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BASIC SCIENCES

Phytochemical characterization and biological effects of *Thymus Marshallianus* l. extracts on in vitro induced hyperglycemia

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Introduction. Polyphenolic compounds administration may prevent neurodegeneration, inhibit inflammations and reduce age – related cognitive decline by scavenging free radicals, activating various signaling pathways (NFkB) or inhibiting the release of cytokines (TNF- α). We aimed to chemical characterize and evaluate the comparative effects of two extracts of *Thymus marshallianus* L. (TM), from wild flora (TMW) and from culture (TMC) on in vitro induced hyperglycemia.

Materials and methods. The phytochemical profile of lyophilized extracts was qualitatively and quantitatively analyzed by two HPLC-MS/MS methods, assessing the individual polyphenolic compounds. In vitro studies were performed on HUVEC cell line, using TMW and TMC extracts in two different dilutions (1/10000, 1/100000), under normoglycemic and hyperglycemic conditions. NF-kB, activated pNF-kB, HIF 1 α and γ H2AX were assessed by western blot; MDA levels were analyzed by spectrofluorimetry.

Results. Rosmarinic acid (RA) was the phenolic marker with the highest level determined in both TMW and TMC extracts. TMW extract contained higher amounts of ferulic acid, apigenin and kaempferol, while luteolin amount was the highest in TMC extract. Catechin and protocatechuic acid were found in TMC extract. In vitro, TMW and TMC extracts diminished MDA, NF-kB and γ H2AX levels and increased pNF-kB and HIF 1 α expressions.

Conclusions. Our findings indicate that TM extracts administration might represent a good option in diabetes – related complications. Both compounds exerted beneficial effect by increasing the antioxidant defence, survival molecules and diminishing DNA lesions.

Association analysis between co-morbidities and early post-intervention mortality in patients with colorectal cancer

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Introduction. Our study aimed to analyze the association between a number of co-morbidities and mortality in the clinical management of patients with colorectal cancer.

Material and methods. A six years retrospective study was conducted on subjects with colorectal cancer treated at the Third Surgical Clinic, “Prof. Dr. Octavian Fodor” Regional Institute of Gastroenterology and Hepatology Cluj-Napoca, Romania, from January 2014 to September 2019.

Results. A total of 1,688 patients with a median of age of 69 years were included in the study. Forty patients died during the hospitalization (2.4%). The frequency of death was similar among genders (2.3% for women and 2.5% for men, P=0.7892). The patients who died were significantly older as compared to those who survived (median of 74 years vs. 69 years; P-value = 0.0128). In half of dead patients an emergency intervention

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was applied (the emergency intervention of those who survived was applied on 16.3% of cases; $P < 0.0001$). Neither smoking nor alcohol consumption were significantly associated with post-intervention dead ($P > 0.6$). The frequency of DM among patients who died was significantly higher compared to those who survived (27.5% vs. 15.2%; relative risk = 2.07, 95%CI [1.05 to 4.10], $P = 0.0359$). No significant association was observed between IID, CP, CRD and dead ($P > 0.7$). None of the patients who died had intestinal inflammatory disease, colic polyposis, or colo-rectal diverticulum. The TEM approach as exclusively applied for inferior rectum tumors, and in most of the cases (83.1%) the classical intervention was applied.

Conclusions. A profound understanding of colorectal pathology leads to a correct management of the disease, consecutively resulting in low mortality rates.

Assessing the knowledge, attitudes and practices concerning hormonal emergency contraception among female university students from Cluj-Napoca

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Introduction. Emergency contraception (EC) is the prevention of unwanted pregnancies in case of lack or failure of a contraceptive method. Romania is among the European Union's countries with high abortion rates. Thus, the aim of the study was to evaluate the knowledge, attitudes and practices of Romanian female students related to EC.

Material and method. A web-based questionnaire was distributed to female students, aged 18-26 years, regardless of sexual activity, from medical and non-medical faculties at three universities in Cluj-Napoca. The questionnaire contained 36 questions, divided into 3 sections: the first section collected demographic and general data, the second required general information on the use of hormonal contraceptives, and the latter asked for specific information on emergency contraception.

Results. In total, 386 completed questionnaires were included. Most students were aware that no prescription is required for EC (84.71%), but only 20.06% of the sexually active students knew the correct timeframe of EC administration. Of all students, 25.33% declared not knowing the correct frequency of EC administration/year. The main reasons for not using EC, when needed, were: the impossibility to obtain EC immediately after the event (40.77%), religious reasons (34.95%) and the belief that EC can induce abortion when the ovum is fertilized (17.47%). General beliefs regarding EC were: it is an effective method that can avoid unwanted pregnancies (72.3%) and it is indispensable medication in certain situations (29.6%). Just 46.17% responders declared having used EC, out of them 59.09% were counseled about EC use, counseling was given mostly by pharmacists (95.19%).

Conclusion. Although female students have a general idea about EC, their knowledge should be improved in order to avoid beliefs and attitudes not based on scientific data. Better knowledge about EC could avoid unwanted pregnancies, thus avoiding the physical and psychological trauma of an abortion.

Candesartan as a potential protective agent in anthracycline-induced cardiotoxicity

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Introduction. Cancer and cardiovascular diseases are the leading causes of mortality worldwide. Death rates dropped tremendously in the last decade due to the usage of early diagnosis methods and targeted therapies. Anthracyclines are used in the treatment of solid tumors and blood cancers. Doxorubicin (DOX) is an anthracycline used in the treatment for aggressive forms of cancer. It works by intercalating DNA and RNA, poisoning topoisomerase II activity and by producing ROS, ultimately leading to apoptosis.

A worrisome side effect of anthracyclines is cardiotoxicity, induced by incompletely understood mechanisms. This affects more than 40% of the patients, during or after treatment. Candesartan (CAN) is an angiotensin II receptor antagonist commonly used in the treatment of idiopathic heart conditions. During chemotherapy, CAN may exhibit cardioprotective effects: restoring LVEF, attenuating aortic fibrosis, improving cardiotoxicity markers. This study investigates the toxic effects of DOX on heart, liver, kidney, aorta and blood, and the protective effects of CAN during DOX therapy. We show here only the changes induced in blood parameters.

Materials and methods. Wistar rats were divided into 3 groups: C (control), DOX, and DOX-CAN. DOX was given i.p. in a unique weekly dose of 2.5 mg/kg. CAN was given orally, in a daily dose of 10 mg/kg. After 6 weeks, the rats were killed by exsanguination under anesthesia. Blood parameters were assayed with a SYSMEX XP-300 analyzer and compared using Student's test ($p < 0.05$).

Results. DOX treatment did not change RBC count, whereas CAN significantly lowered it, compared to C and DOX groups. Both DOX and DOX-CAN groups had a lower WBC count than C group. Platelet no. and plateletcrit had increased values in the DOX group and were significantly lowered in DOX-CAN. MCH was elevated by DOX and CAN, showing a cumulative effect in DOX-CAN group.

Conclusion. CAN exhibited significant modifications of RBC and platelet parameters.

The risk of bias in randomized clinical trials reporting on the treatment of endometriosis

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Introduction. Clinical trials are studies that test a therapeutic intervention, with or without administration of a drug, in a sample of patients experiencing a medical condition. The purpose of this study was to assess the risk of bias in randomized clinical trials reporting a therapeutic intervention for endometriosis.

Material and method. Three bibliographic databases, namely PubMed, PMC, and ScienceDirect, were used to identify randomized clinical trials (RCT) published in English between 2008 and 2018. The keywords used were: endometriosis and therapy and efficacy. RCTs were evaluated based on four bias risks: random sequence generation,

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allocation concealment (selection bias); blinding of outcome assessment (detection bias) and incomplete outcome data (attrition bias).

Results. We found 387 articles on endometriosis therapy, of which 38 were RCTs: 30 double-blinded RCTs (DB-RCTs) and 8 open-label RCTs. Bias analysis was conducted just for DB-RCTs. Six of these articles had both high and uncertain risk of bias in the evaluated categories, 13 articles presented just high bias risk in at least one category and 7 articles had unclear bias risk in at least one category. Random sequence generation, as well as allocation concealment, were categories with high bias risk observed in 46.67% (14/30) DB-RCTs. Assessing articles' bias categories, high or unclear risk of bias was identified in: 80% DB-RCTs for random sequence generation, 60% of them for allocation concealment, 56.7% DB-RCTs for blinding of outcome assessment and 16.67% DB-RCTs for incomplete outcome data. Only four articles out of 30 showed a low risk of bias in all four bias categories.

Conclusion. High quality reporting (implying a low bias risk) in RCTs on endometriosis treatment was observed in a very small number of articles, four out of 30. In order to assure an efficient research transfer into clinical practice there is a need to increase the quality of RCTs reporting endometriosis treatment.

Does social media usage reveal personality traits and mental health status? A review of literature

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Internet addiction was first described in 1998 by Young. Later the co-existence of internet addiction with psychiatric disorders or personality disorders was also described. The mechanisms of the development of internet addiction are mostly unknown. Problematic use of Social Media (SM) is a concept that aims to encompass multiple SMs currently used with the presence of accounts on several social networks.

A systematic review following the PRISMA guidelines was conducted. Studies that described social media, examining participant's behavior related to social media, stored in PubMed were analyzed. Studies in English were included if they reported primary or secondary research, with analytic quantitative designs used to provide insight on problematic use of social media, relating psychiatric or personality disorders. Both interventional and observational studies were included. Social media was defined according to Kaplan and Haenlein's classification scheme, including collaborative projects, blogs or microblogs, content communities, social networking sites, and virtual worlds. The PubMed database was searched in October 2019 for relevant articles using 22 search queries. The search was undertaken and included papers published up to then. Data extraction was done using home-made standardized forms, and any duplicates were removed. Firstly, titles and abstracts were screened for inclusion. Secondly, eligibility was assessed through full-text screening.

A data extraction form was developed and pilot-tested on a randomly selected subsection of studies. The data extraction form ensured that the review extracts pertinent data to provide a comprehensive synthesis of the literature regarding social media analysis of medical information usage. As per the PRISMA guidelines, data were extracted from each study that met the inclusion criteria, including participants, interventions, results, social media behavior analysis methodology.

Correlations between Matrix Metalloproteinases MMP-2, MMP-9, Tissue Inhibitor of Matrix Metalloproteinases (TIMP-1) and IL-25 in nasal polyposis

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Introduction. Matrix metalloproteinases (MMP) are involved in physiologic tissue remodeling, inflammation and tumor spread and they are capable to break down almost every component of the extracellular matrix (ECM). The active forms of MMP-2 and MMP-9 can sunder type IV collagen. They are activated by inflammatory factors and their extracellular activity is regulated by a tissue inhibitor of matrix metalloproteinase (TIMP). The EMC degradation in which MMP are involved, is a constitutive part for developing nasal polyposis. IL-25 plays a crucial role in nasal polyposis development and is also a biomarker present in most patients with nasal polyposis associated with asthma.

The objective of this study was to evaluate MMP-2 and MMP-9, TIMP-1 and IL-25 expression in nasal polyps and in normal mucosa and the correlation between these factors.

Material and methods. We designed a case-control study which included 60 patients (30 with nasal polyposis and 30 control patients) and we determined the expression of MMP-2 and MMP-9 by zimography, TIMP-1 by Western Blot and IL-25 by ELISA.

Results. Statistical analysis established that MMP-2, MMP-9 and IL-25 have a greater expression in nasal polyps comparing with the control group.

Conclusions. MMP are involved in nasal polyposis development and can be further studied for a better understanding of the physiopathology of this process.

The effect of Celecoxib on apoptosis, melanogenesis and angiogenesis in cutaneous melanoma treated with Trametinib

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Introduction. Cutaneous melanoma is a very immunogenic tumor. Chronic inflammation and genomic instability dictate the changes in melanoma microenvironment. It is well known that cyclooxygenase-2 (COX-2) has an intricate role in tumor cell proliferation, angiogenesis, therapeutic resistance and immune suppression. Therefore, its inhibition becomes a logical approach. The current *in vitro* study evaluated if Celecoxib, a selective COX-2 inhibitor, might be a suitable adjuvant for Trametinib, a selective MEK inhibitor, on an experimental melanoma model.

Materials and methods. All *in vitro* experiments were conducted on human melanoma cells (SK-MEL-28) and human fibroblasts (BJ), in co-culture. After performing viability tests in order to choose the suitable dose, cells were treated as follows: 2.5 nM Trametinib (group 2), 50 nM Celecoxib (group 3), and the therapeutic combination of Celecoxib+Trametinib (group 4). Results were compared with a control group

represented by untreated cells (group 1). After 72h we evaluated cell death induction - flow cytometry, LDH – colorimetry, melanogenesis via tyrosinase and MITF – WB, angiogenesis via VEGF – ELISA and proliferation signaling pathways via NF- κ B, pNF- κ B and AKT - WB.

Results. Celecoxib managed to increase the inhibitory effect of Trametinib on cell proliferation compared with Trametinib group ($p < 0.0001$). Moreover, the drug combination increased cell death via apoptosis, membrane lysis, inhibited angiogenesis and apoptosis compared with the control and Trametinib group ($p < 0.0001$).

Conclusion. Celecoxib proved to be a suitable adjuvant for Trametinib on SK-MEL-28+BJ co-culture cells after inhibiting cell proliferation, promoted apoptosis, inhibited angiogenesis and melanogenesis.

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The relationship between treatment, bone remodeling biomarkers and pathophysiological process in spondyloarthritis

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Introduction. The treatment of spondyloarthritis (SpA) follows the control of clinical manifestations. In the management of SpA accurate biomarkers are needed both to track the activity of the disease and to predict the response to treatment. A better understanding of the relationship between the inflammatory process and the mechanisms of new bone formation is essential for tailoring the treatment. Bone biomarkers DKK-1 and sclerostin (SOST) are mediators of the new bone formation process involved in the pathogenesis of SpA. Their serum level may indicate a lack of inhibition of the osteoformation process in relation to the administrated treatment.

Material and method. We performed an observational, retrospective and cross-sectional study, conducted on a cohort of patients diagnosed with SpA and followed-up at the Rheumatology Ambulatory of the Clinical Hospital of Infectious Diseases Cluj-Napoca. Demographic, clinical and treatment data were extracted from patients' charts. Serum level of DKK-1 and SOST and inflammatory parameters (CRP) were measured in the same day. Radiographs not older than 1 year were scored by an expert rheumatologist. The variables were included in the database and analyzed using the statistical software SPSS version 20. The choice of statistical tests was made according to the distribution of data. T-test for independent samples and Spearman correlation test were applied.

Results. A positive, statistically significant correlation was identified between the serum level of SOST and the severity of sacroiliitis on the radiographs in the biological treatment subgroup. We did not find correlations between serum DKK-1 or SOST level and disease activity (BASDAI).

Conclusion. Serum levels of DKK-1 and SOST biomarkers cannot be used as markers of monitoring SpA disease activity. Serum levels of SOST may be indicative of reduced new bone formation process in patients with anti-TNF α treatment.

The effects of Luteolin, Cornus mas extract and gold nanoparticles conjugated with Cornus mas extract on Caco2 cells exposed to gliadin

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Introduction. Celiac disease (CD), an enteropathy caused by the intolerance to gluten/gliadin peptides, with genetic and environmental determinisms, is mediated by an interaction between innate and adaptive immune responses. At present, the only accepted treatment is the gluten free diet. Further studies are required to discover novel or adjuvant therapies for CD. The present study aimed to evaluate comparatively the effects of Cornus mas fruits extract (CM), gold nanoparticles capped with CM (AuCM), and natural antioxidant Luteolin (LT) on objective measures of oxidative stress, apoptosis mediation and inflammation in Caco-2 cells, exposed or not to gliadin.

Material and methods. The total phenolic content of the CM fruit extract was assessed using the Folin-Ciocalteu reagent. Gold nanoparticles characterization was determined by transmission electron microscopy (TEM) and ultraviolet-visible spectroscopy. The evaluated parameters were: markers of oxidative stress (malondialdehyde level, catalase and superoxide dismutase activities), and factors involved in cellular signaling, apoptosis and inflammatory response (NF-κB, pNFκB, NOS2, TNFα, TRAIL, Bax, Bcl-2, p53).

Results. The pretreatment with AuCM, CM extract and LT diminished the oxidative stress levels, regulated the antioxidants enzymes and NOS2 activity and lowered the NF-κB and pNFκB expressions. The production of p53 was increased by AuCM and CM treatment and Bcl-2 level was decreased especially by AuCM.

Conclusion. According to our results, the most promising are AuCM, which reduced the oxidative stress and inflammation, recommending them as candidates for further studies.

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Probiotic bacillus spores protect against acetaminophen-induced acute liver injury in rats

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Introduction. Acetaminophen (APAP), is one of the most used analgesic and antipyretic agent in the world. Intoxication with APAP is the main cause of acute liver toxicity in both the US and Europe. Spore-forming probiotic bacteria have the ability to resist harsh gastric and intestinal conditions.

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The aim of this study was to investigate the possible protective effect of *Bacillus* (B) sp. spores (*B. Licheniformis*, *B. Indicus*, *B. Subtilis*, *B. Clausii*, *B. Coagulans*) against hepatotoxicity induced by APAP in rats.

Material and methods. A total of 35 rats were randomly divided into seven groups: group I served as control; group II received Silymarin (SIL); group III received MegaSporeBiotic (MSB); group IV received APAP and served as the model of hepatotoxicity; group V received APAP and SIL; group VI received APAP and MSB; group VII received APAP, SIL and MSB.

