements like contraindication during pregnancy, the need for contraception and regular pregnancy tests. PPP can be designed on a case by case scenario, however there is a need for regulatory guidance on proper development, as well as evaluation of the benefits and burden of PPPs in pursuit of constant optimization of the intervention.

The 3D-FDM printability assessment in terms of pharmaceutical polymers/polymeric blends

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Introduction. The three dimensional printing (3DP) in the pharmaceutical domain constitutes an alternative, innovative approach compared to the conventional production methods. Fused deposition modelling (FDM), is a simple, cost-effective 3DP technique, however the range of pharmaceutical excipients that can be applied for this methodology is restricted. The study set to define the requirements of the FDM printability, using as technical support custom made, pharmaceutical polymer based filaments and to evaluate if these new dosage forms can live up to the current GMP/GCP quality standards.

Materials and methods. Formulation rationale was assessed in accordance to the apparatus functionality. The technological process implied the use of FDM coupled with hot melt extrusion (HME), while printability was defined by means of thermal, rheological and mechanical measurements. From the pharmaceutical standpoint, the consistency of the in vitro dissolution kinetics was monitored ‘at release’ and ‘in stability’, while the

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print process impact was evaluated based on the previously determined processability potential.

Results. Results showed that FDM printability is multifactorial. The increase in shear-thinning and flexural modulus can enable broader processability intervals, which in turn proved to be essential in limiting degradation product formation. The 3DP tablets released the API in an extended rate, however the temperature and humidity along production and storage should be carefully considered as it may affect the product quality in time.

Conclusions. HME+FDM can be considered as an alternative production methodology, with prospects of applicability in the clinical sector, however for some formulations extensive packaging development will be necessary before confirming their suitability.

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In vitro exposure of a 3D-tetraculture representative for the alveolar barrier at the air-liquid interface to silver particles and nanowires

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Introduction. The present study aimed to evaluate the potential differences in the biological effects of two types of spherical silver particles of 20 and 200 nm (Ag20 and Ag200), and of uncoated silver nanowires (AgNWs) with a diameter of 50 nm and length up to 50 µm, using a complex 3D model representative for the alveolar barrier cultured at air-liquid interface (ALI).

Material and methods. The alveolar model was exposed to 0.05, 0.5 and 5 µg/cm2 of test compounds at ALI using a state-of-the-art exposure system (Vitrocell™Cloud System). Endpoints related to the oxidative stress induction, anti-oxidant defence mechanisms, pro-inflammatory responses and cellular death were selected to evaluate the biocompatibility of silver particles and nanowires (AgNMs) and to further ascribe particular biological effects to the different morphologic properties between the three types of AgNMs evaluated.

Results. Significant cytotoxic effect was observed for all three types of AgNMs at the highest tested doses. The increased transcription of the pro-apoptotic gene CASP7 suggests that apoptosis may occur after exposure to AgNWs. All three types of AgNMs induced the transcription of the anti-oxidant enzyme HMOX-1 and of the metal-binding anti-oxidant metallothioneins (MTs), with AgNWs being the most potent inducer. Even though all types of AgNMs induced the nuclear translocation of NF-kB, only AgNWs induced the gene expression of pro-inflammatory mediators. The pro-inflammatory response elicited by AgNWs was further confirmed by the increased secretion of the 10 evaluated interleukins.

Conclusion. In the current study, we demonstrated that the direct exposure of a complex tetra-culture alveolar model to different types of AgNMs at ALI induces shape- and size-specific biological responses. From the three AgNMs tested, AgNWs were the most potent in inducing biological alterations.

Pharmacokinetic interactions study between carvedilol and some antidepressants in rat liver microsomes – a comparative study

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Introduction. Cardiovascular diseases and depressive disorders are some of the most frequent diseases. The probability of concomitant prescription of antihypertensive and antidepressant medication is increasing. The aim of this study was to investigate the enzyme inhibition by bupropion, sertraline and fluvoxamine on the metabolism of carvedilol using rat pooled liver microsomes and to assess the importance of these interactions from the pharmacokinetic mechanism point of view.

Material and methods. Two substrate concentrations (0.5 and 1 μM) and four inhibitor concentrations (0, 0.1, 0.75 and 1.5 μM) were used for each inhibitor tested.

Results. The in vitro experiments indicated significant decrease of the metabolic rate of carvedilol to 4'-hydroxyphenyl carvedilol, as well as increase of the area under the concentration-time curve for carvedilol was observed for all of the tested inhibitors. The most potent inhibitor was sertraline, followed by fluvoxamine and bupropion.

Conclusion. The co-administration of tested antidepressants led to a significant alteration of carvedilol's metabolism in vitro. CYP2D6 inhibition is the main pharmacokinetic mechanism which can explain these drug-drug interactions, with clinical implications.

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Evaluation of adherence and beliefs about medicines among the elderly

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Introduction. Adherence is characterized as a rational decision-making process that results from a balance between perception of the need to take medication and concerns about their negative effects.

The Beliefs about Medicines Questionnaire (BMQ) represents a useful tool for assessing patients' beliefs and worries about taking medication for their disease.

Objective. Assessing the adherence and beliefs of the elderly patients about disease and treatment using the BMQ.

Materials and methods. This study was observational, prospective and it was conducted in a community pharmacy located in Cluj-Napoca, Romania, over a period of one month.

Patients were considered eligible for our study if they were ≥65 years old and suffering of a cardiac or respiratory chronic disease.

Results. 55 patients responded positive to our invitation to complete the BMQ. They had a mean age of 79 years [71-87], 26 were men (48%) and 29 were women (53%). Out of the patients enrolled in the study, 42 had only cardiac disease, 5 had only respiratory disease and 8 patients suffered from both diseases.