Liver for histopathological examination and blood samples were collected on the last day of the experiment. Were determined GPT and GOT, total antioxidant capacity (TAC), zonula occludens (ZO), tumor necrosis factor (TNF) α and interleukin (IL1 β).

Results. APAP overdose increased GOT, GPT. It slowly decreased TAC compared to the control group, but pre-treatment with silymarin and MSB increases TAC level. Elevated plasma concentrations of ZO-1 in groups treated with APAP overdose compared with groups without APAP or with those receiving APAP in combination with silymarin, MSB or both were identified. The changes are positively correlated with the levels of other pro-inflammatory cytokines (TNF α , IL1 β). Also, histopathological hepatic injury was improved by pre-administration of MSB or silymarin versus the disease model group.

Conclusion. *Bacillus* sp spores have a protective effect on acute hepatic injury induced by APAP. Pre-treatment with MSB resulted in a significant reduction in serum GOT, GPT, TNF α , IL-1 β , ZO-1, TAC and also hepatocyte necrosis, similar to the well-known hepatoprotective agent - silymarin.

The influence of surface treatments on the bioactivity of porous titanium implants

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Introduction. Bone tissue engineering and regenerative medicine gained tremendous development in the last decades. Pure titanium and its alloys are commonly used in dental and orthopedic applications due to their biocompatibility and mechanical properties. For binding the bone tissue, the implant material would be more desirable to be bioactive. The present work aims to characterize the structure and to evaluate in vitro the effect of different surface treatments on the bioactivity of medical grade Ti6Al7Nb alloy implants manufactured by selective laser melting.

Material and methods. The Ti6Al7Nb implants manufactured by selective laser melting (SLM) were investigated before and after heat treatment, chemical treatment and impregnation with calcium phosphate precipitates and silica-titania gel in order to evidence the changes induced by the applied treatments especially on their surface that would primary interact with the body fluids in biomedical applications. The samples were characterized before and after immersion by scanning electron microscopy, X-ray diffraction and X-ray photoelectron spectroscopy.

Results. The elemental composition on the surface of SLM derived samples pronouncedly differs from that of Ti-6Al-7Nb compact implant material that is first due to the occurrence of passive oxide layer and elements rearrangement on powdered Ti-6Al-7Nb alloy. The bioactivity tested in vitro in SBF was proved by the self-assembling of an apatite type layer clearly evidenced by SEM/EDX analysis.

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Conclusion. XPS results referring to the outermost layer indicate that both calcium and phosphorus are attached on all investigated samples after immersion in SBF.

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Influence of *Nigella sativa* oil on oxidative stress markers in experimentally induced chronic inflammation in rats

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Introduction. *Nigella sativa* (black cumin) (NS) has been used for many centuries as spice or in traditional medicine due to its pharmacological activities such as anti-asthmatic, gastro-protective, anti-inflammatory, antioxidant, anti-hyperlipidemic, anti-diabetic, anti-cancer, immunomodulatory and antimicrobial. Because of the contradictory studies existing in the literature more research is needed.

Materials and methods. The antioxidant effect of NS oil was evaluated using an experimental model of induced chronic inflammation in rats by Complete Adjuvant Freund (CFA). Fifty Albino Wistar rats (weighing between 150 and 200g) were randomized and divided into five groups. Group (A) received normal saline solution; group (B) received sodium diclofenac (5mg/ kg), group (C) received NS oil (4 mL/kg) 7 days before and 7 days after FCA injection, group (D) received NS oil (4 mL/kg) 7 days after FCA injection and group (E) which received both sodium diclofenac and NS oil. The oxidative stress parameters like malondialdehyde (MDA), reduced glutathione (GSH), oxidized glutathione (GSSG), GSH/GSSG, hydrogen donor capacity (DH) and superoxide dismutase (SOD) were determined from the rats serum.

Results. The MDA (6.4 nmol/mL) and GSSG (1.9 nm/mL) analysis had statistically significant differences between control group (A) and all the others (with values of 2.3, 3.6, 3.1, and 2.4 nm/ml in case of MDA for groups B, C, D and E respectively and 0.5, 0.7, 0.55 and 0.58 nm/ml in case of GSSG for groups B, C, D and E respectively). The positive control group (B) presented statistically significant differences only when compared to control group. The inhibition of MDA and GSSG was effective in all cases (preventive (C), treatment (D) or adjuvant (E)).

Conclusions. The use of NS oil was effective in reducing the oxidative stress associated with the inflammatory process by inhibiting MDA and GSSG and partially by normalizing the other oxidative stress parameters.

Stem cells in the treatment of diabetes mellitus type 1

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Introduction. Type 1 diabetes is characterized by the destruction of pancreatic β cells and its treatment is based on exogenous insulin intake. An alternative could be cell therapy, involving the replacement of β -cells with mesenchymal stem cells. The present research aims to quantify the performance of these cells in regulating blood glucose according to their source of harvest, in rodents suffering from type 1 diabetes.

Material and methods. A literature search was conducted in ScienceDirect database and retrieved 7 studies. To analyze the performance of cell therapy, blood glucose and body weight measured after therapy were quantified from each study using a systematic analysis.

Results. The selected parameters were grouped according to the collection source of mesenchymal stem cells from human subjects (bone marrow, dental pulp, umbilical cord blood, hair follicle, Wharton gelatine, menstrual blood and amniotic fluid). For each harvesting source, the performance of the transplant was calculated according to the blood glucose values. The best results regarding the glucose level were obtained by stem cells acquired from amniotic fluid, in contrast to cells procured from umbilical cord blood. The cells obtained from umbilical cord blood had poor results, with no influence on body weight, in contrast with cells from dental pulp and hair follicles.

Conclusions. The results obtained by stem cell therapy with cells extracted from hair follicles and dental pulp were promising regarding the glucose values and weight gain. Stem cells from umbilical cord blood had zero impact on rodent blood glucose, probably due to their rejection by the host. In conclusion, these results encourage to improve the cell therapy techniques because the current treatment for type 1 diabetes is chronic and it has no effect on the substrate of the disease.

MEDICAL SCIENCES

Influence of diabetes mellitus and central obesity on central arterial stiffness parameters

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Introduction. Diabetes and obesity are representing important risk factors, interconnected between them and with cardiovascular diseases. Studies assessing arterial stiffness have focused on its assessment at peripheral level; the predictive importance of “central” parameters has been also shown to be important. The purpose was to evaluate the interrelationship between diabetes-obesity-central central arterial stiffness parameters.

Materials and methods. The study included 285 patients, mean age 59.13 ± 10.81 years, 67% women. Abdominal waist was measured, abdominal obesity being defined as waist circumference ≥ 94 cm for men and ≥ 80 cm for women. Patients were categorized in obese only (66.1%), diabetics only (0.4%), associating obesity and diabetes (22.7%) and non diabetics-non obese (10.8%). Arterial parameters (central systolic blood pressure–SBPAo and aortic pulse pressure–PPAo) were determined using TensioMedTMArteriograph.

Results. Globally, mean values registered for PPAo and SBPAo were 104.83 ± 54.01 mmHg, respectively 115.87 ± 58.56 mmHg. The values of PPAo registered in the four groups were: in diabetic+obese patients 125.84 ± 45.38 mmHg, diabetics only 114.99 mmHg, obese only 97.79 ± 55.61 mmHg, non obese-non diabetics 98.68 ± 55.37 mmHg (between groups $p=0.006$); the differences between groups were significant just in women (in men $p=0.165$, in women $p=0.017$). The values of SBPAo registered in four groups were: in diabetic+obese patients 140.45 ± 47.38 mmHg, diabetics only 130.33 mmHg, obese only 107.96 ± 60.77 mmHg, nonobese-non diabetics 107.08 ± 58.31 mmHg ($p=0.002$ between groups). No significant difference was found in men between groups ($p=0.158$), in women $p=0.007$.

Conclusions. Central arterial stiffness parameters were increased especially in diabetic patients, particularly in women. The association between diabetes and abdominal obesity determine an additive negative effect on central arterial parameters, weight loss being recommended to reduce cardiovascular risk.

Amiodarone-induced thyroid dysfunction in elderly patients

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Introduction. Amiodarone is the most efficient antiarrhythmic agent currently available. Is the only drug that can be used to maintain sinus rhythm in patients with significant impairment of the left ventricular ejection fraction or severe aortic stenosis, both of which are often encountered in the geriatric population. The complex electrophysiological profile of amiodarone and the large amount of iodine in its composition attract an important retinue of adverse effects, the most frequent being dysthyroidism. This can occur because of specific enzymatic activities inhibition, competitive antagonism on thyroid hormone receptors, as well by direct cytotoxic effect.

Materials and methods. It is a retrospective study that included consecutive

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geriatric patients (minimum 75 years old), hospitalized between January 2016 and March 2019. All patients benefited for at least one reevaluation in cardiology or geriatric department of Cluj-Napoca Municipal Hospital.

Results. A total of 184 patients were included, the average age was 82 ± 6 years, with the predominance of the female sex (61%). Re-evaluation was performed at 98 ± 26 days. The main indication for amiodarone was rhythm control strategy (71%), followed by ventricular rhythm disorders. The abandonment rate of amiodarone was 34%, mostly for cardiologic effects (bradycardia, long QT) followed by thyroid disorders. Hypothyroidism was found in 27% of cases, with a female-to-male ratio of 1.9: 1. Hyperthyroidism was identified in 4.5% of patients, with a male-to-female ratio of 2.5: 1. Severe forms of thyroid storm and myxedema were rarely encountered (3.3%).

Conclusion. Elderly patients treated with amiodarone are at a high risk for developing dysthyroidism compared to younger patients. This exerts a negative impact on cognitive function and increases frailty.

The impact of continuous positive pressure therapy (CPAP) on the quality of life in patients with OSA

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Introduction. Obstructive sleep apnea syndrome (OSA) has become a public health problem, affecting 10% of adults worldwide. OSA decrease the quality of life (QOL) due to the effects on the patient's physical and mental function. QOL in sleep apnea may improve under CPAP therapy. The purpose of this study was to assess the OSA patients quality of life at the diagnosis and after 3 and 6 months of CPAP therapy.

Materials and methods. We conducted a cross-sectional study between October 2017 and August 2018, including 143 subjects diagnosed with OSA in the Sleep Laboratory of Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca. We used the Calgary Sleep Apnea Quality of Life Index (SAQLI) in order to quantify the quality of life.

Results. From all subjects included, 81.7% were men and the mean age was 49.83 ± 11.87 years. The mean abdominal circumference was 115 ± 23.90 cm and the mean body mass index (BMI) was 32.12 ± 8.52 kg/m². The mean value of Epworth Sleepiness Scale (ESS) was 11.3 ± 5.08 at the diagnosis. The mean apnea-hypopnea index (AHI) was 42.46 ± 30.83 events/hour of sleep. In all 4 domains of SAQLI was observed an improvement in mean total score after therapy compared to baseline 3.22 ± 0.41 versus 4.42 ± 0.45 ($p < 0.01$).

Conclusions. The quality of life in sleep apnea patients was improved after 3 months of CPAP therapy and highly different at 6 months of treatment according to SAQLI and clinical status. This is a useful tool to evaluate the quality of life in patients with sleep apnea, in order to highlight the benefits of CPAP therapy and should be used in daily clinical practice in sleep medicine.

Interrelation between inflammatory profile and tobacco consumption in foster care teenagers

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Introduction. Foster care teenagers, a particular social category, have documented an increased risk for the development of chronic health conditions, because smoking is a major risk factor for many conditions with inflammatory component. In smokers, some biomarkers reflect the reactivity of the body to the toxic effects of cigarette smoke. These changes of inflammatory profile indicate subclinical changes that may constitute the basis for the subsequent occurrence of various pathologies.

Methods. Since young people in foster care system appear to be at increased risk for various chronic diseases, we aimed to evaluate whether smoker status was associated with an inflammatory response as an additional potential risk factor. We performed a cross-sectional pilot study for assessing the correlation between tobacco consumption status and inflammatory profile among foster care teenagers in the central region of Romania. A number of 175 teenagers aged 10-18 were enrolled. Blood samples were collected for complete blood count (CBC), fibrinogen, Interleukin-6 (IL 6), C reactive protein (CRP). Smoking status was confirmed by urinary cotinine.

Results. Urinary cotinine accurately reflected smoker status. In smokers, the average urinary cotinine was 1639 µg/l. In our study, smoking did not affect hemoglobin levels or other hematological parameters. C-reactive protein was higher in foster care smokers. Plasma fibrinogen, assessed by the Clauss coagulation method, correlated with the daily number of cigarettes. Interleukin-6 did not correlate statistically significant with the smoker status or the daily number of cigarettes consumed.

Conclusions. This research highlights the existence of an inflammatory response correlated with tobacco consumption in foster care teenagers. Determination of smoking risks in this special social category has been a strong point of this research.

Usefulness of arterial stiffness assessment in oncologic patients with venous thromboembolism

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Background. Venous thromboembolism (VTE) and atherosclerosis (ATS) are related processes, even enhanced in cancer patients. In their cases, first clinical manifestation may be VTE, accelerated ATS may develop and acute ischemic events may occur.

We tested the hypothesis that assessment of arterial stiffness (AS), a marker of infraclinical ATS, in patients with cancer and VTE, may identify a subgroup vulnerable for arterial events.

Methods. We selected in our hospital patients admitted for VTE in a four year period. If cancer was also present or diagnosed during hospitalization, patients were included. Arterial risk and vascular age were calculated using SCORE diagrams. AS was

assessed using pulse pressure (PP). Patients with clinical manifestations of the ATS, with diabetes, younger than 40, or older than 70 were excluded.

Results. 180 patients with VTE and cancer were admitted. After applying the exclusion criteria, 44 patients (21 men, 23 women) with a mean age of 63.72 ± 7.50 years, were included. The mean SCORE risk level was $4.75 \pm 4.1\%$, with a significant difference between genders. The mean value for PP was 52.5 ± 11.23 mmHg. The mean SCORE vascular age (67.13 ± 10.19) was statistically significantly higher compared to the real age ($p=0.0031$). A SCORE risk level greater than mean value was significantly correlated with AS assessed by PP ($p=0.0007$, $r=0.49$). We also found that PP had a statistical significant correlation with vascular age ($p=0.005$, $r=0.41$), but no significant correlation with real age ($p=0.16$, $r=0.21$).

Conclusions. Our study showed that in a population of oncological patients with VTE, with no clinical manifestation of ATS disease, SCORE vascular age is higher than real age. This indicator of high arterial risk was correlated with PP, a simple tool of AS assessment.

Further studies would be useful in order to confirm our results, and to identify diagnostic and treatment options for prevention of arterial events in this vulnerable population.

The use of Schwartz formula in kidney grafted patients: does it help?

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Introduction. Chronic allograft dysfunction is an alteration of the renal graft's structure that causes renal function to deteriorate. Kidney function is evaluated by measuring the glomerular filtration rate using reference methods such as urinary clearance of inulin or iothexol. This study aimed to investigate the concordance between Schwartz formula and renal inulin/iothexol clearance in renal grafted recipients.

Patients and methods. 61 kidney recipients were enrolled. Simultaneous measurements of inulin/iothexol urinary clearance were performed.

Results. The mean value of GFR after 1 year of renal transplantation was 79.60 ± 12.10 ml/min/1.73. There was a difference of GFR means between the methods: 72.10 ± 10.40 ml/min/1.73 using urinary clearance of inulin or iothexol vs. 93.17 ± 13.17 ml/min/1.73, with $p=0.01$. There was a positive correlation between inulin/iothexol clearance and the presence of microalbuminuria, with $r^2 = 0.34$, $p<0.001$.

Conclusions. Estimation of the glomerular filtration rate from plasma creatinine using the Schwartz formula is not a reliable marker of renal function loss in the transplantation patient; nor is it a good predictive marker of graft loss.

The management of inappropriate ICD therapies in patients of the Clinical Rehabilitation Hospital Cluj-Napoca

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Introduction. The implantable cardioverter defibrillator (ICD) is a salutary device used for the prevention of sudden cardiac death, however 10-15% of the ICD careers experience inappropriate shocks (i-Sck) and this complication impairs the quality of life; it tends to be an important issue since the number of ICD implants continuously increases.

That's why we aimed to assess the prevalence of inappropriate shocks in our ICD patients during a mean 3 years time period and to identify possible risk factors for these.

Materials and methods. We retrospectively enrolled 39 patients (out of 112 patients) implanted in our hospital from January 2015 to December 2017. They were assessed during 36 months at both regular follow up and the unscheduled visits for perceived shock. The subgroup of i-Sck was compared with the subgroup of the remaining patient.

Results. The study group consisted of 28 (71.8%) males and 11 (28.2%) females, mean age 54.22 ± 9.3 years. The inappropriate shocks were recorded on 9 patients (23%) and the mean age (52.56 ± 13.74 years for i-Sck, vs 54.73 ± 13.7 years) gender distribution (78% males in i-Sck vs 70% males in control) among subgroups was similar. The cause for i-Sck was high rate atrial fibrillation (AF) (4p, 44%), sinus tachycardia (3p, 33%), T-wave oversensing (1p, 11.1%), lead damage (1p, 11.1%). The management consisted of device reprogramming in 3p (33.3%), drug treatment (betablockers, amiodarone and digitalis) in 5p (55.5%) out of which 2p (22.2%) received medication and reprogramming, and 1p (11.1%) undergo lead replacement. The i-Sck did not correlate with NYHA class, occurrence of ventricular arrhythmias or LVEF, but was significantly prevalent among AF and ischemic etiology.

Conclusions. In our cohort, the i-Sck were registered in around one tenth of the patients and this seems to be more prevalent among AF patients and ischemic cardiomyopathy. The most of them were fixed by device reprogramming and by medication adjustment.

Arterial stiffness assessment for cardiovascular prognosis in end-stage renal disease patients on chronic hemodialysis

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Introduction. Cardiovascular (cv) mortality in end-stage renal disease (ESRD) populations is high, related to accelerated atherosclerosis and arterial stiffness (AS). In the attempt to achieve dry weight target through hemodialysis (HD), ultrafiltration determines a powerful activation of the sympathetic nervous system. The consequence is an important variation of heart rate, blood pressure and AS. We aimed to establish the

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prognostic value of some AS parameters regarding incidence of cv death.

Materials and methods. We conducted a prospective study in 45 subjects with ESRD treated chronic by HD. Traditional and novel risk factors, along with AS pre- and post-dialysis were assessed at the beginning of the study. Arterial system function was assessed through brahial pulse pressure (PP), digital volume pulse-derived stiffness index (SIDVP) and a calculated pulse wave velocity (cPWV). For a ten year period incidence of cv death was observed.

Results. During the follow-up period a total of 27 deaths occurred. Among risk factors, age ($p=0.0003$, $r=0.51$), diabetes melitus ($p=0.0082$, $r=0.38$) and inflammation markers (albumin- $p=0.0093$, $r=-0.38$; high-sensitive C-reactive protein- $p=0.004$, $r=0.42$) were correlated with death incidence. We noticed a high rate (33.3%) of not detectable SIDVP values. AS was related or not with death incidence, depending on the method used (PP, SIDVP, cPWV) and the moment of determination (pre- or post-dialysis) ($p<0.012$, $r=0.57$ for PP pre-, $p=0.138$, $r=0.22$ for PP post-; $p=0.27$, $r=0.28$ for SIDVP pre-, $p=0.75$, $r=-0.25$ for SIDVP post-; $p=0.0041$, $r=0.41$ for cPWV pre- and $p=0.0001$, $r=0.54$ for cPWV post-).

Conclusion. In a ESRD population treated with chronic HD, multiple traditional and novel risk factors were statistically correlated with the 10 year death incidence. Regarding AS assessment, cPWV post-dialysis value had the best prediction for cv vulnerability, while SIDVP measurement was not an appropriate method for all patients.

Multimarker risk stratification in patients with unstable angina

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Introduction. The complete and quick evaluation of patients with unstable angina (UA) allows their inclusion into a risk class and the choice of the optimal therapeutic strategy. The risk stratification of UA patients can be achieved by means of TIMI NSTEMI and GRACE scores; however, these do not always manage to achieve a proper short-term risk stratification of UA patients. The aim of this study was to determine if the combined measurement of biomarkers involved indifferent pathophysiological axes of UA can improve the TIMI NSTEMI risk score. Inflammatory and thrombotic biological markers were studied because atherosclerotic plaque inflammation and thrombosis represent the main mechanisms involved in UA physiopathology.

Materials and methods. We enrolled 40 patients with UA admitted to the Cardiology Department of the Cluj-Napoca County Emergency Hospital. Risk stratification of these patients was performed upon admission, based on the TIMI NSTEMI risk score. They were evaluated in hospital by means of clinical observation, electrocardiography, echocardiography, angiography, and some biochemical markers: hsCRP, IL18, serum albumin and sCD40 ligand.

Results. The only biomarkers that were associated with the evolution of the patients during hospitalization were: sCD40 ligand (AUC:0.789, $p=0.002$, 95% CI [0.631;0.947]), serum albumin (AUC:0.691, $p=0.043$, 95% CI [0.528; 0.855]) and hsCRP (AUC:0.699, $p=0.019$, 95% CI [0.529;0.836]). We did not find a significant association between IL18 and the short-term evolution of patients with UA (AUC:0.462, $p=0.689$, 95% CI [0.272; 0.653]). The multimarker risk score significantly improved the C-statistic (AUC:0.776, $p=0.005$, 95% CI [0.616; 0.915] to (AUC:0.834, $p=0.001$,

95% CI [0.703; 0.965]) when sCD40 ligand, hsCRP and serum albumin were added to the TIMI NSTEMI risk score ($p < 0.05$).

Conclusion. Multimarker scores could improve the capacity of TIMI NSTEMI risk score stratification in patients with UA during hospitalisation.

Cardiologic features and effects of enzyme replacement therapy in Romanian children with mucopolysaccharidosis type II

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Introduction. The severity of cardiovascular disease in patients with mucopolysaccharidosis (MPS) is progressive, consisting in severe cardiac valve disease and ventricular hypertrophy. Enzyme replacement therapy in MPS may improve the organ impairment. The aim of the study was to characterize the cardiac disease and the results of enzyme replacement therapy in children with MPS type II.

Materials and methods. We evaluated by echocardiography 18 patients with MPS type II. We assessed the function of valves, left ventricular chamber dimensions, septal and posterior ventricular wall thicknesses, systolic and diastolic function of the ventricles, pulmonary hypertension at every 6 months. The treatment consisted in weekly administration of recombinant form of human iduronate 2-sulfatase in dose of 0.5 mg/kg, iv.

Results. At diagnosis, all patients presented echocardiographic alterations. Mitral valve thickening with regurgitation was diagnosed in all patients, aortic regurgitation was present in 50% of patients and mitral stenosis in 5% of patients. Left ventricular hypertrophy was diagnosed in 35% of patients. Mild pulmonary hypertension was present in 11% of patients. The mean age of the patients at starting therapy was 5.9 years. The treatment results after 2 years were: valvular heart disease were stable in 62% of patients, mild improvement in 25% of patients and aggravation in 13% of patients. Ventricular hypertrophy remained unmodified in 75% of patients and disappeared in 25% of patients. After 4 years of treatment the results were: valvular heart disease were stable in 62% of patients, mild improvement in 13% of patients and aggravation in 25% of patients. Ventricular hypertrophy remained unmodified in 37% of patients and improvement was recorded in 63% of patients.

Conclusions. The most prevalent cardiac changes in children with MPS are valvular lesions. Enzyme replacement therapy had little effect on cardiac disease in children with MPS.

Acute liver failure in infants - hereditary fructose intolerance

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Introduction. Hereditary Fructose Intolerance (HFI) is an AR disease characterized by the deficiency of aldolase B activity in the liver, kidney and intestine, leading to growth failure, chronic liver and kidney disease. The estimated prevalence in Europe is 1 in 20,000 children.

Case-report. We report a 2 month old boy who was referred for hematemesis and melena, hepatomegaly and abdominal distension. These symptoms appeared after treatment with acetaminophen for fever. Laboratory investigations showed severe anaemia and hypoglycaemia, hypoalbuminemia, coagulopathy and elevated liver enzymes. We excluded viral causes of hepatitis, galactosemia and tyrosinemia. However, considering a possible metabolic disorder, we initiated exclusive parenteral nutrition. The outcome was favourable, with complete recovery and normal laboratory tests.

During follow-up, the boy presented multiple urinary tract infections, hypercalcemia and nephrocalcinosis. At the age of 6 months, when introducing complementary food (fruits, vegetables), the child started vomiting, losing weight in association with altered neurologic status. Laboratory investigations showed severe coagulopathy and increased transaminases again. Our strong suspicion was HFI, which was confirmed by genetic tests for aldolase B mutations (homozygote A175D). The treatment for HFI included the exclusion of fructose, sucrose and sorbitol from the diet. With specific diet, the boy presented normal weight and neurologic development, normal liver tests, with similar changes on renal ultrasound. Reconsidering the case, the first episode of ALF was most likely secondary to the acetaminophen syrup ingestion, which contains sucrose.

Conclusions. In the presence of acute liver failure in infants, it is essential to take into consideration the possibility of an inborn metabolic disorder. Among these diseases, the early diagnosis of HFI is important in order to exclude fructose from diet, to prevent permanent physical damage.

The cascade of care for patients living with HIV infection in Cluj AIDS Center

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Introduction. The HIV pandemic is spreading across the globe, and the World Health Organization (WHO) is trying to take action to limit its spread. By 2020, the WHO target is: 90% of those infected to be diagnosed, 90% to be under antiretroviral treatment, 90% to have undetectable viral load.

Materials and method. We evaluated the patients living with HIV infection who are in the records of the Cluj AIDS Center on December 31, 2018 to analyze the fulfillment of the WHO requirements.

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Results. At the end of 2018, 673 patients with HIV infection were active, 606 (90.04%) of them were in antiretroviral treatment. 471 (77.72%) of those under treatment had undetectable HIV viral load (<100 copies / ml). The antiretroviral treatment include at least 3 active drugs. 299 (49.33%) patients are being treated with protease inhibitors, 75.85% of them having undetectable viral load. 203 (33.5%) have integrase inhibitors in therapy, 73.4% of them are having undetectable viral load. 104 (17.16%) have non-nucleoside reverse transcriptase inhibitors in treatment, 92.3% of them have undetectable viral load.

Conclusions. The WHO threshold regarding the antiretroviral therapy of patients in the Cluj AIDS Center has been reached, 90.04% of the patients living with HIV infection are under antiretroviral treatment. Adherence to antiretroviral therapy is below that estimated by WHO, 77.72% of patients have undetectable viral load, to reach the WHO target is necessary to increase adherence to antiretroviral therapy. Most patients undergoing treatment with non-nucleoside reverse transcriptase inhibitors have undetectable viral load.

Pericardial malignant mesothelioma. Case presentation and review of literature

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Originating from the mesothelial cell layer, the pericardial malignant mesothelioma is a very rare neoplasm. Cardiac CT and MR may be of help in diagnosis, but surgery with biopsy generally make the diagnosis. Sometimes the diagnosis is made only at autopsy. The best treatment in these patients is surgery. The tumor is very aggressive, having a bad prognosis, with a very short survival.

We present the case of a 51 years old woman which was admitted in our department presenting the clinical symptoms of malignancy, initially suspected and treated for tuberculous pericarditis. She was a nonsmoker, and denied asbestos exposure in the past. Lab values were quite in normal range. ECG showed low voltaged QRS complexes, whereas the transthoracic echocardiography documented pericardial echo free space, with some echogenic masses in the pericardial wall. Cardiac MR revealed a diffuse pericardial tumor, compressing the atria, suggesting either a mesothelioma or a cardiac lymphoma. The surgical intervention with biopsy documented a malignant pericardial mesothelioma. The tumor could not be resected completely and a treatment with carboplatin and pemetrexed was started, with no clinical improvement, the patient dying after two months.

Ventricular activation assessed by vector cardiography in patients with neurally mediated syncope

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Introduction. We have demonstrated previously that patients with neurally mediated syncope (NMS) who have an isolated QRS complex of very low voltage in the limb leads on electrocardiogram are more likely to have recurrent syncope. We hypothesized that these changes might be related to a specific left ventricular geometry and/or electrical activation pattern that could predispose to NMS.

Materials and methods. We included 171 patients (age 52±8 years, 122 women) with NMS with a positive (N=82) or negative (N=89) response to tilt table testing (TTT+ and TTT- groups). QRSmin was the lowest voltage in the limb leads.

Results. The TTT+ group had significantly lower QRSmin and QRS duration when compared to the TTT- group (Table). The QRS loop was significantly smaller in area, more elongated as well as narrower in TTT+ patients when compared to TTT- patients. The QRS loop area correlated significantly with LV end diastolic and LV end systolic diameters measured by echocardiography ($r=0.30$ $p=0.017$ and $r=0.25$ $p=0.033$ respectively).

| Variable | TTT+ | TTT- | p-value |
|-----------------------------|-----------|-----------|---------|
| QRSmin (mV) | 2.83±1.38 | 4.30±1.76 | <0.001 |
| QRS loop area frontal (mV2) | 0.25±0.22 | 0.37±0.35 | 0.001 |
| QRS loop width (mV) | 0.33±0.23 | 0.24±0.19 | 0.006 |

Conclusion. Patients with NMS with a positive TTT have smaller and more elongated frontal plane QRS loops than patients with negative TTT. This highlights the potential importance of ventricular geometry and activation pattern in NMS.

Psoriasis: a defining affliction of the 21st century

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Introduction. Psoriasis is an inflammatory, chronic, systemic pathology, affecting primarily the teguments, having an important genetic and immune component. Psoriasis vulgaris represents the most common form, affecting people of all ages, most commonly between 50-69 years old, and all races, with at least 100 million individuals worldwide. It is a potentially debilitating disorder with a progressive evolution, linked to multiple comorbidities and characterized by underlying immunologic and inflammatory elements.

Clinical manifestations. There is a wide variety of clinical forms of psoriasis such as plaque, guttate, pustular, erythrodermic, palmoplantar, inverse and nail psoriasis. The most frequent form is plaque psoriasis, otherwise known as psoriasis vulgaris, representing the overwhelming majority of 90% of cases.

Management of psoriasis. During the last few years, numerous achievements have been made in apprehending the complex physio-pathological mechanisms of psoriasis.

Topical therapy as the single form of treatment shows little rate of improvement, patients often report ongoing clinical symptoms such as redness, pruritus or scales. In the event topical therapy alone disappoints in delivering the expected outcome, practitioners must be prepared for the alternative strategies, such as systemic and biological therapies which up until now have known a fair share of progresses.

Determinants of atrial fibrillation in diabetic patients with symptomatic heart failure

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Background. The prevalence of atrial fibrillation (AF) is increased in both diabetic patients, as well as in those with heart failure (HF), with symptoms being worse when the three conditions meet.

Purpose. The aim of this study was to analyze the main determinants of atrial fibrillation in patient with heart failure and diabetes mellitus.

Methods. 108 subjects with decompensated heart failure (NYHA class II-IV) and left ventricular ejection fraction (LVEF) less than 50% were enrolled, with a mean age of 70.3 ± 9.6 years, 60.2% men and 48.15% of them with a previous diagnosis of DM. All patients were evaluated clinically, biologically and echocardiographically.

DM patients were further divided into two groups: those with microvascular complications- 57.7% and those without- 42.3%.

Results. 64.8% subjects had at least an episode of AF, with a percentage of 61.5% in the DM group vs 67.9% for those without ($p=0.49$).

The mean NT-pro BNP value was 2121 pg/ml in AF subjects vs 2147 pg/ml in those free of AF ($p=NS$). There were no statistically significant differences even when adjusting for microvascular complications of DM.

The mean LVEF was $36.4 \pm 11.3\%$, without significant differences between the groups.

Subjects with a history of AF had a tendency of exhibiting lower serum creatinine levels- 51.1 ± 23.9 ml/min/1.73m³ vs 75.9 ± 29.1 ml/min/1.73m³ ($p=0.0015$).

Among DM patients there were no significant difference regarding glycemic control as a determining factor for developing AF (130.4 ± 52.2 mg/dl in the AF group vs 129.4 ± 41.9 mg/dl in the non-AF one, $p=NS$).

Conclusion. Our study found the prevalence of atrial fibrillation to be higher among heart failure subjects who associated diabetes mellitus and decreased renal function. However, the glycemic status, BMI and low LVEF were not determinant factors for developing AF in our cohort.

Alagille syndrome - cause of cirrhosis in a child with social disadvantage

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Introduction. Alagille syndrome is a rare liver disorder characterized by chronic cholestasis due to paucity of intrahepatic bile ducts, pulmonary artery stenosis, vertebral anomalies, specific facies, ocular abnormalities, pigmentary retinopathy and dysplastic kidneys.

Case report. We report a case of a 5-year-old boy with Alagille syndrome, with progressive neonatal jaundice, acholic stools and dark urine. He was referred with cirrhosis due to suspicion of biliary atresia. On admission, we noticed the triangular facies, jaundice, pruritic skin lesions, large abdomen and hepato-splenomegaly. Spinal X-ray could not show the typical “butterfly vertebrae”. The liver elastography was suggestive for cirrhosis. The upper gastro-intestinal endoscopy showed grade 2 esophageal varices. The echocardiography displayed turbulent flow in the pulmonary artery, suggesting stenosis. A pathogenic variant in JAG1 gene was identified, conclusive for the final diagnosis. During his admission, our patient presented hematemesis and melena, that required therapeutic endoscopic intervention (variceal ligation). The treatment is mostly symptomatic (nutritional support, fat-soluble vitamin supplementation, ursodeoxycholic acid, anti-pruritic medication and non-selective beta blocker). Our patient’s long-term prognosis is poor, his only chance of long-term survival remaining the liver transplantation. There are important social issues: our patient is abandoned, living in a foster care and his parents could not be living donors due to medical reasons. His only chance will remain a deceased donor liver transplantation. After that, he will require medical assistance and help from a foster care social worker or a hired nurse.

Conclusion. Diagnosis of Alagille syndrome remains a challenge. In our case there is a poor prognosis, only chance for survival being a deceased donor liver transplantation and due to the social issues, this will be an important challenge.