When asked about beliefs about medicines in general, 95% of patients felt the

need to take their medicines to have less health problems. More than 90% of patients completely trusted their physicians and followed their recommendations. 76% believed that their health depends on the medicines they must take at the moment, while 47% felt worried about having to take their medicines. When asked about their own therapy, 42% patients expressed concern about becoming addicted to the drugs they take. 89% of patients believed that drugs only work if they are taken correctly and on a regular basis, while 44% considered that they should take a break from taking their medication from time to time.

Conclusion. Concerns about becoming addicted should be addressed by healthcare professionals and patients should be educated about the importance of adherence to their prescribed therapy.

Polyphenolic content and antioxidant activity of pomace and canes extracts from several varieties of Vitis vinifera

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Introduction. The aim of this study was to obtain and to characterize the chemical composition and antioxidant activity of different extracts from by-products of the wine industry: pomace and canes.

Material and methods. Five varieties of Vitis vinifera were used, 3 for red wines: Feteasca neagră, Cabernet Sauvignon, Mamaia and 2 for white wines: Muscat Ottonel, Sauvignon Blanc. Aqueous and ethanolic solutions (50%, 70%) were prepared by hot, cold or ultrasonic extraction, as well as glycerin macerates (1:10 - dry material: solvent). The total polyphenolic, flavonoid, caffeic acid derivatives and tannins contents were spectrophotometrically determined. The samples were screened for antioxidant activities using the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging method.

Results. The results showed that the phenolic amount of the vegetal extracts varied as follows: hot ethanol extract (50%) > hot ethanol extract (70%) > cold ethanol extract (50%) > cold ethanol extract (70%) > glycerol macerate > ultrasonic ethanol extract (50%) > ultrasonic ethanol extract (70%) > hot water extract > ultrasonic water extract. In the hot ethanolic extract, the polyphenolic quantities have decreased as follows: Muscat Ottonel pomace < Sauvignon Blanc pomace < Cabernet Sauvignon pomace < Feteasca neagra pomace < Mamaia pomace < Feteasca neagra canes. The Muscat Ottonel pomace extract showed the highest total antioxidant activity (83.45%), reducing power and DPPH radical scavenging activity in accordance with the phenolic content (59.95 mg GAE/g), flavonoidic content (3.15 mgRE/g) and caffeic acid derivatives content (21.65 mg CAE/g).

Conclusion. These preliminary results indicate that pomace extracts could have a great cosmetic potential due to their high content of antioxidant compounds.

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Optimization of bioactive compounds extraction in hazelnut (*Corylus avellana* L.) involucre: Phytochemical profile and biological activity

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Introduction. Tree nuts by-products could contain a wide range of phytochemicals, natural antioxidants, which might be used as dietary supplements, and pharmaceuticals or cosmetic ingredients.

Materials and methods. In this research, we examined the phytochemical profile and the antioxidant activity of the acetone extracts of hazelnut involucre (HI). An experimental design was developed in order to obtain the optimum extraction conditions for HI rich in bioactive compounds.

Results. The best results per gram of dry weight (dw) HI were 377.43 mg gallic acid equivalents, 43.11 mg quercetin equivalents, and 28.07 mg catechin equivalents for total phenolic content (TPC), total flavonoid content (TFC), and condensed tannin content (CTC), respectively. The highest value for total antioxidant activity (TAA), determined by TEAC method, was 1,811.42 mg Trolox equivalents per gram of dw HI. There was a positive relationship between TPC, TFC, CTC and TAA. The best results for TPC, TFC, and CTC were achieved at equal mixture (1:1) acetone and water, as extraction solvent. After LC-MS/MS assay, the best results for individual polyphenols were achieved using binary-solvent systems, 25% water in acetone for epicatechin, catechin, syringic acid, gallic acid, protocatechuic acid, vanillic acid, p-coumaric acid and ferulic acid, or 50% water in acetone for hyperoside, quercitrin and isoquercitrin. For the three phytosterols (stigmasterol, campesterol, beta-sitosterol) quantified, the best outcomes were reached at 25% or less water in acetone as solvent. Further, for the richest polyphenolic HI extract, the tyrosinase inhibitory activity and the antioxidant capacity, using DPPH and FRAP assays, was determined.

Conclusion. This is the first study to analyze the composition in both hydrophilic and lipophilic bioactive compounds in HI. Our findings revealed that hazelnut involucre presented strong biological activity and could potentially be considered as inexpensive source of natural antioxidants for food, pharma or cosmetic industry.

Evaluation of the cucurbitacin content and biological activities of *Ecballium elaterium* (L.) A. Rich

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Introduction. *Ecballium elaterium* (L.) A. Rich. is a species known in traditional medicine for its anti-inflammatory, anti-bacterial, analgesic, laxative and purgative activities. The aim of the present study consisted in the analysis of the cucurbitacin content and evaluation of the anti-plasmodial and cytotoxic activities of the crude extracts obtained from the main parts of this species.

Material and methods. Analysis of cucurbitacins was performed by a HPLC-DAD method, using a Hypersil ODS C18 column. Water and acetonitrile were used as mobile phases, in gradient mode. Detection of compounds was performed at 235 nm.

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The anti-plasmodial activity was assessed on two strains of *Plasmodium falciparum*, that are chloroquine sensitive (3D7) and chloroquine resistant (W2). Cytotoxic activity was tested on cancerous cell lines (*A549* - lung cancer and *HeLa* - cervical cancer). One healthy cell line (*WI38* - fetal lung fibroblasts) was used in order to assess the cellular toxicity of the species.