The influence of vitamin D receptor gene polymorphisms and vitamin D supplementation on serum markers associated with colorectal cancer

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Introduction. Studies have shown that lower serum levels of vitamin D3 (cholecalciferol) correlate with an increased prevalence of colorectal cancer. Changes in the insulin-like growth factor-1 (IGF-1) and insulin-like growth factor-binding protein 3 (IGFBP-3) ratio have been found to be related with colorectal polyps and colorectal cancer. Vitamin D supplementation may modulate the serum levels of IGF-1 and IGFBP-3, but can also modify local and systemic inflammatory responses. The results of vitamin D supplementation may be also influenced by polymorphisms of the vitamin D receptor gene.

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Material and methods. Our research is an interventional and longitudinal study on approximately 100 patients diagnosed with colorectal polyps and a control group of 50 patients. We will determine at presentation the serum values of IGF-1, IGFBP-3, transforming growth factor 1 (TGF- β 1), and nuclear factor Kappa B (NF- κ B) activity. We will also determine the rs1544410 and rs2228570 genotype in our patients. After 10 weeks of vitamin D supplementation (4000 UI/day), we will determine again the same serum markers and compare them to baseline.

Results. The primary outcome is to determine if a 10 week course vitamin D supplementation did cause a change in the serum values of IGF-1, IGFBP-3, TGF- β 1, and influenced NF- κ B activity. Changes in serum values of cholecalciferol, calcitriol, and total calcium will also be evaluated. These changes will be correlated with the rs1544410 and rs2228570 genotypes.

Conclusion. The mutant variant genotype of rs1544410 has been associated with a lower incidence of colorectal cancer across several meta-analyses, and rs2228570 is the only polymorphism known to change the aminoacid sequence of the vitamin D receptor. It has not been determined yet how these genetic variants influence the response to vitamin D supplementation in patients at risk of colorectal cancer.

Toxic acute liver failure in children from the North-West of Romanian

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Introduction. Toxic liver injuries represents one of the most important cause of acute liver failure (ALF) in children, with a prevalence of 20-25%. The most important causes of toxic ALF are mushroom poisoning and drugs (acetaminophen, valproate, albendazole). The aim of the study was to analyze the main causes of severe hepatotoxicity in children from North Western Romania.

Materials and methods. This retrospective (2000-2014) and prospective (2015-2018) study includes 123 children hospitalized in the Emergency Clinic Hospital for Children Cluj-Napoca with toxic ALF. We have analyzed the cause of toxic ALF, clinical manifestations, laboratory parameters and final evolution.

Results. There were 89 children with ALF after mushrooms ingestion and 34 cases of ALF secondary to drugs ingestion: acetaminophen overdose (18; 52.94%), antiparasitic medication (11; 32.25%), isoniazid (2; 5.88%), and valproate, colchicine or fluconazole (1; 2.94%). The mean age of the patients was 7.74 \pm 3.94 years in mushrooms poisoning and 12.39 \pm 4.59 in drugs. In almost all ALF cases due to mushroom poisoning (98.97%) the first symptoms were gastrointestinal: vomiting, diarrhea, abdominal pain. Hepatic encephalopathy at the time of admission was present in 64 children (71.91%), jaundice in 40 cases (44.94%), bleeding in 34 cases (38.20%) and acute renal injury was associated in 15 cases (16.85%). Uncommon symptoms were convulsions (8.98%) and ascites (1.12%). The mortality in children with ALF due to mushrooms poisoning was 51.68%, while only 5.88% among patients with severe hepatotoxicity after drugs ingestion. The main prognosis factors for fatal evolution in toxic ALF were age, presence of the encephalopathy or renal injury, value of transaminases, bilirubin, INR at the admission.

Conclusion. Toxic ingestion represents one of the main causes of ALF in children from the North-Western part of Romania, and an important cause of death without emergency liver transplantation.

Hepatic adenomas in Glycogen Storage Disease type Ib – the importance of a better metabolic control

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Introduction. Glycogen storage disease (GSD) type Ib is an autosomal recessive disorder, caused by a mutation in the SLC37A4 gene, which encodes glucose-6-phosphate translocase. First signs and symptoms appear early in infancy: hypoglycemia, seizures, lactic acidosis, cholestatic hepatitis, hyperlipidemia. In evolution, patients may develop neutropenia, nephropathy, hepatic adenomas, osteoporosis, delayed or stunted growth.

Case report. We report a case of a 13-year-old boy diagnosed with GSD type Ib during infancy. At 8 months of age he was admitted with failure to thrive, hepatomegaly, dyslipidemia, hypoglycemia, metabolic acidosis with high lactate and neutropenia. The liver biopsy confirmed the diagnosis. He was admitted in our service 7 years after diagnosis, with enlarged liver, stunted growth, increased transaminases, high lactate and uric acid, and frequent episodes of hypoglycemia. After the start of corn starch diet and reduction of lactose and fructose, his parameters had favorable evolution, without known episodes of hypoglycemia. In evolution, hepatic ultrasound showed a 3 cm adenoma and at 13 years of age, he developed multiple hepatic adenomas of different sizes due to the non-adherence to the diet, with proven unbalance status of glycemia.

Conclusion. Early diet may improve prognosis of GSD patients by preventing hepatic disease, including adenoma and hepatocellular carcinoma. With careful monitoring the metabolic status can be improved, and the patients live into adulthood. Long term complications are kidney damage, osteoporosis, tumors of the liver and growth retardation. Teenage is an age with predisposition to non-adherence to treatment or diet in chronic diseases and a close surveillance is needed to detect the early onset of any possible complication.

Alpha-1-antitrypsin and IL-1 receptor antagonist in relation to serum urate and inflammatory markers - comparison between patients with gout, asymptomatic hyperuricemia and healthy controls

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Introduction. Gout is an inflammatory form of arthritis with acute episodes highly dependent on neutrophil involvement. In the center of inflammatory process in gout it is very well known the place of IL-1 β and its natural inhibitor IL-1 receptor antagonist (IL-1Ra). Alpha-1 -antitrypsin (AAT) is an inflammatory modulator due

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to the effects on neutrophil mediated inflammation. In this study we assessed the association between the AAT, IL-1 Ra, serum urate levels (SUA) and inflammatory parameters in patients with gout, asymptomatic hyperuricaemia and a control group of healthy subjects.

Materials and methods. We included 114 patients with gout, 100 asymptomatic hyperuricaemic patients with SUA level >7 mg/dl, and 89 normouricaemic controls matched in age. The erythrocytes sedimentation rate (ESR), C reactive protein, and SUA levels were determined by routine laboratory test. AAT and IL-1Ra were determined by ELISA assay using EDTA plasma samples. Statistical analyzed was perform using Spearman correlation test.

Results. A significant negative correlation was found between circulating AAT and SUA concentration in the control group. There was also a significant positive correlation between AAT and ESR in patients with gout. We obtain a positive correlation between SUA concentration and IL-1 Ra plasma levels in our hyperuricaemic and control group of patients. Also, we observed a positive correlation between the CRP levels and IL-1RA levels in our control and hyperuricaemic cohort.

Conclusion. We were able to validate previous reported findings in which a negative correlation between SUA levels and AAT was observed, possibly due to the role of uric acid to inhibit the production of AAT. We also validate the positive correlation between inflammatory marker, CRP and plasma levels of IL-1Ra, which could possible explained the positive correlation between SUA and IL-1Ra.

A comparative study of single versus dual chamber pacemaker in sick sinus syndrome

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Introduction. The current guidelines on cardiac pacing recommend the implantation of dual chamber pacemakers in patients with sick sinus syndrome, for the risk of atrial fibrillation and reoperation for upgrade in patients initially receiving a single chamber atrial device. Our study aimed to compare the evolution of the single (atrial) chamber (AAIR) and dual chamber (DR) pacemaker patients along one year of follow-up.

Materials and methods. We retrospectively enrolled 44 patients implanted in Clinical Rehabilitation Hospital Cluj-Napoca and divided them into two subgroups: single chamber (28 patients) and dual chamber (16 patients) pacemaker; in both subgroups the AV conduction was assessed as normal at the time of implantation. At one year follow-up visit we assessed the percentage of the atrial and ventricular pacing, the occurrence of atrial fibrillation and the occurrence of atrioventricular block.

Results. We enrolled 22 males and 22 females. The ratio males/females remained the same in the two subgroups, and also the mean age (67.3 years in AAIR subgroup vs 65.06 years in DR subgroup). The LA size (39.74 vs 40.5 mm), the indication for pacing (sinus bradycardia 46.4% vs 43.7%, tachy-brady syndrome 53.6 vs 56.3%), the prevalence of underlying cardiac disease (ischemic heart disease- 10.7% vs 18.7%; valvular heart disease 25% vs 31.2%) comorbidities, and antiarrhythmic medication did not significantly differ. At one year follow-up visit we observed an increased

atrial pacing percentage (58.4% to 68.12%, due to beta-blockers and amiodarone recommended after implantation) but no change in ventricular pacing percentage in DR patients suggesting that AV conduction remained normal despite antiarrhythmic drugs. Atrial fibrillation occurred in 17.9% of the AAIR subgroup and 25.4% in the DR subgroup ($p=0.241$).

Conclusion. The single chamber atrial pacing proved to be safe and effective in sick sinus syndrome patients with preserved atrioventricular conduction.

Portable ultrasound examination: Is the smaller the better?

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Introduction. The National Institute for Health and Care Excellence (NICE) recommend the use of ultrasound in many clinical procedures such as guided catheterization (placing central venous catheters, localization of devices, glaucoma treatment, etc.). Mobile and portable ultrasound are new small and light devices that bring ultrasound examinations to the patients' bedsides. This study aimed to systematically evaluate the performances of the pocket ultrasound devices used in medicine.

Materials and methods. PubMed database was used to retrieve the studies reporting the use of pocket ultrasound in medical care. The following keywords were used to search the database as per 29 October 2019 "(hand-held OR pocket) and (ultrasonography OR ultrasound)". Studies that feature truly hand-held (not hand-carried) devices that compare the results with those of standard ultrasound were included in the evaluation. The studies that do not mention the type of pocket ultrasound that was used and those who used ultrasound devices that were not pocket-sized were excluded.

Results. A total of 3015 articles were found. The screening of the title and abstract reduced the pool of articles to 127. Nineteen articles were included in the final analysis. The majority of the studies showed good concordance between pocket and conventional high-end ultrasonography. The articles established strong correlations when evaluating atrial and ventricular morphology and function (correlation coefficient >0.8), the presence of abdominal aortic aneurysm (correlation coefficient = 0.98), or the presence of pericardial and abdominal effusions (Se=80%, Sp=99%).

Conclusion. Despite their heterogeneity, the studies that were evaluated indicate that hand-held ultrasound is a useful tool for assessing targeted conditions. Further studies are needed in order to establish the role of pocket-sized ultrasound devices in the clinical practice.

Personalized nursing interventions – a factor improving the quality of life in patients with chronic venous insufficiency of the lower limbs

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Introduction. The aim of our study was to evaluate the quality of life in patients with chronic venous insufficiency of the lower limbs (CVI) in hospital and after one month of applying a personalized plan of nursing interventions, compared with the standard nursing care plans provided by the hospital medical staff.

Materials and methods. The study was performed during December 2018 till May 2019 in the CF Clinical Hospital, being previously approved by the local ethics committee. We formed 2 groups of patients with CVI: 25 patients who received standard care from the medical staff and 25 patients who, beside standard care, benefited from a personalized nursing care plan from a student of the Nursing Faculty. They were interviewed and completed the SF- 36 questionnaire and the CIVIQ-14 questionnaire. After one month, a phone-visit recorded the results of the same questionnaires and we compared the results.

Results. 90% of the patients were females, and 60% of these patients were over the age of 60 years old. They were randomly assigned in one of the 2 groups, and we recorded the scores from these 2 questionnaires during the hospitalization. In group 2 we applied a personalized nursing intervention based on non-pharmaceutical approach, which involved a 30 minutes discussion with each of the 25 patients. After one month, patients from group 2 reported a significantly improved quality of life (evaluated by SF-36) compared with patients who only received standard nursing care ($p < 0.01$). The total score assessed by the CIVIQ-14 questionnaire was improved significantly after one month follow up in group 2 versus group 1 ($p < 0.01$).

Conclusion. The study showed that a personalized plan of nursing interventions added to the standard medical care during hospitalization significantly increased the quality of life in patients with CVI at 30 days after hospital discharge.

Newborn with intrauterine growth restriction - development in the first 6 months of life

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Introduction. Intrauterine growth restriction (IUGR) is, after prematurity, the second cause of perinatal mortality and is associated with an increased risk of perinatal complications. The cause is multifactorial including genetic mechanism, maternal and paternal factors, placental insufficiency.

Materials and methods. It is a prospective study, which evaluates the early morbidities and the growth rate in neonates with fetal ultrasound diagnosis with IUGR at the age of 1 month and 6 months.

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Result. We analyzed 40 newborns with RCIU at birth, 62.50% were female. The average gestational age was 35.83 ± 3.17 weeks. 80% were born through caesarean section. The predominant pregnancy pathology was preeclampsia 27.5%. The ideal growth rate was not respected in 88% of cases at 1 month and 17.33% respectively at 6 months. Significant differences were obtained by analyzing the breakdown by gender (female 28% vs male 60% $p = 0.046$) at the age of 1 month. The growth rate was different in those associating IUGR and prematurity compared with those who were born on time and just with IUGR. The number of days of weight gain from birth did not differ significantly for newborns with female IUGR compared to those of male gender. Analysis of the neurological evaluation showed that 22 of the newborns with IUGR had neurological disorders during the first 6 months of life. In the majority of cases (90.9%) neurological disorders were minor such as hypotonia and 2 cases showed a tendency for spastic development.

Conclusions. The ideal growth rate was not respected in 88% of cases at the age of 1 month and in 17.33% at 6 months respectively. In the majority of cases, neurological disorders were minor only 2 children showed a tendency for spastic development.

A retrospective study regarding the epidemiological characteristics of the non-small cell lung cancer patient

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Introduction. Pulmonary cancer has gained a top place in the cancer-related incidence and mortality worldwide and in our country in both sexes. The main risk factor is smoking, incriminated in over 80% of the cases and most frequently related to squamous histology. According to the literature, pulmonary cancer is diagnosed mostly in advanced stages at a median age of 70 years. After intense research, non-small cell lung cancer is considered molecularly heterogeneous due to the driver mutations which led to targeted therapy. Regarding the tumor, there has not yet been identified as a prognosis factor although the left and the right part are anatomically different. The aim of this study is to identify the characteristics of the non-small cell lung cancer patients, in order to identify the epidemiological trend and possible risk and prognosis factors.

Materials and methods. In this retrospective study we have included 243 patients diagnosed with non-small cell lung cancer from our Department between 2014 and 2019 by applying the inclusion and exclusion criteria.

Results. We have observed the predominance of male patients, urban living environment with the most affected age group 61-70 years. Most of the patients were diagnosed with adenocarcinoma stage IV (pulmonary) in the superior lobe and the predominance of the left side. According to the anamnesis, only 72 of the patients admitted smoking which is in concordance with the squamous histology identified and only 22 of the patients undergone professional exposure (dust, powder, steam). In our study we have also analyzed the associated pathologies of the patients and the molecular testing.

Conclusion. The parameters identified in our study help us to create the profile of the non-small cell lung cancer patient with its particularities. The epidemiological study represents the foundation of the further research activities and we consider that it can provide a background in non-small cell lung cancer domain.

Synovial and serum levels of Osteocalcin, Osteoprotegerin and β -crosslaps in patients with calcium pyrophosphate deposition disease

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Introduction. Calcium pyrophosphate deposition (CPPD) disease is defined by deposition of calcium pyrophosphate crystals in hyaline cartilage and fibrocartilage. The study of bone markers is of great interest in CPPD disease from different points of view. The aim is to measure synovial and serum levels of three bone turnover markers in patients with CPPD.

Materials and methods. Using ELISA kits, Osteocalcin, Osteoprotegerin and β -CrossLaps were measured in the serum and the synovial fluid of eight patients with CPPD disease in a pilot study.

Results. Synovial fluid Osteocalcin was lower than serum levels (2.1 ± 0.6 versus 9.21 ± 46 , $p=0.02$). Synovial fluid Osteoprotegerin levels were higher than the serum levels (55.5 ± 284 versus 8.44 ± 7 ; $p=0.0001$). β -CrossLaps in synovial fluid wasn't statistically different from the serum (6146 ± 66818 versus 6077 ± 12212 ; $p=0.5$). Ratios between synovial fluid and serum levels were 0.22 for Osteocalcin, 6.57 for Osteoprotegerin and 1.01 for β -CrossLaps.

Conclusions. Osteocalcin and Osteoprotegerin levels were significantly different in synovial fluid from the serum ones. β -CrossLaps had similar values in serum and synovial fluid.

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VACTERL association: from diagnosis to treatment through a series of pitfalls

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Background. VACTERL stands for vertebral defects, anal atresia, cardiac defects, tracheoesophageal fistula, renal anomalies, and limb abnormalities. Other features may include growth deficiencies and failure to thrive, facial asymmetry, external ear malformations, intestinal malrotation and genital anomalies. The objective of this case report is to highlight the difficulty of diagnosis and possible complication in management of complex malformation.