Results. Analysis of cucurbitacins revealed mainly the presence of Cucurbitacin B, D, E and I, which were found in larger amounts in the roots and fruits of the species. Anti-plasmodial activity of the crude extracts was absent, while cytoxicity was found to be significant especially in the case of fruits and roots. Mature and young stems proved moderate cytotoxicity, while leaves and aerial parts proved no cytotoxicity on cancerous cell lines. Toxicity on healthy cell lines was proved to be very low for all the tested crude extracts.

Conclusion. These results offer a new perspective on this species, proving it as an important source of cucurbitacins and showing the important cytotoxic potential of its fruits, roots and stems.

DENTAL MEDICINE

Advanced Glycation End Products (AGEs) assessment by ultrasounds at skin and mucosa levels in oromaxillofacial area

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Introduction. Advanced Glycation End Products (AGEs) are involved in low level inflammation. AGEs can be assessed in human tissues using ultrasound non-invasive technique due to their mucosal and skin hypersignal. The aim of the study was to assess the AGEs in skin structures and oral mucosa using two ultrasounds devices.

Material and methods. The study was conducted on a group of 20 subjects in good health or with associate disease. Skin phototype was recorded.

A L64 linear array transducer (18-MHz) with stand-off device (Arietta, Hitachi, Ltd. 2013, 2017, Q1E-EZ1295) and a linear B-Scan mode applicator (38 MHz) (DUB SkinScanner Taberna pro medicum, ScanLoop 2000) were used. The linear transducer was positioned at the level of the zygomatic area and lower lip mucosa.

The following skin structures were evidenced: epidermis, subepidermal band (papillary dermis), dermal band (reticular dermis), hypodermis, elasticity and density.

Images provided by both ultrasound investigation systems were exported to process soft and quantitative measurements were performed.

Results. AGEs hypersignal was analyzed in skin and inferior lip mucosa. Results were compared with skin phototype, associate diseases and patient's age. The dermis is the main skin component for AGEs accumulation. AGEs were found more expressed in zygomatic skin compared to oral mucosa. Subject with IV skin phototype had lower AGEs concentration compared with II either III skin phototype. Also, in older subjects AGEs were more expressed compared to younger subjects. Sun-exposed skin was thinner compared to oral mucosa, revealing the elastosis process.

Conclusions. The AGEs accumulation are influenced by aging, sun-exposure and associated diseases. The ultrasound assessment has the advantages of non-invasiveness, easy handling, multiple measurement, with accurate and reproducible results.

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Subjective evaluation of implanto-prosthetic treatment by edentulous patients - autoperception (self-esteem)

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Introduction. Previous studies have shown that lack of teeth is perceived as a serious handicap, as an important disability that affects the quality of life (like any other loss in the human body). The success factors of implanto-prosthetic treatment are: the materials used, the optimal choice of implant and implantation area, edentation size, postoperative body response, and last but not least, patient expectations.

Purpose. The purpose of the present study is to determine the degree of satisfaction of edentulous patients treated with implant-supported prostheses.

Material and method. The study was performed on 50 implanto-prosthetic treated edentulous patients in the maintenance phase of the implant works. The selected patients were chosen after: implant supported prostheses no older than 5 years, total maxillary edentulous ridge, total mandibular edentulous ridge, lack of special events (complications) during treatment, treatment by specialists. An evaluation questionnaire with 26 questions, divided into 3 parts (I-III) was used. Questions were asked for: patient satisfaction after treatment performed, the attitude towards oral health of patients, the treatment with conventional prostheses in the past, the frequency of dental problems.

Results. Most patients showed a higher degree of satisfaction after implant supported prostheses treatment. Some positive effects are: increasing the mastication capacity, increasing the comfort, improving the physiognomy, lack of implant pain, lack of mobility of the implants and last but not least regaining self-confidence.

Conclusions. The study aimed to determine the degree of satisfaction among the edentulous patients with implant-supported prostheses. We used questionnaires with questions divided in 3 categories, subjects from different backgrounds and being treated in different clinics.

Dental implant testing using fine element analysis

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Introduction. Before entering mass production, medical devices have to undergo a long series of tests, to ensure they are able to perform as expected. The first series of tests are usually in vitro experiments, to prove the functionality and endurance of the concept. Even before these tests, medical devices can benefit from a new type of testing (fine element method - FEM). This computerized testing method offers extremely fast and cheap cost-efficient results compared to classical testing and provide similar results.

Material and methods. In our study we compared mechanical tests on a new type of dental implant (according to ISO14801 – Dynamic fatigue test for endosseous dental implants) using a standard testing machine, with the results we obtained by using FEM for the same implants, in the exact same conditions.

Results. Similar results were obtained by using the two different testing techniques. The fatigue testing results were better for FEM, but the implant behavior was extremely similar to mechanical testing. FEM took only a few hours to obtain the final results, compared to several weeks for the milling of the physical implant bodies and their mechanical testing. Also, the costs of FEM were considerably lower. Another obvious advantage of FEM was the fact that maximum stress or low resistance areas could easily be visualized and instant modifications could be made.

Conclusion. FEM proved to be an efficient testing method for dental implants, due to its extreme effectiveness (time and cost) and also to the fact that it provides similar results to mechanical testing. Although its advantages are obvious, it still has its limitations, which makes it of extreme value in addition to mechanical testing, but not able to totally replace them.

Insertion of salivary biosensors in dental appliances

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Introduction. The metabolic diseases are constantly increasing in Romania and their detection and monitoring is done through laboratory analyzes of biological fluids such as blood and urine.

Objectives. For the early detection of metabolic disorders, we can use integrated biosensors in dental appliances and dentures for AGEs (Advanced Glycation End products) measurement in saliva.