Case presentation. We present the case of a 10-weeks-old infant from twin pregnancy, born prematurely with C-section at 35 weeks of gestation, with 1890 g. His brother was diagnosed after birth with esophageal atresia and tracheoesophageal fistula but died after severe complication during surgery. Our infant with facial asymmetry and breathing problems was investigated in Pediatric ICU for poor feeding,

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excessive drooling, fast breathing, cough and intermittent bowel movement disorders (excessive bloating with constipation alternatively with watery stools). Based on the clinical, laboratory findings and a series of imagistic and invasive investigations we made a diagnosis of atrial septal defect, maintain the suspicion of tracheoesophageal fistula, excluded Pierre-Robin syndrome and other chromosomal disorders, cystic fibrosis, congenital infections. Due to bowel movement disorders he was suspected of Hirschsprung's disease. During surgical intervention the suspected tracheoesophageal fistula was identified and resolved; colostomy for segmental bowel resection has been done. The histologic examination excludes congenital aganglionic megacolon and the anal/rectal stenosis was attributed to VACTERL association. The clinical evolution was favorable with normal weight gain, but the infant underwent two more operations (removal of the esophageal patch and stoma reversal surgery).

Conclusion. Despite a wide range of diagnostic options for VACTERL described in the literature, the final diagnosis tool might be surgical exploration.

A rare association in the 21st century: *Shigella flexneri* enterocolitis and scabies in a severely malnourished infant

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Background. Shigellosis continues to be an important public health problem in developing and undeveloped countries. The disease is difficult to prevent, because only a small number of bacteria can cause illness. On the other hand, scabies is a contagious skin infection rare in newborns. The purpose of this clinical case report is to highlight the unusual association of two concomitant unlikely infection at a malnourished infant and a possible diagnostic pitfall.

Case presentation. We report the case of a 10-weeks-old premature infant brought in for multiple episodes of watery diarrhoea, fever and multiple disseminated cutaneous papulous lesions. At that time the infant was severely malnourished. Based on the clinical and laboratory findings a diagnostic of bacterial enterocolitis, hypoproteinemia, hypoalbuminemia, hyponatremia and severe anemia, complicated with septicemia was made. Because of the excoriated papules and family history (both siblings presented the same lesions) a high suspicion of scabies was made. We initiated treatment with intravenous antibiotics, iv fluids, anti-diarrheal medication, albumin and blood transfusion. After the isolation of *Shigella flexneri* from the stool culture, the patient was transferred in the Infectious Disease Department, where he received Ceftriaxone, iv fluids and Benzyl Benzoate for the cutaneous lesions. The patient's evolution was favorable with the partial remission of the diarrhoeal stools, cutaneous lesions. Due to the severe malnutrition the infant was afterwards transferred to the Dystrophic Department, where they suspected further cow's milk protein allergy and secondary lactase deficiency. After passing to a lactose free and extensive hydrolysed protein formula all symptoms disappeared and the infant gain weight.

Conclusions. This case illustrates the unlikely association of two rare infections in the 21st century at a malnourished infant and the overlap of symptoms between these infections and the cow's milk protein allergy.

Methylmalonic acid as a biomarker measured by NMR spectroscopy in the evaluation of B12 vitamine response in a potential lethal inborn error of metabolism

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Elevation of urinary methylmalonic acid (MMA) is found in a large number of monogenic mitochondrial disorders and non-genetic disorders such as nutritive cobalamin deficiencies. The most common monogenic cause of high MMA excretion is methylmalonyl-CoA mutase (MMUT) deficiency, that has an estimated incidence of ~ 1: 50,000. Patients present either shortly after birth with acute deterioration, metabolic acidosis and hyperammonemia (in severe forms), or later at any age with a more heterogeneous clinical picture, leading to early death or to severe neurological handicap in many survivors. Except for vitamin B12 responsive forms of deficiencies, the outcome remains poor, despite the existence of apparently effective therapy with a low protein diet and carnitine. Secondary MMUT deficiency may also be caused by deficient biosynthesis of its cofactor cobalamin.

We present the results of B12 vitamin response obtained for a child (that have been in acute decompensation with high MMA) using the NMR spectroscopy method. This evaluation included the i.m. loading test with hydroxocobalamin – 1 mg/day for one week, according to the international guidelines. The work-up in a stable metabolic state is with 1 mg hydroxocobalamin/day i.m. for several days and careful biochemical monitoring (urinary MMA should fail by >50%). In this case, homocysteine was not increased, and the urinary MMA values decreased from 113.5 mmol/molcreatinine to 36.2 (after 4 doses of hydroxocobalamin) and to 29.6 mmol/molcreatinine (after 7 doses), respectively. The molecular diagnostic is linked to a gene panel approach, several genes being known to be associated with isolated methylmalonic academia, but the B12 response should always be tested.

We outline the importance of biochemical genetics approach in metabolic decompensations linked to inborn errors of metabolism and the potential of urinary NMR-spectroscopy for diagnostic and evaluation of the response in a specific loading test.

Linking cell biology with monogenic diseases: revealing psychiatric manifestations in inborn errors of metabolism

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Inborn Errors of Metabolism (IEM) form a large group of disorders caused often by enzyme deficiencies with: (i) substrate accumulation (intoxication pattern), (ii) complex molecules defects or (iii) defects in energy production, causing impairment of one or several systems. Searching IEM that present as major psychiatric syndromes

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in both children and adults, we used the PubMed database for articles containing the keywords “inborn errors of metabolism” and “psychosis”, “anxiety”, “depression”, “psychiatric disorders” or “psychiatric manifestations”. We selected 8 landmark articles that were published between 2006-2018.

According to recent publications, psychiatric signs may be the first manifestations of an IEM; this may manifest as illness that alter brain function via main two neuropathological processes: 1. by altering neurodevelopment as progressive metabolic illness and 2. by disrupting brain function as acute/episodic illness (i.e. in hyperammonemias). Recent works point to relevant functions of purines, pyrimidines, lipids, and autophagy in the molecular mechanisms which regulate neuronal connectivity and brain growth. Altered neurodevelopment may disrupt long association cortico-cortical and cortico-subcortical fibers, compromising the ability to test reality, to regulate emotions and behavior. After the clinical evaluation, among specific blood tests (including ammonia level), imaging, a targeted biochemical and/or genetic test should be considered for a specific diagnosis.

Substrate reduction or enzyme replacement therapies, stimulation of transport and intracellular processing involving vitamins, chaperons, chelation treatment, etc. are used to treat several groups of IEM.

Lack of knowledge regarding the psychiatric manifestations of IEM may lead to serious misdiagnoses. Identifying the molecular defect in several psychiatric disorders is crucial in order to provide a potential disease-specific treatment before irreversible complications arise.

Cardiotoxicity associated with breast cancer chemotherapy

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Introduction. Chemotherapy in breast cancer patients results in cure or improved survival, but it may be associated with severe secondary effects. Whereas the anthracyclines may induce dilated cardiomyopathy with irreversible cardiac failure, the monoclonal antibodies - trastuzumab, may generate hypertension, arrhythmias, myocarditis, heart failure. Aromatase inhibitors (tamoxifen) may provoke pulmonary embolism and strokes, whereas the anti endothelial growth factors may generate thrombo-embolic and hemorrhagic episodes, or pulmonary edema.

Materials and methods. We evaluated the left ventricular systolic and diastolic performance, by transthoracic echocardiography and Doppler examination in 30 female patients with breast cancer, treated with anthracyclines. Systolic performance was documented by determining the volumetric ejection fraction, whereas the diastolic performance by measuring the diastolic transmitral flow index.

Results. We documented an altered left ventricular diastolic performance during and after cancer chemotherapy, in our patients. The systolic left ventricular performance was not significantly altered.

Conclusion. Antineoplastic chemotherapy with anthracyclines, in female patients with breast cancer significantly alters the left ventricular diastolic performance. These alterations may preclude the deterioration of the left ventricular systolic performance with associated signs of dilated cardiomyopathy.

The value of shear wave elastography in the evaluation of primary Sjogren syndrome and diagnosis of parotid lymphoma complication

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Objectives. Ultrasonography is the preferred imaging method for investigating patients with primary Sjogren syndrome (pSS), as grey scale modifications were recently defined and quantified. Shear wave elastography (SWE) is considered to be a user-independent ultrasonographic method for tissue stiffness. Non-Hodgkin lymphoma (NHL) represents the most frequent complication of pSS patients, and in spite of the well-established clinical and biological criteria, early diagnosis is still difficult. The aim of this study is to evaluate parotid stiffness using 2D-SWE technique and to determine the contribution of this technique to the diagnosis of pSS and NHL.

Materials and methods. In this prospective, transversal study were included 35 patients with pSS and 35 healthy patients. All of the patients were evaluated by 2 independent examiners. NHL was confirmed by US guided echography or surgical removal.

Results. Positive diagnosis of pSS was established in 88.57% of cases by using grey scale US parameters, with a cut-off of 5 points. SWE was able to identify stiffer parenchyma of the parotid glands in comparison with healthy subjects ($p < 0.001$). A cut-off value of 6.45 kPa increased the number of diagnosed patients to 94.28%. Eight patients with pSS were diagnosed with MALT type NHL of the parotid glands. In these particular cases the area and the stiffness of the parenchyma were higher than the rest of the patients with pSS ($p < 0.001$). Applying a score which includes clinical swollen parotid glands, area of the parotid, US score, presence of hyperechoic bands, the size of the largest hypoechoic area and the stiffness, allows the detection of parotid lymphoma with a sensitivity of 92.3%, specificity 100%, positive predictive value 98.3% and negative predictive value 100%, if the score is higher than 4.

Conclusions. SWE is a useful tool not only for increasing the sensibility of pSS diagnosis, but more importantly for the detection of parotid NHL.

Pediatric autoimmune liver disease - case report

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Introduction. Pediatric autoimmune liver disease is a hepatic inflammatory process characterized by hepatic cytolysis, circulating autoantibodies and/or increased levels of IgG. Three liver disorders present autoimmune mechanism: autoimmune hepatitis (AIH), autoimmune sclerosing cholangitis (ASC) and de-novo AIH post-liver transplantation. ASC has often the same features with AIH, the diagnostic being possible only based on the cholangiography.

Case-report. We report the case of a 5-year-old female patient, who was transferred to our hospital for elevated serum aminotransaminase levels and cholestasis.

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A few weeks before, she was admitted to the Infectious Diseases Hospital for jaundice, and the laboratory tests revealed increased transaminases, cholestasis, a low prothrombin index, high levels of IgG and mild thrombocytopenia. The serology was negative for EBV, CMV, HIV, HSV, HBV and HCV. At admission in our service she presented jaundice and hepato-splenomegaly. The laboratory findings showed also reduced cholinesterase levels, positive antinuclear antibodies (ANA), other autoantibodies being negatives. The transient elastography indicated elevated liver stiffness, corresponding to F4 fibrosis stage and the endoscopy showed no esophageal varices. Given the presence of cholestasis, MRCP was performed, showing mural irregularities of the intrahepatic biliary ducts, typical lesions for sclerosing cholangitis. The final diagnostic was type 1 AIH-related liver cirrhosis, associated with ASC. The treatment with ursodeoxycholic acid and prednisone was started, resulting in lower transaminase levels, but still not within the normal limits.

Conclusions. The specific feature of this case is the overlap syndrome between type 1 AIH and ASC. In such cases the progress towards liver cirrhosis is faster, therefore it is important to check for bile duct lesions when diagnosing an AIH with associated cholestasis.

Sleep disorders and pruritus affect the quality of life in hemodialysis patients

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Introduction. Pruritus and insomnia are common disorders in hemodialysis (HD) patients. Both have a major clinical impact as they are associated with poor quality of life and increased mortality. Pruritus affects up to 40% of end-stage renal disease patients, while sleep disorders are experienced by approximately 50%-75% of HD patients. However, their coexistence and impact on survival in HD patients have rarely been investigated.

Materials and methods. This study focused on comparing the survival of HD patients with both pruritus and insomnia versus HD patients with insomnia or pruritus only and versus HD patients without these complaints. It also compared clinical and laboratory features between these 4 groups of HD patients. After the inclusion/exclusion criteria, 170 patients treated by HD or on-line hemodiafiltration were assigned in 4 study groups. We analyzed the survival difference between groups after 20 months and we searched if there were significant differences in terms of clinical and laboratory features: age, dialysis vintage, body mass index, dialysis type, vascular access type, hemoglobin, albumin, C-reactive protein (CRP), Daugirdas single-pool Kt/V, ultrafiltration volume (UF), blood processed volume, transferrin saturation (TSAT), ferritin, calcium and phosphate.

Results. Survival at 20 months was lower in patients with both pruritus and insomnia. This study also shows that haemoglobin and albumin are statistically significant prognostic factors for better survival. Patients with pruritus and no insomnia had a lower Kt/V than those with no complaints or insomnia alone. Those with no complaints had lower C-reactive protein and higher albumin levels than patients with insomnia alone or both conditions.

Conclusion. Sleep disorders and pruritus should be actively investigated in patients undergoing hemodialysis and correlated with some clinical and laboratory features, as they represent important prognostic factors with an impact upon survival.

The ankle, hindfoot and heel ultrasonographic findings – predictors for the pain and low quality of life in rheumatoid arthritis patients

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Introduction. In rheumatoid arthritis (RA), foot involvement occurs from the early stages and results in deformities with impact on the patients' quality of life (QoL). However, clinicians neglect foot evaluations, because the disease activity measuring tools omit it. Aim: evaluation of clinical, ultrasonographic (US) and baropodometric changes of the ankle, hindfoot and heel, responsible for the pain and poor QoL in RA.

Materials and methods. The ankle [tendons and tibio-talar joint (TT)], hindfoot [talonavicular and subtalar (ST) joint] and heel of 35 RA patients and 35 healthy control (HC) were evaluated using physical examination, Disease Activity Score 28-Joints count with C-reactive protein (DAS28-CRP), Routine Assessment of Patient Index Data 3 (RAPID3) for functional status, Rheumatoid Arthritis Quality of Life (RAQoL) questionnaire, ultrasound (US) and baropodometry.

Results. The US inter-observer agreement was good for ST joint and very good for the other examined structures. US-visible ankle and hindfoot synovitis, erosions, tenosynovitis, and heel modifications were more frequent in RA patients than in HC. The flat foot was present at physical examination in 50% of the examined feet of the RA patients, 83.3% of these simultaneously having hindfoot valgus with ST joint synovitis, less visible from lateral approach (32.4% vs 55.6%, $p=0.041$). Body mass index, RAPID3 and ST synovitis were found to be independent predictors for the ankle pain ($p<0.05$). RA patient had higher midfoot and heel plantar pressures than HC, but in the presence of ST joint synovitis they were lower (heel support avoidance). The poor QoL of RA patients was independently predicted by DAS28-CRP, RAPID3, disease stage, hindfoot valgus, TT and ST synovitis, tendinopathy, enthesophytes, calcaneal erosions, plantar fasciitis ($p<0.05$).

Conclusion. The ankle, hindfoot, and heel US findings do predict the ankle pain and significantly influence the QoL of RA patients.

How big is the gap between guidelines and clinical practice in antimicrobial therapy? Gastrointestinal vs. respiratory infections

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Background. Infectious diseases are the most common health problem of childhood. Although most of them are sole viral infections, there is a significant number of mixed viral-bacterial and sole bacterial infections. As a result, antibiotics are among the most common drugs prescribed to children. The study aimed to assess to what extent the way antibiotics are prescribed in a hospital is consistent with the existing guides.

Methods. 253 patients were included in the study, divided into 2 categories:

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children with gastrointestinal and respiratory infections. We evaluated the pattern of administration, duration and class of antibiotics used, and finally we compared them with the recommendation in the existing guidelines.

Results. 100 children with acute diarrhea were included into 3 categories: viral gastroenteritis (30%), bacterial (12%) and unspecified (in which the etiology could not be determinate). From the last category, 24% (those with inflammatory syndrome) received antibiotics (50% third-generation cephalosporin, TGC), the rest second-generation cephalosporin (SGC) or sulfonamide. 92% of children with bacterial enterocolitis received antibacterial treatment (48% TGC, the rest SGC, macrolides or polymyxin). Children with respiratory infection (153) were admitted with pneumonia (32.7%), bronchiolitis (22.3%) and upper respiratory tract infections, URTI (45%, pharyngitis, tonsillitis and laryngitis). 92% of the patients with pneumonia received antibiotics (65% TGC, the rest SGC, or association of cephalosporin with aminoglycosides). 29% of the children with bronchiolitis (70% SGC) and 59% of URTI were also treated with antibiotics.

Conclusions. Antibacterial use is generally correlated with the confirmation of bacterial etiology or with the presence of the inflammatory syndrome. The most used antibiotics are TGC and SGC. The classes of antibiotics were chosen according to guidelines in case of respiratory infections but differ in case of acute diarrhea.

Heart function monitoring in a rat model of heart failure associated with obesity

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Introduction. Nowadays, obesity has become a prevalent pathology, especially in the developed world and is associated with the activation of numerous pathophysiologic mechanisms which may lead to cardiovascular diseases. The aim of our study was to assess cardiac function in a rat model of heart failure and obesity.

Materials and methods. Sprague-Dawley male rats (wild type, WT, n=24) were either fed with standard diet (WT+SD, n=12) or with hypercaloric diet (SD+HD, n=12). Transgenic rats overexpressing β_3 -adrenergic receptors in endothelial cells (TG β_3 , n=24) were also divided into 2 groups: receiving standard diet (TG β_3 +SD, n=12) and receiving hypercaloric diet (TG β_3 +HD, n=12). For 35 weeks body-weight (BW), feed and water consumption, systolic blood pressure (SBP), echocardiographic structural and functional parameters were monitored.

Results. HD induced an increase in BW in HD groups (~10.08% for WT and ~10.45% for TG β_3) since week 8 (W8), trend maintained until the end of the study (~19.42% for WT and ~20.59% for TG β_3). Regardless of WT or TG β_3 status, SBP (mmHg) was significantly increased by HD (~12%), as measured at W35. Also, a decrease in early-to-late filing ratio (E/A ratio) in TG β_3 +HD vs. TG β_3 +SD was observed (0.97±0.04 vs 1.09±0.07) starting with W25, while for WT+HD vs. WT+SD, reduction occurred at W35 (0.99±0.06 vs 1.25±0.05). E'/A' ratio followed the same trend, at W25: TG β_3 +HD vs. TG β_3 +SD (0.93±0.05 vs 1.07±0.05), at W35: WT+HD vs. WT+SD (0.99±0.06 vs 1.19±0.04). At W35, no significant change was registered in ejection fraction (%) between all groups (~63%), suggesting no systolic dysfunction at this timepoint.

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Conclusions. Alteration of the diastolic function occurs at around W35 in obese WT rats, whereas in obese TGβ3 rats diastolic function alteration occurred earlier (W25).

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Neutrophil to lymphocyte ratio among overweight or obese children

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Introduction. Obesity is characterized by a pro-inflammatory state which plays an important role in the onset of multiple comorbidities. Neutrophil-to-lymphocyte ratio (NLR) was found to be a good indicator of infectious or inflammatory conditions. We aimed to evaluate the relationship between NLR and anthropometric indicators in obese and overweight children.

Materials and methods. The medical charts of overweight and obese children age from 2 to 18 years who were evaluated from January 2017 to December 2018 in one Endocrinological Ambulatory Center from Cluj-Napoca, Romania were reviewed. Data regarding anthropometric characteristics and neutrophils and lymphocytes blood levels were retrieved. The AnthroPlus application v1.0.4 was used to compute the Z-scores and percentiles for BMI-for-age, height-for-age and weight-for-age according with WHO criteria.

Results. Out of one hundred and one overweight or obese children addressed from January 2017 to December 2018 to our center, sixty-four children (63%) aged from 2 to 18 years old, 32 girls and 32 boys, were included in the analysis. The majority of children were pre-adolescents (54.7%), followed by adolescents (39.1%), without significant difference in gender (Fisher exact test: P-value = 0.5779). The Z-score of the body mass index-for-age proved statistically significant higher for boys (median = 2.79, IQR = (2.33 to 3.10) compared to girls (median = 2.05, IQR = (1.76 to 2.88)) (Mann-Whitney test: P-value= 0.0185). The NLR varied from 0.45 to 4.76 with a median of 1.39 and without significant differences across gender groups (Mann-Whitney test: P-value= 0.9411).

Conclusion. NLR was not associated with body mass index-for-age, nor to other anthropometric measures and did not change between genders. The NLR values range we found was higher than reported value range in obese adolescents (1.33 and 0.53). Relation with inflammatory biomarkers in obesity may be further investigated.

Paraoxonase 1 serum concentration and PON1 gene polymorphisms in patients with non-alcoholic steatohepatitis

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Background. Non-alcoholic steatohepatitis (NASH) is a part of a liver condition known as Non-alcoholic fatty liver disease (NAFLD), which became the number one cause of liver impairment in the world. Paraoxonase 1 (PON1) is an enzyme that exerts an important antioxidant role. The aim of the study was to examine the PON1 gene polymorphisms role as a risk factor for NASH.

Materials and methods. We studied a group of 81 patients diagnosed with NASH and a group of 81 patients without liver diseases (controls). In each patient, we collected clinical information, performed routine blood tests, and measured the serum concentration of PON1 using ELISA kits. By using the PCR-RFLP method, we also evaluated the PON1 gene polymorphisms L55M, Q192R, and C-108T.

Results. We observed a statistically significant difference ($p < 0.001$) between the PON1 serum concentration in the NASH group compared to the control group. A statistically significant variability between groups was observed only for the L55M polymorphism. Thus, the variant LM was observed in 58% of the patients in the NASH group and in 33.3% of the patients in the control group ($p = 0.002$). A multivariate binary logistic regression showed that the only variables independently linked to NASH were the BMI ($p < 0.001$) and LM+MM genotypes of the L55M polymorphism ($p = 0.04$). In a multivariate linear regression model created to identify the variables which influenced the PON1 concentration, we found that only the presence of NASH was associated with PON1 concentration ($p < 0.001$).

Conclusions. PON1 concentration is diminished in patients with NASH compared to subjects without NASH. The LM+MM genotypes of the L55M polymorphism were an independent predictor for NASH, while NASH was the only variable linked with the PON1 concentration. These findings could help for the incorporation of these parameters in a non-invasive score able to detect NASH without the need for a liver biopsy.

SURGICAL SPECIALTIES

Transperitoneal versus extraperitoneal approach in laparoscopic radical prostatectomy depending on risk group

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Introduction. Radical prostatectomy remains the main treatment option for patients with localized prostate cancer. The highest mortality rate among European countries is found in the eastern countries, thus in many situations a proper evaluation for choosing the best option between transperitoneal (TP) and extraperitoneal (EP) approach is needed. Extended lymph node dissection is required in patients with high-risk prostate cancer.

Materials and methods. We retrospectively reviewed 42 cases of radical prostatectomy performed by a single surgeon in our department 18 of which underwent (TP) approach and extended lymph node dissection, respectively 24 with (EP) approach and standard lymph node dissection. All cases were preoperatively evaluated and the best surgical approach being was chosen in each case. All patients underwent 3D laparoscopic radical prostatectomy with 5 trocar setting, using 5mm LigaSure™, titan clips and scissor for dissection and monofilament fast resorbable thread for the anastomoses.

Results. Pre-, intra- and post operatory data was gathered from each case, including complications. No major complications accrued that required conversion. (TP) vs (EP) approach results consisted of: mean operating time 171 vs 132 minutes, mean blood loss 250 vs 260 ml, bowel movement resumption 55 vs 22 hours, hospital stay 7 vs 4.7 days and mean excised lymph node 13.4 vs 9.5. Four patients that underwent the (EP) approach presented with lymphoceles of which 3 were percutaneously drained and one was laparoscopically fenestrated due to its position regarding the intestines.

Conclusions. (TP) approach can be opted in cases of high-risk prostate cancer for extended lymph node dissection, having lower risk of lymphoceles but high long-term complications, whereas (EP) approach is the desired option in low-risk prostate cancer for offering a shorter surgery intervention and hospital stay, early bowel resumption but a higher risk of lymphocele.

Secondary retroperitoneal fibrosis after radical hysterectomy and radiotherapy treatment by 3D laparoscopic surgery

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Introduction. Retroperitoneal fibrosis is a rare pathology, described by the presence of retroperitoneal tissue with chronic inflammation and fibrosis, which can, many times, incorporate the ureters and other abdominal organs. In 70 percent of cases it presents as an idiopathic form (known as Ormond disease). The secondary form has been reported after malignancies, infections or medication. Women can develop this pathology following surgical and radiotherapy treatment for cervical cancer, with obstructive repercussions to the upper urinary system. We evaluated the minimally invasive surgery

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by 3D laparoscopic approach in treating patients with cervix cancer that developed retroperitoneal fibrosis after surgery and radiotherapy.

Materials and methods. We analyzed the cases treated by one surgeon in the Urology Department of the Oncology Institute “Ion Chiricuță” of Cluj-Napoca, between January 2018- October 2019 using the 3D laparoscopic transperitoneal approach by 4 trocars manner. In two cases unilateral ureterolysis and reimplantation was performed, two cases required bilateral reimplantation and for one patient ureterolysis was done.

Results. Mean operative time was 155 minutes, and intraoperative blood loss was 240 ml. Patients had early postoperative mobilization. Mean hospital stay was 6.8 days. Urinary bladder catheterization was maintained for 14 days. Double-pigtail ureteral stents were extracted after 12 weeks.

Conclusion. 3D Laparoscopy as minimally invasive procedure for patients previously treated for cervix cancer by surgery and radiotherapy that have developed retroperitoneal fibrosis is a safe option in resolving the obstructive urinary complications of this pathologies.

The role of endoscopic nasal surgery in oral surgery rehabilitation

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Introduction. Dental implants and the reconstruction of the sinus floor occupies an important part of dental pathology. Rhino-sinusal land preparation is very important for the increased rate of success of oral rehabilitation works.

Material and methods. Presentation of clinical cases with rhino-sinusal pathology (cysts, mucocoele, concha bullosa, maxillary sinusitis, nasal polyps) and solving them minimally invasively through FESS, but with increasing success rate of subsequent dental work; the authors intend to highlight the risks and complications associated rhino-sinusal in the absence of pathology solving.

Conclusions. Making implantology and reconstruction works Floor sinus (sinus lift) require careful preparation and prior solving problems associated rhino-sinusal through minimally Techniques type FESS.

Intracranial vascular malformations at the pediatric age – our experience

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Introduction. Intracranial vascular malformations (VMs) represent a rare and potentially debilitating pathology. Arteriovenous malformations (AVMs) are the most frequent cause of hemorrhagic stroke in the young population. Hemorrhage from cavernous malformations (CMs) can result neurological deficit, being especially life-threatening within the brainstem. We present the experience of a single surgeon over the course of 11 years in the neurosurgical management of pediatric intracranial VMs.

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Material and methods. We performed a retrospective study on the case series of VMs in pediatric patients operated in our department in the last 11 years by the senior neurosurgeon. There were 22 patients in the AVM group and 9 in the CM group.

Results. Mean age was 15.08 years in the AVM group and 10.12 years in the CM group. 13 (59%) of AVMs presented with hemorrhage. 6 (44.4%) of CMs presented with hemorrhagic stroke, and 3 with epilepsy. From the AVM group, 1 patient (4.5%) presented with grade I and another patient (4.5%) with grade V, 9 (41%) with II, 7 (32%) with III, and 4 (18%) with IV. 3 AVM patients admitted with massive intracranial hemorrhage and comatose were lost, while the rest were discharged with a favorable outcome. There was no mortality within the CM group.

Conclusions. Intracranial VMs in the pediatric age can be safely and successfully treated via microsurgery. State of consciousness upon admission and presence of hemorrhage are the most decisive factors under the same morphological conditions of VMs and surgical team experience.

Total thyroidectomy and parathyroid glands in thyroid surgery

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Introduction. Transient or persistent hypocalcaemia can occur after total thyroidectomy. 24h postoperative PTH low values are studied as predictive for long term evolution of hypocalcaemia. Detached parathyroid reimplantation in subhyoidian muscles is thought to lower hypothyroidism risk.

Material and method. 96 patients with total thyroidectomy for benign disease were followed up for 2 years focusing on operative technique, clinical signs of hypocalcaemia, pre and postoperative data of Calcium and PTH value.

Results. No clinical signs of hypocalcaemia occurred in 57.29% of cases even though 65.45% of them registered immediate decrease of PTH; 31.25% were noticed with transient decrease of serum calcium but only 33.33% of them had clinical signs; 11.45% presented with 2 months Calcium and PTH decrease, but only 3.12% were persistent after 2 years. No statistical significant relationship was found between low 25h postoperative values and long term evolution of hypocalcaemia. Subhyoidian muscle reimplantation of detached parathyroid glands were carried out in 20 patients because of technical reasons. Persistent hypocalcaemia disappeared in these patients and transient hypocalcaemia lowered significantly by maintaining higher 2 months postoperative levels of PTH.

Conclusions. Careful dissection of the rear part of thyroid lobes in total thyroidectomy as well as subhyoidian muscle reimplantation of accidentally detached parathyroid glands significantly improves on persistent hypocalcaemia. 24h PTH observation did not predict any long term result.

Primary jejunal adenocarcinoma - case report

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Introduction. In this case report, we will see an unusual presentation of proximal jejunum neoplasm that was hiding under an anemia iron deficiency, loss of appetite and weight loss for more than 1 year that invaded the mesentery, mesocolon transverse and transverse colon.

Material and method. A 54 year old male presented on 15 Nov 2015 with the diagnosis of secondary iron anemia for over 1 year and a small bowel tumor that bleed, the diagnosis was based on CT exam. Over the past year, the patient followed more treatments for his iron deficiency, PPI, prokinetics, but without a positive result. He also had 2 gastroscopy and 2 total colonoscopy that showed internal hemorrhoids and an average axial hiatal hernia. Associated with these symptoms, the patient had asthma and high blood pressure. The clinical examination showed mucocutaneous pale, with no other changes. Laboratory tests showed iron anemia (Hb - 9.9 g/dl, Ht - 32.8%, Iron - 25 microg/dl), leukocytosis (17,600/mm³), reactive thrombocytosis (700,000/mm³), a nonspecific inflammatory syndrome (VSH - 57 mm/h, PCR - 24) and hypercholesterolemia (236 mg/dl). The ACE marker was normal - 0.59 ng/ml, also the LDH - 198UI/L. The surgery, was performed in November, under general anesthesia, it was an enterectomy segmental of jejunum (50 cm) with entero-enteral anastomosis terminal-terminalis, segmental resection of transverse colon, anastomosis colo=colic terminal-terminalis procedures.

Results. Postoperative evolution was favorable. The definitive pathological examination revealed a tubular adenocarcinoma G2 pT4N0MxL1V0.

Conclusions. The management of this case is an ongoing process, the patient is having adjuvant chemotherapy with XELOX protocol (IV cycles). Performing an oncologic surgery can be the best outcome in patients with nonmetastatic disease. Primary adenocarcinoma of the small bowel is a rare malignancy that challenges physicians in both diagnosis and treatment.

Exaggerated placental site - a rare finding in gynecological practice

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Exaggerated placental site is a form of intermediate trophoblast, a benign lesion, characterized by an extensive infiltration of the endometrium, myometrium and arterial walls. An intermediate trophoblast is a distinctive trophoblastic cell population from which four trophoblastic lesions are thought to arise, exaggerated placental site (EPS), placental site nodule (PSN), placental site trophoblastic tumor (PSTT), and epithelioid trophoblastic tumor (ETT). EPS can occur following normal or ectopic pregnancy, abortion (it is seen in 1.6% of first trimester abortions but can also occur after full term pregnancy), or hydatiform mole. Rarely, it can cause life threatening hemorrhage. We report a case of 21-year-old patient (3G1P) with multiples episodes of uterine bleeding

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after a drug-induced abortion for a intrauterine fetal demise (IUFD), followed by a uterine curettage. In an interval of four weeks, between 6th and 10th week after abortion, the patient has presented three times to different medical facilities with severe vaginal bleeding, for which repeated curettages have been performed. Considering repeated hemorrhagic episodes with the appearance of massive life threatening bleeding, surgical treatment is decided and subtotal hysterectomy is performed. The morphopathological study reports an exaggerated placental site.

A microscopic study of nerve and ganglia distribution within the human female bladder trigone

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Introduction. The nerve fibers emerging from the spinal roots that are responsible for micturition have been described macroscopically, but the microscopic characterization of their distribution within the bladder wall is not clearly documented. This information could be useful when performing minimally invasive interventions for refractory overactive bladder, such as intravesical botulinum toxin injections, sacral neuromodulation or percutaneous tibial nerve stimulation. The purpose of this study was to report the nerve and ganglia densities in the human bladder, with a focus on identifying areas with a higher density.

Material and methods. Three fresh, frozen human female urinary bladders were obtained from our University's Department of Morphological Sciences, in accordance with the ethical and legal requirements. Following tissue processing and slides staining with haematoxylin eosin, S100 and CD56, a total of 100 slides were analyzed. The density of the nerve fibers (NFD) and ganglia (GD) in different areas of the bladder trigone were calculated.

Results. The NFD in the central compartment was significantly higher than in the peripheral ($p=0.0005$) as well as in the intermediary ($p=0.01$) compartment. The GD was the highest in the peripheral compartment, followed by the central and intermediary compartment, respectively. However, there was no significant difference at the multiple comparison between these compartments.

Conclusions. The microscopic study of nerve structures within the female bladder trigone showed a distribution pattern with a dominance of nerve fibers in the central compartment and a rather homogenous distribution of the ganglia.

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Are medical students interested in disaster medicine education?

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Introduction. Considering the dynamics of modern society, man-made or nature-inflicted disasters have marked the recent decades and triggered international response initiatives to alleviate these burdensome situations. Medical students (MS) represent a valuable resource in disasters, if awareness and introductory training are provided, such as the International Training on Disaster Medicine (ITDM). Nonetheless, most European medical universities do not include DM training within their bachelor curricula. The aim of our observational study is to document MS's interest in disaster medicine education and generate appropriate learning contexts.

Material and methods. A survey is currently conducted among the 6th year medical students of Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca at the end of their Emergency Medicine rotation. The questionnaire collects data about the students' previous training/ experience in DM, as well as their educational and professional interest in DM. Their responses consist of numbers on a scale (from 1 to 5), as well as multiple choice answers.

Results. Approximately 600 MS will be offered the possibility of enrolling in the survey. Data will be analyzed in order to obtain the interest percentage along with the current knowledge level of the students. A proposal list will be consequently drafted, in order to enhance the DM professionalization process.