Material and method. Based on models of hard-gypsum plaster were made different prosthetic parts depending on the edentations extension and position. In the case of integrity of dental arches two mouthguards (one from a durable, rigid self-curing acrylate and the other from a thermoformed transparent vinyl foil) were made. At the frontal area of the acrylic piece we created a slit for inserting the biosensor. In the case of the thermoformed one, the biosensor was attached with adhesive material. In the case of an edentation, a Kemmeny prosthesis were made with a lingual face for the biosensor insertion. The biosensor is a flexible band that allows easy manipulation and change after each measurement.

Conclusions. The various devices and surgical prostheses can be used as a portblock. The biosensor size may vary from a few millimeters to 1-2 cm depending on the size of the alveolar ridge. Inclusion of biosensors in these systems are work-accessible and cost-effective methods.

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Current treatment modalities of orthodontically induced white spot lesions and their outcome – a literature review

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Introduction. White spot lesion is a demineralization of the enamel that appears as a white spot on the surfaces of the tooth. The cause of this spot is determined by the activity of the bacterial plaque and it represents the initial stage of a carious lesion. This lesion is a common side effect for patients with fixed orthodontic appliances mainly because of the brackets' position that favors the accumulation of plaque that ultimately leads to the formation of the white spot.

Material and methods. We conducted an electronic search by using a single database, PubMed. "Orthodontic", "white spot lesions", "enamel demineralization treatment" and "remineralization" were the terms used. We found 324 articles, but we took in consideration only the ones from the last 10 years, which resulted in 223 articles.

Results and discussion. The first step after research was article selection: first by scrutinizing the title and secondly by reviewing the abstracts or full texts. The exclusion criteria were: meta-analysis, reviews, original articles regarding prevention of white spot lesions and their prevalence or incidence. We included the articles that seemed relevant for the treatment of white spot lesions, made either on extracted teeth either on orthodontic patients. We found 75 articles to be eligible for this research and we eliminated 5 because

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of the lack of an abstract or full text and a further 22 were rejected because they didn't fit the aforementioned criteria.

Conclusion. Although some traditional methods for the treatment of white spot lesions seem to have undesirable results, nowadays with new technologies and thorough investigations in nanotechnology, the eradication of the lesion appears to be short term.

Whitening effect of bleaching products for at home protocols upon composite resins

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Introduction. Dental bleaching is considered to be a popular procedure for treating discolored teeth. It is of interest both the efficiency and the secondary effect of bleaching on dental surfaces and on restorative materials.

This study aims to analyze the bleaching effect of 3 whitening gels in a 16% concentration of carbamide peroxide, indicated for at home dentist supervised bleaching: Bite and Smile (Cavex), White Smile Home Whitening (White Smile) and Opalescence (Ultradent).

Materials and methods. A total of 56 samples were fabricated from Amelogen Plus (Ultradent), in two shades: A1 and A2. After light-curing, samples were polished to a final thickness of 0.9-1.1 mm and divided into four groups (n=7): (1) control and (2-4) bleached with the abovementioned materials. Initially and at the end of every bleaching application, samples were analyzed for color parameters with Vita EasyShade (Vita) spectrophotometer (on a neutral gray background) and for surface roughness with Mitutoyo SJ-201 Surface roughness tester; based on initial and final lightness L* and chromatic coordinates a*,b*, color difference DE2000 and Whiteness index WI were calculated.

Results. The surface roughness decreased after the bleaching procedure: for control samples from an average value 0.18Ra to 0.16Ra, for samples bleached with WSHW and Opalescence from 0.19Ra to 0.16Ra, for samples treated with Bite and White from 0.18Ra to 0.14.Ra.

Color variation (DE2000) on A1 samples ranged between 1.15 - 7.37 for the control samples, 0.8 and 0.92 for Bite and White, 2.7 and 4.99 for WSHW 1.66 and 8.48 for Opalescence.

Color variation on A2 samples ranged between 2.12 and 15.17 for the control samples, 0.64 and 21.83 for Bite and White, 0.82 and 10.72 for WSHW, 0.62 and 7.33 for Opalescence.

Conclusions. Low concentration of bleaching gels can induce color changes on restorative materials such as dental composites.

New fiber reinforced composite material for custom-made craniofacial implants

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Introduction. The conducted studies aimed obtaining a new composite material characterized by superior biological and mechanical properties, with increased resistance to the action of the microorganisms. It also aimed solving the technological processes by which the material can be modeled into complex, three-dimensional, predefined form, specific to bone defects to be reconstructed.

Material and methods. A new formulation of fiber-reinforced composite (FRC) was obtained from a polymeric matrix (mixture of dimethacrylic oligomers of bis-GMA, UEDMA, TEGDA, HEMA, PMMA), along with hydroxyapatite, zirconium oxide (ZrO2), gentamicin and glass fiber fabrics E 300 g/m2. In order to obtain customized implants, an indirect 3D printing method has been used. A total of 12 male rabbits, 3.5 to 4.0 kg of New Zealand breed were divided into two groups representing an experimental group that benefited from a composite implant and a control group to which titanium alloy implants were applied. The subjects were submitted to clinical, imaging and histological studies.

Results. Local and general impact upon animal health, quality of reconstruction, bone and dura reaction to the material showed good biological behavior of the FRC implant and optimal 3D reconstruction.

Conclusion. Implementing this new interventional method will improve the quality of life in a large number of patients, responding excellently to all expectations in the field and being competitive at European level.

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Promoting integrity, trust, and responsibility in academia

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Objective. In the past few years, cases and issues of Research and Integrity have gained visibility, and became an important topic of debates and investigations. How to prevent this phenomenon in Academia? This is the main question of this presentation.