Conclusion. Worldwide, MS present a genuine interest in disaster medicine. Our experience from ITDM Cluj supports this statement, as 92 applications were registered for 40 training vacancies. Trained MS can contribute to a competent and qualitative response action in natural and humanitarian crisis. We speculate that MS would benefit from a DM course and hands-on application as part of their standard bachelor curricula. Means such as peer-to-peer education, table-top and manikin simulations can be employed inexpensively.

Perioperative neutrophil-to-lymphocyte ratio in Klatskin tumors

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Introduction. Klatskin tumor is a cholangiocarcinoma situated at the biliary three confluence in the liver hilum. We aimed to evaluate the changes in the neutrophil-to-lymphocyte ratio (NLR) at baseline (before intervention) compared to early post-intervention.

Material and methods. A cohort study was conducted on patients with Klatskin tumors hospitalized at the "Prof. Dr. Octavian Fodor" Regional Institute of Gastroenterology and Hepatology, Surgery Department Cluj-Napoca, Romania from 1 January 2012 to 31 December 2018. The patients' medical charts were reviewed and demographic (age, gender), the type of intervention, and laboratory data (namely neutrophils and lymphocytes) were collected. Only patients with all data of interest available at baseline and follow-up were included in the study. The cohort was split into two groups according to the eligibility for resection (group 1) or palliative intervention (group 2).

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Results. Forty-seven patients out of 57 patients with Klatskin tumors had all laboratory measurements and were included in the analysis. The age of the patients included in the study varied from 39 to 79, with a mean age of 63.83 ± 8.17 years. The male/female ratio was almost 2:1 (31/16). Twenty three patients had surgical resection of the tumor. No significant differences between groups were identified regarding age, neutrophils, lymphocytes, and NLR (both baseline and follow-up) (Mann-Whitney test: $P\text{-value} > 0.12$). A significantly higher percentage of patient with paleative intervention had baseline $NLR \geq 6$ as compared to those with surgical resection (41.7% vs. 13.0%; Chi-square test: $P=0.028$). Statistically significant post-intervention increases, regardless the group, were observed for neutrophils (Wilcoxon Matched test: $P<0.011$) and NLR ($P<0.04$).

Conclusion. A significantly higher percentage of patients with inoperable Klatskin tumors have NLR above six at the presentation. NLR significantly increases after intervention in both groups.

Minimally invasive approach by 3D laparoscopy salvage radical cystectomy for recurrent bladder cancer after radiotherapy and chemotherapy

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Introduction. Open radical cystectomy and pelvic lymphadenectomy is the standard treatment for locally advanced muscle invasive bladder carcinoma. In selected patients, organ preservation is tempted by choosing a multi-modality therapy. However, there is a 30% percent malignancy recurrence, mostly in the first year after treatment, that requires performing salvage cystectomy. This surgical intervention has higher complication rates. Our objective was to assess the feasibility of laparoscopic 3D transperitoneal cystectomy as salvage treatment for recurrent bladder cancer after multi-modal therapy.

Material and method. We present 2 cases treated by one surgeon in the Urology Department of the Oncology Institute "Ion Chiricuță" of Cluj-Napoca. The patients were both male, with ages of 48 and 61 years. They had both previously received radiation and chemotherapeutic treatment after being diagnosed with muscle invasive bladder cancer and were readmitted with malignancy recurrence.

Results. 3D laparoscopic cystoprostatectomy and lymphadenectomy was performed by transperitoneal approach, using 5 trocars placed in standard position. The surgeries lasted for 230 minutes and 240 minutes, with a mean blood loss of 250 ml. There was one intraoperative complication represented by injured right external iliac vein resolved by suturing. Two drain tubes were placed at the end of the surgery. Urinary drainage was done by bilateral cutaneous ureterostomy in the iliac fossae. Bowel movement resumed after day 4 and 5, and drain tubes were suppressed in day 4 and 5 respectively. Histopathological exams showed pT3bN0MxL1V0 with 8 metastatic-free lymph nodes and pT4aN0(0/5)MxL1V1R1 with 5 metastatic-free lymph nodes.

Conclusion. 3D Laparoscopic approach for salvage cysto-prostatectomy is a safe procedure and can be a choice option for patients treated in highly experienced laparoscopy centers.

Tailgut cyst – a gynecologist’s pitfall: case report and literature review

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Retrorectal cystic hamartomas (“Tailgut cysts”) are rare developmental cysts that appear in the retrorectal space, arising from aberrant remnants of the post-anal primitive gut in case of an incomplete embryogenetic involution. We present the case of a 30-year-old woman with a history of chronic lower abdominal pain. Other digestive symptoms, like rectal fullness, constipation, pain on defecation, rectal bleeding or genitourinary obstruction symptoms were not associated. During a period of 3 years she had undergone several surgical procedures for ovarian cysts, without relieving the symptomatology. CT scan showed a presacral tumor with a right pararectal development. A surgical resection of the lesion using an anterior approach was performed, with the final pathological diagnosis of a retrorectal cystic hamartoma (“tailgut cyst”). This case underlines the fact that retrorectal masses can be challenging to diagnose and tailgut cysts must be taken into consideration in cases of perirectal tumors at patients with a history of multiple failed procedures and surgeries.

Risk factors for cervical spine injury in patients with traumatic brain injury

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Introduction. In patients with altered mental status due to moderate to severe Traumatic Brain Injury (TBI), identifying a Cervical Spine Injury (CSI) is frequently difficult. The incidence and severity of the CSI increase with the severity of the TBI. This study aims to identify the incidence and risk factors that indicate the association between CSI and TBI.

Material and methods. This retrospective observational study included consecutive TBI patients who also suffered a CSI and underwent evaluation in the Emergency Department of Cluj-Napoca, over a 12-months period (Jan. to Dec. 2018). All these patients were examined using X-rays or CT scans to evaluate the head and spine injuries. Data was collected on age, gender, injury mechanism, Glasgow Coma Scale (GCS) and the presence of other injuries.

Results. 3.650 TBI patients were identified, of which 102 were diagnosed with a concomitant CSI (3%). There were 72 (70.6%) male patients and 30 (29.4%) female patients, whose ages ranged from 18 to 93 years (mean age, 55 years). Regarding the mechanism of injury, most common cause was road traffic accidents - 40 (39.2%), especially in male drivers and pedestrians >55 years old. Other mechanisms included falls >1 m - 32 (31.4%), falls <1m - 24 (23.5%) and assault - 6 (5.9%). According to the initial GCS, the patients were grouped into 3 categories: GCS 15 – 57.8% patients, GCS 14-9 – 28.4% and GCS ≤8 - 13.8%. 14% of patients with an initial GCS score ≤14 were hypotensive. The most common cervical lesions were fractures 74.5% and subluxations 18.6%, especially located at C1 (19%) and C2 (25%). In patients with TBI and systemic lesions in the upper half of the body, (chest trauma 51%, facial fractures 24.5% and upper limb fractures 13.5%) CSI were commonly associated.

Conclusion. For patients with TBI, the identification of risk factors, the correct assessment of GCS and systemic lesions can help the physicians to accurately diagnose a CSI.

Anatomical, imaging and endoscopic aspects of the sheep head - similarities and differences with the human head

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Introduction. Surgical training in FESS depends on the existence and access to equipped laboratories where endoscopic dissection can be performed on cadaveric heads, but limiting the procurement of cadavers for medical, ethical and moral reasons points to the search for an alternative by implementing an anatomical model accessible with anatomical elements similar to the human skull. For this purpose, methods of reducing the learning curve were sought, the sheep head being proposed as an anatomical ex vivo model, but with limited and reduced number studies in the literature. Through this study we want to implement as anatomical model the sheep head for training in functional endoscopic sinus surgery, starting from the ex vivo anatomical study of the sheep head from an endoscopic and imagistic point of view to the implementation in the surgical training of the debutants.

Material and methods. We performed dissection of 5 freshly preserved sheep heads (10 nostrils) with anatomic and endoscopic aspects and analysis of 5 CT examinations in axial, sagittal and coronal incidents performed on sheep heads.

Results. Highlighting the specific rhinosinusal anatomical elements of the sheep head with the possible particularities that will be determined by the measurement and the statistical analysis of the specified distances.

Conclusion. Similar data from the literature are missing or limited, which is why this study should have a decisive role in the implementation of anatomical model of sheep head for preparation in functional endoscopic sinus surgery in our country, considering the accessibility, reliability, viability of the sheep head and very good results obtained from its use.

Deep neck space infections - case series

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Introduction. Deep neck space infections represent a possible life threatening condition involving the virtual spaces of the neck and fascial planes. A rapid and accurate diagnosis is vital and implies determining the origin and the extension of the infection. The purpose of the study was to present a series of eight cases from diagnosis to management.

Methods. We present a series of eight cases treated in the ENT Department of Cluj-Napoca County Emergency Hospital. Patients were admitted between January 2019 and March 2019 and were either transferred from tertiary centers or presented directly to our department. The parameters taken into consideration were demographics, symptoms, imagistic evaluation, spread of the infection, management and hospitalization costs.

Results. All eight patients were evaluated by CT scans to assess the deep tissue spread of the infection. The majority of patients came from urban areas. Youngest patient was 5 years old and the oldest 82 years old. Etiology could not be determined in all instances. We reported three patients with Ludwig's angina, one case of phlegmonous adenitis, one case of necrotizing fasciitis with mediastinal spread, one case of lateropharyngeal cellulitis-phlegmon and one case of posterior neck phlegmon. All cases needed surgical intervention and sample from the wound was obtained for antibiogram. All cases had favorable evolution except the one case with mediastinal involvement.

Conclusion. Deep neck space infections are potentially life threatening. Against our expectation the majority of patients admitted with cervical suppurations came from urban areas. The appearance of several cases in a short period of time may represent a concern and raise questions about the efficiency of prevention. Inconclusive antibiograms and the poor clinical presentation and evolution may indicate inappropriate empirical antibiotic use or poor selection of first line antibiotics.

Minimally invasive treatment of pheochromocytoma: 3D laparoscopic adrenalectomy

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Introduction. The adrenal glands tumors are usually called incidentalomas, because usually they do not present symptoms, with the exception of those that are metabolically active (that represent a minority). The inferior limit is 4 cm, every tumor above that measurement represents a high risk of malignancy and surgery becomes gold standard treatment, and secreting tumors are excised at any dimension. The anatomical position of the glands represents a challenge even for the open surgery, and one would think that laparoscopic surgery is even more complicated. This may be, but in expert hand, laparoscopic surgery becomes safe and feasible, especially for the quality of life for the patient, aesthetic looks, social reintegration and low morbidity.

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Material and methods. We report 6 cases of laparoscopic 3D adrenalectomy, 3 were benign adenomas, 1 was Conn disease (aldosterone secreting), 1 pheochromocytoma (secreting catecholamines) and 1 primary Cushing syndrome (corticoid secreting). For all the patients we opted for transperitoneal 3D laparoscopy approach using 3 trocars for the left side tumors and 4 trocars for the right-side ones (the extra trocar was for lifting the liver).

Results. The mean operating time was 85 minutes, blood loss less than 100ml for all 6 cases, no intraoperative complications, and 1 tube drain was placed. We mobilized the patients on day 0 (approximately 8 hours postoperatively), bowel movement was restored on the 2nd day postop, the uretro-vesical catheter was suppressed on day 2 and the drain tube on day 3 postop, the patient being discharged on the same day.

Conclusion. Laparoscopic 3D adrenalectomy is feasible, this approach represents an optimal choice for this type of pathology, recovery is fast, quality of life is high postop and the morbidity risks are low.

Treatment of prostatic recurrence: 3D laparoscopic salvage radical prostatectomy after local recurrence of rectal adenocarcinoma

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Introduction. It is rare for patients to suffer from metachrone cancers, and when this happens, treatment, especially for the second cancer becomes a real challenge. There are cases cited in the literature of prostatic adenocarcinomas after rectal cancers that were treated with surgery, radiotherapy and chemotherapy. In such cases, surgical treatment remains the only curative option for prostate cancer patients, but the surgery itself represents a challenge, due to the adhesions created after the first surgery, and the low quality of the tissues after radio and chemotherapy.

Material and methods. We performed a 3D laparoscopic transperitoneal prostatectomy for a patient with a history of rectal cancer (2016), operated and radio-chemo treated. We placed 5 trocars, used the cold scissors for the dissection of adhesions, and for the prostatectomy we opted for the Ligasure, Hem-o-Lock clips, titanium clips and resorbable 2.0 threads for the anastomosis.

Results. Operative time was 140 minutes, of which 45 minutes was the adhesiolysis, estimated intraoperative blood loss - 400 ml. The patient was mobilized on day 0 postop, bowel movement was regained on day 4. Drain tube - suppressed on the 6th postoperative day. The patient was discharged on the 7th day. Bladder catheter was removed on day 14 postop.

Conclusions. Laparoscopic 3D salvage radical prostatectomy after rectal cancer, represents a viable option, but this type of surgery should only be performed in high volume centers.

Takotsubo cardiomyopathy in a patient with thyroid lobectomy for anaplastic carcinoma and respiratory obstruction

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Introduction. We report the case of a 63-year-old female patient with the diagnosis of a tumor formation located in the anterior cervical region. The patient presented with dyspnea and marked dysphagia. With the diagnosis of thyroid tumor, the patient underwent surgery for left thyroid lobectomy, left cervical lymphadenectomy with vagal nerve section and jugular vein. After surgery the patient had cyanosis at the upper limbs and increased levels of troponins. She died twenty hours after surgery with the suspicion diagnosis of Takotsubo cardiomyopathy. The diagnosis was confirmed at the necropsy.

Conclusion. Patients suffering from severe emotional stress and physical stress (surgery) are prone to develop this syndrome post-operatively, also known as “broken heart syndrome”.

FUNDAMENTAL RESEARCH

Early initiation of breastfeeding and associated factors among mothers of children aged less than 2 years in North-Western Romania

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Introduction. The World Health Organization recommends the early initiation of breastfeeding (EIBF), defined as putting newborns to the breast within the first hour of birth. Different studies show that late initiation of breastfeeding leads to an increase in neonatal morbidity and mortality. The aim of this study was to assess the prevalence of EIBF and associated factors among mothers of children aged less than 2 years in North-Western Romania.

Material and methods. A cross-sectional study was conducted from March to June 2019, in the North-Western region of Romania. A total of 1399 mothers of children aged less than 2 years were randomly selected from the community. Data were collected using an interviewer administered questionnaire. Descriptive statistics was used to determine the prevalence of EIBF. Several medical factors were tested for association with EIBF using logistic regression models.

Results. EIBF was 24.3% among all mothers surveyed, while breastfeeding initiation rate for 1-24 h and that for more than 24 h were 47.3% and 28.4% respectively. Mothers who gave birth in a private hospital (Adjusted Odds Ratio [AOR] 5.17; 95% Confidence Interval [CI] 3.86, 6.91) were more likely to initiate breastfeeding within 1 h than those who gave birth in a public hospital. Moreover, mothers who gave birth by C-section (AOR 0.22; 95% CI 0.17, 0.30) were less likely to practice EIBF than those who gave birth by vaginal delivery.

Conclusion. Practice of EIBF in this study was poor. Place of delivery and mode of delivery were strongly associated with EIBF. Information, education and communication on the importance of EIBF must be supported to improve child wellbeing in Romania.

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Synthesis and physicochemical characterization of some new thiazole flavones and hydroxyflavones

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Introduction. Flavones possess a wide range of biological activities: anticancer, antioxidant, antibacterial, antifungal, anti-allergic, anti-inflammatory and neuroprotective. Their structure–activity relationships have generated interest among medicinal chemists, and this has culminated into the discovery of the clinical anticancer agent flavopiridol, as well as several lead molecules in other disease areas. Starting from

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this literature data and in continuation of our research related to the synthetic analogues of natural compounds, we have proposed the synthesis and spectral characterization of some new flavones and hydroxyflavones in order to evaluate their biological potential.

Material and methods. Thiazole ortho-hydroxychalcones were used as substrate for cyclization with hydrogen peroxide in alkaline media and with iodine in order to obtain products from the flavonoid family. The resulted compounds were purified and characterized by melting point, retention factor and their structures were confirmed by spectral methods: ¹H NMR, ¹³C NMR and MS.

Results. Previously synthesized thiazole ortho-hydroxychalcones were cyclized with hydrogen peroxide in basic media and depending on the substituents from their molecules the resulted compounds were either hydroxyflavones or the corresponding aurones. When the thiazole ortho-hydroxychalcones were cyclized with iodine, the corresponding flavones resulted in good yields. All compounds were purified by column chromatography and characterized by melting point and retention factor. The spectral analysis, ¹H NMR, ¹³C NMR and MS confirmed the structures of the newly synthesized compounds, as the predicted flavones, hydroxyflavones or aurones.

Conclusion. New thiazole flavones and hydroxyflavones were obtained by the cyclization of the corresponding thiazole ortho-hydroxychalcones with different oxidizing agents. The spectral analysis confirmed the structures of the synthesized compounds.

Lipophilicity evaluation of some thiazole chalcones and aurones

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Introduction. Lipophilicity is a physicochemical property which influences the pharmacokinetics of the drugs, consequently having a great impact on the compounds' capacity to cross the biological barriers. The prediction of lipophilicity is of great help in drug development, because it also affects the toxicity of the compound. Data from literature reveals many natural and synthetic chalcones and aurones with multiple pharmacological activities. The aim of this study was to evaluate the lipophilicity of some new thiazole chalcones and aurones with antiproliferative activity in order to determine possible structure-lipophilicity-biological activity relationships.