Methods and results. First, by inform and educate people about the right scientific methodology, paper writing in a proper way and good examples and practices for young students. Second, by promoting researchers' integrity and credibility in educational programs and in practice. Researchers involved in educational programs and mentorship must to be a good example from students. Knowledge, behaviors, and ethics are important for researchers who are in the same time even mentors for students. The pressure to teach, to practice and to publish in the same time is not a normal functioning of a human and it must be removed or thought in a different way, in different steps during the university career. Criteria for career promotion must to be reflecting in a proper way the quality and not quantity of papers or research projects. Third, in this field it is an emergency to adopt and implement norms and clear regulations. It is known that in 2013 from 27 countries of the European Union (plus Switzerland, Lichtenstein, Norway and Iceland) only two countries (Denmark and Norway) had a specific law on scientific misconduct, some countries had guidelines in which scientific misconduct is defined and judged in

different ways. But in twelve countries it was not possible to identify or analyze any guideline (The Lancet, 30 March 2013).

Conclusions. Being responsible for your acts and think to the future is an obligation but even a challenge for researchers, students and for all involved in medical practice, research and academic fields. With awareness and commitment, education and intensive work, we can find solutions, adopt regulations and promote integrity and credibility in research.

Bruxism – an interdisciplinary challenge

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Introduction. Bruxism consists in stereotyped movements characterized by teeth clenching and grinding. The literature converges in a multifactorial etiology for this behavior, with multiple hypotesis. The aim of this study was to analyze the association between sleep bruxism, salivary levels of cortisol and anxiety, stress and general state in healthy adults.

Material and method. 60 subjects, 30 with bruxism, 30 without bruxism were included in the study. Initially, the subjects had to answer to a questionnaire which consists in two parts: one part evaluated the presence/absence of bruxism and second one analyzed the general state of the subject and the state in relationship with his/her job. We also performed a clinical examinations of temporomandibular joint (TMJ) and static and dynamic occlusion. The salivary sample was taken to each subject early in the morning, before eating and cortisol level was determined using ELIS technique.

Results. Salivary levels of cortisol were significantly higher in subjects with bruxism (p=0.006). The score reflecting the general state and the score for anxiety were significantly higher in subjects with bruxism compared to the others (p=0.047 and p=0.07). Sleep bruxism did not show significant correlation with stress level analyzed through questionnaires. In subjects with bruxism, salivary levels of cortisol, the scores for general state and anxiety were significantly higher in the males compared to females. The ethnicity had no influence in salivary levels of cortisol or in psychological scores.

Conclusions. The presence of malocclusion, altered general state or anxiety and stress in the occurrence of the bruxism is still a controversial issue. The studies performed until now, including the present one, showed that these factors could be considered favoring factors rather than determinant ones in producing sleep bruxism.

Comparison of the mechanical properties of flowable resin composites

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Aim. The purpose of the present study was the comparison of the compressive strength, flexural strength and flexural modulus of eleven flowable resin composites (FRC).

Materials and methods. We used for mechanical investigation eleven FRC: Tetric EvoFlow (A3, Bleach L), Latit Flow (A2), PermaFlo DC (A2), Filtek Supreme XT (A3), Accolade SRO (A2), Accolade PV (A2), StarFill 2B (Dentin), StarFlow (A2), SYNERGY Nano Formula (A3.5/B3, A4/M5, A2/B2, A3/D3, Super White), els extra low shrinkage (A3) and Wave (A3).

Specimens (n=7) were prepared for compression testing (4 mm in diameter and 8 mm long) and flexural strengths (parallelepiped with 2 mm ± 0.01 × 2 mm ± 0.01 × 25 mm ± 0.01). Samples were cured using XL3000 photocuring source (3M Dental

Products, St Paul, MN, USA) for 60 s. The test specimens were water stored at 37 °C for 24 h before the mechanical tests. The mechanical test was carried out in a universal testing machine (LR5K Plus, Lloyd instruments. Ltd., England) at a loading rate of 0.75 mm/min until fracture.

Results. The results recorded were statistically different ($p = 0.05$) when evaluated with ANOVA statistical analysis. Mechanical properties were well correlated with the filler volume fraction. The mechanical properties of the tested materials were between 182.87 – 310.38 MPa for compressive strength, 59.59 – 96.95 MPa for flexural strength and 2.34 – 6.23 Gpa for flexural modulus.

Conclusions. Future flowable resin composites are recommended to have higher mechanical properties in order to improve the clinical lastingness of the fillings.

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Keywords: flowable resin composites, mechanical properties, modulus of elasticity

Anxiety in the dental office

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Introduction. Anxiety is frequently and widely known problem in dentistry. Even though many of the patients have dental anxiety, there is no certain protocol that can be used for certified results.

The aim was to explore the literature in order to find out what are the solutions to help patients overcome their fear before going to the dentist and during dental procedures.

Material and methods. There was done a descriptive review of 24 articles found by searching the terms "dental anxiety" on Pubmed platform. There were chosen publications regarding the possible solutions for managing dental anxiety.

Results. The solutions proposed by the scientific literature were: Cognitive Behavioral Therapy, relaxation techniques, premedication with sedative drugs (benzodiazepine), music distraction, hypnosis, acupuncture, inhaled sedation, aromatherapy with essential oils parental presence/absence for children and audiovisual distraction.

Conclusion. Cognitive Behavioral Therapy is the most effective technique that was used to help patients overcome their dental anxiety. All the techniques used were more efficient when combined with repeated exposure to dental treatment.

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Dental pulp stress analysis in periodontal resorption

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Introduction. Maintaining the pulp vitality during the orthodontic treatment phase is an important aim during the treatment of periodontal disease. It was hypothesized that due to periodontal resorption the same amount of force determines an increase of maximum stress in the dental pulp, which might affect its vitality. The objective was to quantify stress produced in the dental pulp at 10 different bone levels under transverse and vertical orthodontic loadings, for the special case of a two roots second mandibular premolar.

Material and methods. The alveolar bone and PDL has been reduced in height by 10%, from 0% to 90%, and subjected to 6 constant loadings of 1-10 N/mm2. The von Mises stress values for the dental pulp were calculated.

Results. For 0% bone loss, a 1 N/mm2 intrusive load produced a maximum stress of 5.4E-05N/mm2. When resorption reached 50% the stress value was of 14.3E-05N/mm2 while for the 90% level the stress was 53.5E-05N/mm2. After 30% periodontal resorption (5.7 mm) the stress significantly increase and is assumed to be the starting point for dramatic changes in stress level. The mesial-distal loadings produced the highest stress values in the vital dental pulp for the 80% bone loss. The periodontal resorption determined a steady increase in the equivalent stress.

Conclusion. Results lead to the conclusion that application of higher forces will determine higher stresses in the root apical third, which might affect the vitality of the pulp during the orthodontic treatment phase, and could worsen the periodontal problems.

Digital evaluation of pathologic posture - correlation with dental occlusion

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Introduction. Dental malocclusion can determine over time an adaptive dynamic reaction, an asymmetric hyper tonicity of the cervical paravertebral muscles, spine and even extremities if the stimulus persists., affecting body posture. Clinical postural analysis can be realized using numerous clinical tests (Romberg test, static study, thumb test, lead wire test etc.).

Methods. This study will present the technique for posture evaluation using a digital application- PostureScreen mobile, which is based on photographic method with vertical reference using the lead wire.

Results. Simplicity and affordability are characteristics that recommend this application as a useful tool for dental practitioners in body posture evaluation. They can easily evaluate the impact of dental malocclusion on body posture during the initial examination and monitories the changes induced by occlusal rehabilitations.

Conclusions. Before starting an irreversible and sometimes expensive occlusal rehabilitation treatment, we can evaluate the possible side effects using occlusal splints and body posture analysis.

Treatment protcol for class III patient using minimplant anchorage

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Introduction. Skeletal class III malocclusion usually involve a hyperplasic maxilla, a prognathic mandible or both, and it can be associated with skeletal open bite which may increase the bad prognosis. The treatment protocol includes Rapid Maxillary Expansion combined with Face Mask Therapy. Chin cup is not used anymore do to it's fail to stop mandibular growth. Rapid Maxillary Expansion could be done by using the teeth as anchorage. In this case mesial migration of posterior teeth can create severe anterior crowding. In order to overcame this disadvantages we used Hybrid-Hyrax as expansion device.

Material and methods. In our protocol, we used Hybrid -Hyrax for maxillary expansion combined with Face Mask or Class 3 elastics. Hybrid Hyrax is a bone-borne expander with 2 Benefit Implants inserted in the anterior palate.

Benefit implant were placed using Easy Driver or guided surgery in order to increase the outcome of the Benefit system. By using this procedure, we can place the implant and the RPE in the same time.

We want to present 2 patients treated with this protocol. One is a 12 year old boy and in this case we used ALT-RAmec protocol, expansion one week, constriction one week, and Face Mask in the same time. The other is a 16 years old girl with Hypoplastic Maxilla and open bite. In this case we activated 2 turns per day and class 3 elastic were started at the same time.

Results. In both cases we obtained significant improvement of class 3 parameters.

Conclusion. Even if the efficiency of RPE for the improvement of the maxillary protraction is a disputed subject, the use of it for the treatment of Class III malocclusion is indicated in order to enhance the maxillary advancement.

Different approaches in layering composite materials to achieve maximum aesthetic for indirect prosthetic construction : inlay, onlay, overlay and adhesive bridge

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Introduction. The challenge for each dentist is to create perfectly invisible restorations.

Materials and methods. Two types of composite materials were used, modified to improve both optical and mechanical qualities: 1) G-aenial – GC contains improved filling pre polymerized, shaped silica glass and silica nano-particles, in order to improve the material's optical qualities: reflectance, fluorescence and transmitted light; 2) Essentia – GC contains a micro-hybrid composition with addition of inorganic fillers for dentin and a mix between ultra fine glass filler and filler pre-polymerized for the enamel. In both material cases the color clinical determination was made by using small amounts of material positioned in specific dental areas and photo-polymerized. The reconstruction preparations were performed with little loss of substance according to the dental tissue destruction. Reconstructions were performed on working models in the dental laboratory, after previously it was done fingerprinting prosthetic field.

Reconstructions were adhesive bonded to the teeth involved when in advance the mating surface was sandblasted.

Results and conclusions. The Essentia duo-Layer Concept (one dentin & one enamel) is more simple than G-aenial Multi-Layer Concept. In this way the Essentia reconstruction can emulate the natural tooth structure. The different composition between Essentia-dentin and Essentia-enamel makes that the change of specific light direction in restoration being like in natural tissue. G-aenial reconstruction must layered with a clear thin layer between dentin and enamel to achieve the same effect. Choosing the shade with the Essentia concept is faster than Vita Classic System Shade that we meet in G-aenial materials.

Keywords: composite materials, indirect aesthetic reconstruction, shade system

The effect of root filling materials on bone healing

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Aim. This experimental study involving laboratory animals aims to assess the bone healing process produced in the presence of the three materials used for root canal filling.

Material and methods. We designed an experimental study based on an animal model conducted within the Bio-base of the Department of Physiology of UMF, Cluj-Napoca. We used forty-eight adult male Wistar rats. After anaesthesia, double row and double column osteotomies were performed using a paramedian approach, 2 mm apart from each other. The first orifice was left empty, as control; the other three were filled with the three endodontic filling materials (Epoxi resin- AH Plus, a dual-polymerized resin- RealSeal SE and an experimental hydroxyapatite-based endodontic sealer. Starting with the second week after surgery, four animals were sacrificed every two weeks. After sacrifice, histopathological specimens were obtained and each sample was examined in detail in terms of bone resorption, inflammatory infiltration, remodeling processes and new bone formation.

Results. Generally, the inflammatory response varied similarly in all groups, with a higher intensity in the first 2 and 4-week intervals and a decrease in intensity to a complete remission of the inflammatory process, and even the appearance of new bone structures on some sections towards the end of the experiment. The results underwent statistical validation.

Conclusion. The biocompatibility of the new hydroxyapatite-based root canal filling material is comparable to that of the other two materials that are in use on the market.

Canine retraction methods in fixed orthodontic therapy

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Introduction. The decision upon following an extraction treatment plan depends on some factors like dental overcrowding, anchorage, canine and incisor axial inclination, midline discrepancies, vertical dimension, facial and dental esthetics, dental health, along with the main chief complaint. The most commonly chosen teeth for extraction in order to provide space for alignment of the others, are the first or second bicuspid, followed by canine retraction. The aim of this study was to summarize the different retraction methods and to emphasize their advantages compared with disadvantages.

Material and methods. The chosen working method consisted in a synthesis of the diverse methods used in order to distalize the canines, as seen in the orthodontic literature.

Results. When managing space closure, the ideal force system must meet certain characteristics, including optimal and constant forces for tooth movement, minimal chair time and patient cooperation, and it must be comfortable and hygienic to the patient. Space closure in orthodontics can be accomplished using two types of mechanics: non-frictional mechanics, consisting in closure loops designed on a main or segmented arch, in which teeth movement results from activation of the loop, while the second method involves frictional (sliding) mechanics, that is being produced by the sliding of the braces upon the arch wires. Loss of posterior anchorage has been the object of debate regarding space closure in two phases – canine retraction first followed by incisor retraction – as opposed to "en-masse" six anterior teeth retraction, which is told to reduce treatment time as it is done in only one phase, but resulting in a higher percentage of anchorage loss. Depending on the space necessity for further alignment, anchorage may vary from minimal, medium or maximum; space closure can be done in a reciprocal manner, one direction predominantly, or only from the anterior direction. Whether using power chains, coil-sprigs, different types of loops or retroligatures the final result of space closure has to comprise aligned and upright teeth with contact points and parallel roots.

Conclusions. Following our study, we can affirm that all methods are equally applied in the daily practice, depending on the chosen technique regarding the features of each case, according to the abilities and vision of the practitioner.

Numerical simulation of the important signals generated by the upper canine's orthodontic movement

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Introduction. Canine distal retraction is often necessary in orthodontics, especially in cases with severe crowding which require premolar extractions. This process involves two physical quantities, torque (couple of forces) and generated energy, which enable an elaborate analysis of the orthodontic tooth movement.

Material and methods. The mathematical model of the upper canine's orthodontic movement has been implemented in MATLAB/SIMULINK. The parameters taken into consideration are the following: the average length of an upper canine, point of force application on the tooth crown, initial force applied, period of treatment, tissue resistance (sum of tissue reaction effects constant).

Results. The numerical simulation generates results for the following signals: force evolution in relation to time, rotation center position, tooth crown and root position, torque (couple of forces) and energy generated by the biomechanical process.

Conclusions. Use and interpretation of the obtained evolutions, in relation to time, present important practical value and relevance in the orthodontic and pre-surgical orthodontic treatment. Future elaboration of the program used in this study, may simplify orthodontic teeth movement and elucidate the underlying mechanisms of these biological processes.

Criteria for stability in anterior open bite treatment

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Introduction. Open bite malocclusions are one of the most difficult and challenging orthodontic conditions to properly diagnose, effectively treat, and successfully retain. At the same time, since the anterior teeth define the smile, which is the first facial feature that draws attention, anterior open bite problems tend to be one of the most disturbing malocclusions for patients aesthetically as well as functionally.

Material and methods. Review of the literature on the etiology of anterior open bite malocclusion, diagnosis and treatment modalities according to the etiology.

Results. The common involvement of the tongue in these types of malocclusions creates a great challenge and concern for any orthodontic clinician or researcher. There are several types of abnormal tongue posture and each one of them causes a certain kind of open bite, most of them anterior open bite. Therefore failure of tongue posture adaptation subsequent to orthodontic and/or surgical treatment might be the primary reason for relapse of anterior open bite.

Conclusions. The multifactorial etiology of these orthodontic problems involving skeletal, dentoalveolar, and especially environmental/neuromuscular components requires adequate diagnostic, treatment knowledge and experience together with the understanding that these malocclusions demand continuous and persistent monitoring during retention since stability is frequently a challenge to achieve.

Biomaterials for tooth tissue engineering: injectable scaffolds

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Introduction. Tissue engineering represents a multidisciplinary research field that applies the principles of biomaterials engineering and the strategies of life sciences for the development of biological substitutes that have the ability to repair and regenerate or improve the tooth tissue function.

Material and methods. In this review, we analyze and evaluate biomaterials that form injectable scaffolds capable of supporting hard tissue regeneration over a period of time of weeks to months. These biomaterial scaffolds have been developed by the innovative approach using a combination of cells, proper biomaterials with controlled properties, bioactive molecules (factors) or drugs and current bioreactor technologies which have the purpose to design and fabricate newly-formed injectable scaffolds mimicking the natural bone tissue.

Results. The novel approach supports the major goal of modern dentistry to restore the regeneration of tooth bone, especially dentine and enamel, by using biomaterial scaffolds suitable for the tissue engineering of mineralized (hard) tissues. This objective is a high-priority in regenerative medicine and dentistry. As key elements in tissue engineering procedure, scaffolds are defined as biocompatible structures or networks that support cell growth and supply a suitable environment for the new tissue formation, and allow cell attachment, proliferation, migration, differentiation, and provide mechanical support for the extracellular matrix generation. Ideally scaffolds must be biodegradable, to allow cells to produce their own extracellular matrix and the degrade rate should be done in a controlled manner to create new tissue. Also the products of this degradation process must be non–toxic and possess the ability to exit the body without harming other organs.

Conclusions. Injectable scaffolds were performed and used in a minimally invasive manner. The use of these scaffolds for tissue engineering is challenging but ideal as other highly specialized and multi-functional biomaterials scaffolds. They can easily fill any irregularly shaped defects and also they can improve the delivery of distinct bioactive molecules, which can be jointly mixed and injected in situ, namely in a particular localized place of bones. As clinical applications they can be used for regeneration of dental pulp, dentin, periodontal ligament and alveolar bone as well as for the treatment of craniofacial and various bone defects.

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Perception of localized dental discoloration: patients versus dentist

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Objectives. To compare patients' and dentist's perception regarding teeth with localized discromies.

Materials and methods. A group of 160 dental patients were asked to answer a questionnaire oriented towards the self-perception of their esthetic appearance; most questions addressed localized dental discolorations. The same target was solved by the current dentist, who examined the respective patients and answered the same questions. Both patients and dentist indicated also a tooth with pleasant color, as reference. Color measurements of teeth indicated as dyschromic and of reference teeth were performed with a spectrophotometer (VitaEasyshade IV, VitaZahnfabrik) and color difference was calculated using ΔEab formula.

Results. On the bases of the answers, various situations were identified:

1. "Perfect agreement" between patients and dentists' regarding identification of dyschromic teeth were found in 61.87% of cases (both considered either absence of teeth with dyschromia, or indicated the same teeth with color modifications). ΔEab between teeth considered dyschromic by patients and dentist and reference teeth, ranged 1.57-35.86.

2. Cases with "disagreement" between the perception of dentist and patients (38.12%);

ΔE*ab between teeth considered dyschromic only by the patients and reference ranged between 0.95 – 43.63, whilst ΔE*ab calculated between teeth considered dyschromic only by the dentist and reference ranged between 0.95 – 43.89; overall, most ΔE*ab exceeded acceptability threshold AT=2.7.

Conclusion. Agreement between patients and dentist regarding the perception of dyschromic teeth may be encountered; however, there are situations of disagreement: patients perceive often as "dyschromic" vital, more saturated upper canines, deficient composite or ceramic crowns whilst the dentist judges as modified the color of nonvital teeth and discolored restorations.

Digital impression in orthodontics- virtually perfect?

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Introduction. In the last years improved technology has become more and more important in our daily dentistry practice.

Although digital impressions promise a higher accuracy and seem to be less time consuming this study aimed to assess the advantages and disadvantages of the two techniques.

Material and methods. In order to establish the best way to take an impression in orthodontics, twelve literature reviews on this topic were studied, relating the different opinions of the authors to the daily practice.

Results, conclusions. For orthodontists the use of digital impressions brought great benefits by increasing the accuracy of the impressions and by gaining time for the whole team (dentist-patient-technician). The most common systems used for digital impressions in orthodontics are Cadent IOC/ Orthocad, Dentsply/GAC's OrthoPlex, Stratos/Orametrix SureSmile and EMS RapidForm.

The most important advantage for those who use this technology is to eliminate chemical processes, leading to high quality impression. In orthodontics the digital impression has a good impact on the patient (uncomfortable perception of the classic impression is known) and allows both the doctor and the patient to immediately visualize the results and to discuss the therapeutic options.

The main disadvantage although remains the high cost of the equipment and of the maintenance.

Raman Micro-spectroscopy (RMS) of Dental Pulp Stem Cells (DPSCs): An approach to monitor the effects of Cone Beam Computed Tomography (CBCT) Low-Dose Ionizing Radiation

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Introduction. Ionizing radiation produces biological damage leading to health effects of varying severity. The effects and subsequent health implications caused by exposure to low-dose radiation, such as diagnostic exposure, remain ambiguous. The objective of this study was to determine the molecular and biochemical changes in dental pulp stem cells (DPSCs) due to consecutive low-dose ionizing radiation exposures using label-free Raman micro-spectroscopy (RMS).

Material and methods. The biological changes in irradiated DPSCs were assessed after three consecutively CBCT exposures. A group of non-irradiated stem cells was used as control. The Raman images of fixed cells were acquired using a Renishaw Raman spectrometer coupled to an Olympus IX73 microscope. The Raman spectra of ten DPSCs selected from each cell group were analyzed in order to evaluate the differences of the spectral components between the irradiated and non-irradiated stem cells. Principal components analysis (PCA) of the stem cells was performed in Matlab. The Raman biological markers specific to the irradiation process were identified as the calculated differences between the averaged spectra of control and irradiated DPSCs.

Results. We identified Raman biomarkers characteristic to low-dose cone beam computed tomography (CBCT) irradiation of DPSCs. The biomarkers were monitored inside the cells using the relative intensity distribution of the 785 and 1734 cm^{-1} bands.

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The control cells presented a higher relative intensity of nucleic acids specific Raman bands, while the irradiated cells revealed an intensity increase of lipids specific bands.

Conclusion. The results obtained in this study demonstrate the capability of RMS for the detection of cells' response to diagnostic radiation dose levels. This may indicate the potential of the technique for future applications such as monitoring the radiation responses in pediatric patients suffering repeated radiological exposures.

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