Material and methods. The experimental lipophilicity parameters were determined by reverse-phase thin layer chromatography (RP-TLC) and five different concentrations of isopropanol-water as mobile phase (55%, 60%, 65%, 70%, 75% isopropanol for the chalcones and 65%, 70%, 75%, 80%, 85% isopropanol for aurones). Several computed lipophilicity parameters were generated by several software and internet websites.

Results. Various experimental lipophilicity parameters were determined by RP-TLC and a good correlation between them and different theoretical lipophilicity parameters has been observed. On the basis of the lipophilicity chart and the lipophilicity space, the evaluated compounds were divided into different groups, based on their structural similarities.

Conclusion. The lipophilic character of 30 previously synthesized thiazole chalcones and aurones was investigated by RP-TLC and the experimental results were correlated with several computed log P values. Based on the substituents from their structures, the evaluated compounds were distributed into different groups, by applying the PCA analysis.

Electrochemical detection of adenosine using a sandwich molecularly imprinted polymer based sensor

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Introduction. Adenosine, an endogenous purine present in all cells of the human system, is involved in the regulation pathways of numerous physiological processes at the cellular level. Abnormal concentrations of adenosine have been used as a marker to diagnose several metabolic disorders and diseases. The purpose of this study was to develop an electrochemical sensor for fast and reliable detection of adenosine in biological samples.

Material and methods. A novel electropolymerized sandwich molecularly imprinted polymer (MIP) was designed. The MIP film relies on the formation of sandwiches between boronate-affinity bithiophene layer (consisting of 2,2'-bithiophene and a boronic acid functional monomer (3-thienyl boronic acid)), target nucleoside, and poly(3-indolacetic acid). Indirect electrochemical analysis of adenosine was achieved, using cyclic voltammetry and a redox probe ($[\text{Fe}(\text{CN})_6]^{3-}/[\text{Fe}(\text{CN})_6]^{4-}$).

Results. The carboxyl groups will form ionic bonds with the adenosine amino group. By forming stable cyclic esters through covalent interactions between the cis-diol moieties of template molecule and TBA, a high selectivity can be achieved, based on a double recognition mechanism, both through functional and spatial complementarity. The MIP based sensor can be used multiple times without significant loss in the signal intensity, exhibiting a linear response in the range of 1 – 100 $\mu\text{g/mL}$ in pH 7.0 phosphate buffer solution. The selectivity of the MIP sensor towards adenosine against other nucleosides was demonstrated.

Conclusion. A highly selective interface capable to detect the target molecule in a complex biological matrix was developed.

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Ferrocene-labelled DNA-based sensor for tetracycline electrochemical detection

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Introduction. Tetracycline (TC) is one of the most common used antibiotics for the treatment of infectious diseases in veterinary medicine and due to its high accumulation, important levels can be found in animal based products and environmental samples. Therefore, there is an imperative need to develop highly sensitive and selective methods with easy operation and on-site applications for tetracycline detection.

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Material and methods. Gold nanoplatform: AuNPs were electrodeposited by potential-assisted method (10 potential pulses at -1.4 V for 50ms, OCP for 1 s; then, chronoamperometry for 60 s at -0.57 V) at polystyrene-modified glassy carbon electrodes (GCEs) from 1.2 mM HAuCl₄ in 0.5 M H₂SO₄. Ferrocene-Aptamer (Fc-Apt) was immobilized by multipulse amperometry (-0.5 -> +0.2 profile pulses for 10 ms, 360 s).

Results. The development of a novel and selective electrochemical sensor based on an aptasensing strategy was envisaged. Choosing the best platform design for the Fc-Apt immobilization and TC detection represent a crucial step. Firstly, gold was electrodeposited at GCEs to obtain different 3D-nanostructures (nanoparticles AuNPs and nanovoids AuNVs) confirmed by microscopy analysis (AFM and SEM). Different strategies for Fc-Apt immobilization at AuNVs/GCE platform were investigated and multipulse assisted-method showed the best results in terms of ferrocene signal $I(\mu\text{A})/\text{STDEV}$ ratio.

Conclusion. Affinity-based biosensing strategies can contribute to antibiotics detection as valid and innovative analytical approaches. A ferrocene-labelled aptasensor for tetracycline detection was developed based on a gold nanopatterned platform and possible sensor applications will be presented.

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Sensitive detection of folic acid using 3D polymeric structures of 3-carboxylic polypyrrole with cone-like shape

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Introduction. Folic acid (FA) is a vitamin with important functions for the human body, such as the development and healthy growth of the fetus. FA cannot be stored in the human body. Because of that regular intake of dietary products or vitamin supplementation is necessary for a healthy lifestyle, as much as it is necessary to monitor the levels of FA in the body fluids in case of deficiency or in the case of pregnancy. Therefore, it is necessary to develop in situ quantification methods that can be applied for biological samples, drug and food control.

Materials and methods. Cone-like carboxylic functionalized polypyrrole was synthesized via the electrochemical polymerization of 3 carboxylic pyrrole in the presence of LiClO₄ and polyvinylpyrrolidone, on a graphite-based screen-printed electrode, by cyclic voltammetry(CV) scanning the potential ten times from -0.5 to 1.1 V/Ag with a scan rate of 100 mV/s. For the FA detection a pretreatment was carried through differential pulse voltammetry (DPV) by scanning the potential from 0.8 to 1 V/Ag in the presence of the analyte solution and the detection itself was achieved by CV using the same solution. Real samples analyses were performed on 1:100 diluted human serum as well as from 5 mg FA pharmaceutical tables.

Results. A detection limit of 0.8 μM FA was calculated for the sensor with a linearity between 2.5-200 μM . Real samples analysis had excellent recovery rates and was confirmed via spectrophotometric analysis. Interference studies showed good

recovery in the presence of dopamine, serotonin, ascorbic acid while the stability of the sensors showed excellent reproducibility up to 30 days.

Conclusions. The sensor was able to quantify FA from biological and pharmaceutical samples on a wide concentration range with very good recoveries. The novelty of this work resides in the simplicity of the method.

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Phytochemical evaluation of *Cotinus coggygia* and *Fragaria x ananassa* callus cultures by UPLC-MS

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Introduction. Strawberry (*Fragaria x ananassa*) extracts are known to protect human dermal fibroblasts against UV A radiation and hydrogen peroxide oxidative damage, but less is known about their anticarcinogenic effect. Previous results obtained within this project showed significant antiproliferative effects of extracts obtained from callus cultures of *Fragaria x ananassa* and *Cotinus coggygia* on human epidermoid carcinoma cell lines. Therefore, our objective was to obtain a phytochemical characterization of those extracts, in order to better understand the pathways underlying the observed effects.

Materials and methods. The methanolic extracts were analyzed by liquid chromatography coupled with high resolution mass spectrometry.

Results. The analyzed extracts contained significant amounts of phenolic compounds (catechin, procyanidins) and triterpenes. Significant differences were observed between the cell cultures of *Fragaria x ananassa* grown in the dark and the pigmented ones, proving that light has a significant effect on metabolism.

Conclusion. The most relevant classes of metabolites produced by the three studied cell cultures were identified.

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Study on the eating habits of adolescents in Romania - preliminary results

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Introduction. Nutrition plays an essential role in growth and development during childhood and adolescence. The intake for energy and nutrients is higher during adolescence than in any other time of life, excepting pregnancy and breastfeeding. The aim of the present study was to evaluate the life style and eating habits of high school students (aged 14-18 years) from different counties of Romania, the results obtained being useful in promoting healthy eating among them, tracking unhealthy habits and correcting them.

Material and methods. A cross-sectional study was conducted from September 2018 to May 2019, in 12 counties of Romania. Data have been collected using a complex questionnaire administered in high schools (students aged 14-18 years). A total of 1146 questionnaires were collected. Descriptive statistics was used to assess the consumption frequency of the main food groups.

Results. 70% of the respondents know the concept of healthy food pyramid. Only 25% of teenagers do at least 60 minutes of physical activity per day, walking and fitness being the first two choices. Breakfast is the most frequently missed meal, especially by high school students in the urban area. More than half of the respondents (60.72% girls and 54.77% boys) consume between 1 and 2 liters of water daily. White meat is more commonly consumed compared to red meat. Sausages are consumed by approx. 12% of respondents as the main mode of consumption of meat. A total of 77.68% girls and 84.48% boys consume dairy products daily or several times a week. Adolescents tend to consume one or two types of fresh fruit daily.

Conclusion. Adolescents are aware of the need to make changes in their diet, which could increase its quality and long-term development of healthy eating habits.

Consumption assessment of energy drinks among young people in Romania

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Introduction. Energy drinks are defined as non-alcoholic drinks with a high content of caffeine and sugar in combination with other substances known for their stimulant properties. They are used for both mental and physical stimulation. A real problem linked with the high consumption of energy drinks is precisely the high caffeine content that often exceeds the dose mentioned on the label. Thus, the present study aimed to evaluate the consumption of energy drinks among young people aged between 14-39 years in Romania.

Material and methods. The study was conducted from June to July 2019 in Romania. Data have been collected using a complex questionnaire administered on line,

using various social media groups and pages. A total of 1234 questionnaires have been collected. Descriptive statistics was used to assess the consumption frequency of the energy drinks products.

Results. 48.5% of women, respectively 77% of men consume energy drinks at least once a month. The preferred time for the use of energy drinks indicated by the consumers (57%) was between 2:00 pm and 10:00 pm for both sexes. In both males and females, the most important criterion for the selection of an energy drink is the taste, which has an average percentage of over 55%.

Conclusion. The consumption of energy drinks, following the study, is common among people, particularly aged 18-26 years. It is advisable to replace energy drinks with other foods or drinks (coffee, black tea, green tea) with similar effects.

In silico drug discovery of naturally-derived inhibitors to the serine pathway

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Introduction. Altered metabolism is a hallmark of cancer cells with the serine biosynthetic pathway emerging as a source for sustaining malignant cells. Phosphoglycerate dehydrogenase (PHGDH) is the first enzyme in this pathway and its role emerged as a potential target following the discovery of two potent inhibitors, NCT-503 and CBR-5884, obtained through screening assays. Drug development increasingly involves assessment of absorption, distribution, metabolism and excretion (ADME) in the initial drug discovery process. Thus, a characterization of these properties for the two inhibitors provides further insight into filtering all the natural compounds found within NPACT database. The main objective was the screening of natural compounds and their classes developed towards inhibition of the serine synthesis pathway.

Material and methods. In this study, plant derived natural compounds that exhibit anti-proliferative activity (NPACT database) were subjected to the molecular docking simulations targeting PHGDH (PBDId: 2g76) using the FlexX structure-based algorithm embedded in SeaSAR software (BioSolvIT, GmbH, Germany) with HYDE affinity assessment. The SwissADME web tool was used to predict pharmacokinetics and “drug-likeness” for the inhibitors.

Results. This structure-based molecular docking simulation combined with “drug-likeness” strategy generated a list of natural compounds from the NPACT database ranked by affinity to PHGDH. In terms of ligand efficiency and binding affinity, the results revealed that natural compounds categorized under the family names Terpenoids, Alkaloids and Flavonoids possess interactions with the NAD binding pocket of the target protein PHGDH.

Conclusion. This novel computational information in tandem with “drug-likeness” properties facilitated an improved understanding of PHGDH inhibition, emphasizing the implementation of this strategy towards the development of new naturally-derived therapeutic compounds.

Synthesis of novel 1,3-thiazole and 2-hydrazinyl-1,3-thiazole derivatives as anti-Candida agents: in vitro/in silico antifungal screening and spectroscopic investigation of their binding interaction with bovine serum albumin

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Introduction. In the context of a noteworthy increase in invasive candidiasis, along with the emergence of fungal resistance to the available treatment, there is an acute need for the development of novel antifungals. 1,3-thiazole and 2-hydrazinyl-1,3-thiazole derivatives are known to possess potent anti-Candida activity. Thus, we report the synthesis of two novel series of compounds as potential antifungal agents, keeping constant the key pharmacophores and introducing different moieties in the C4 position of the thiazole ring.

Materials and methods. The novel thiazole derivatives were obtained through a multistep synthesis protocol, using the classical Hantzsch condensation. Their antifungal activity, in terms of MIC and MFC, was evaluated in vitro against three pathogenic Candida sp. strains. The binding affinity to the catalytic site of the fungal lanosterol-C14- α -demethylase was predicted by a molecular docking study. Their binding interaction with bovine serum albumin was investigated through fluorescence spectroscopy.

Results and discussion. The corresponding chemical structures were confirmed by elemental analysis and spectral data. Three compounds showed promising inhibitory activity against the pathogenic C. albicans strain, exhibiting substantially lower MIC values compared with the reference drug fluconazole. Their antifungal activity was also supported by the performed molecular docking study. The data obtained from the fluorescence measurements assess a reversible, moderate interaction in BSA-ligand complex, linked to a faster diffusion rate to reach the target site in vivo.

Conclusion. The above-mentioned data represent a helpful support for the development of novel antifungal drugs with improved activity and pharmacokinetic properties.

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Performance evaluation of doxorubicin loaded core-shell microcapsules

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Introduction. Drug delivery systems are highly researched pharmaceutical formulations which bring important advantages in the treatment of cancer. In this study, core-shell microcapsules based on hyaluronic acid, chitosan and bovine serum albumin were subjected to an encapsulation process with doxorubicin and the encapsulation efficiency and release profile were evaluated.

Material and methods. The encapsulation of doxorubicin and release profile were realized in different conditions of pH and were evaluated using a new optimized electrochemical method. The results were compared with the ones obtained using UV-Vis spectrophotometry as control method. The aspect of doxorubicin loaded microcapsules was analyzed using Confocal laser scanning microscopy and cytotoxicity of the loaded microcapsules, as well as the unloaded ones, was determined on both healthy cells (MSCs) and tumor cells (HepG2).

Results. The results showed a better encapsulation of doxorubicin using DMSO as solvent of the feeding solution than buffer solution. The best release profile was obtained in media of buffer solution of pH 5, this being an advantage considering the slightly more acidic pH of the tumor tissue reported in specialty literature. The cell viability study showed a high affinity and selectivity of this type of microcapsules for tumor cells.

Conclusion. Hyaluronic acid, chitosan and bovine serum albumin based microcapsules are promising targeted drug delivery systems for cancer treatment and further studies should be done regarding them. The developed electrochemical method is a cheap and accessible method of doxorubicin encapsulation and release evaluation from different drug delivery systems.

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Molecularly imprinted polymer-based electrochemical sensor for Azithromycin detection

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Introduction. Antibiotic resistance has a significant impact on health and therapeutic efficacy, the World Health Organization (WHO) recommending a careful monitoring of the use and disposal of this class of drugs. Therefore, there is a rising demand for highly sensitive sensors able to selectively detect traces of antibiotics from

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different matrices in a fast and decentralized manner.

The purpose of this study was to develop an electrochemical sensor for the detection of azithromycin from various biological samples, by combining the convenient synthesis and analytical robustness with the tailored selectivity offered by molecular imprinting.

Material and methods. For molecular recognition and signal transduction a thin imprinted polymeric film, using 3-thienyl boronic acid as functional monomer and 2,2'-bithiophene as crosslinker, was electropolymerized on the surface of a glassy carbon electrode. The detection of azithromycin was achieved by an indirect electrochemical approach using cyclic voltammetry in the presence of a redox probe ($[\text{Fe}(\text{CN})_6]^{3-}/[\text{Fe}(\text{CN})_6]^{4-}$).

Results. The MIP-based sensor exhibited a very wide linear response for azithromycin on the range of 10 – 50,000 ng/mL in pH 7.0 phosphate buffer solution as supporting electrolyte and could be reused multiple times without significant loss in the signal intensity. The sensor demonstrated good selectivity towards azithromycin over other similarly structured antibiotics, with appreciable long-term stability (shelf life) and batch-to-batch reproducibility. Moreover, the fabricated sensor was successfully applied for the quantitation of azithromycin from different biological samples (urine, plasma, tears).

Conclusion. A highly selective and stable MIP-based electrochemical sensor was developed for Azithromycin detection in biological samples.

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Imprinted polymer-based plasmonic nanosensing platform for interfacial liquid-state surface enhanced Raman spectroscopy

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Introduction. Noble metal nanomaterials are ideal for sensing platforms because of their unique and tunable extinction properties, that can be exploited for signal enhancement and transduction. The plasmonic coupling adopted by closed-packed formations upon their assembly at a liquid interface can further enhance sensitivity, whereas the surface deposition of a thin layer of molecularly imprinted polymer (MIP) can add another dimension in detection selectivity.

Material and methods. Particular bone-shaped gold nanorods (nanobones) were synthesized by the seed mediated method. Their Raman signal enhancement efficiency in comparison with the conventional gold nanorods was assessed before and after their assembly at a liquid interface in the presence of a known Raman probe, rhodamine 6G. Furthermore, a thin layer of polydopamine-based molecularly imprinted polymer (MIP) was deposited on the nanobones. MIP film deposition was performed by the self-polymerization of dopamine in a slightly basic medium (pH 8.4). The optimization of the nanobone and MIP synthesis protocols, as well as their shape and size particularities were assessed by UV-Vis spectroscopy and microscopic (TEM) characterization.

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Results. Gold nanobones with a longitudinal plasmon band situated at ~ 700 nm were synthesized, showing a superior Raman signal enhancement at the liquid interface (3 fold increase) in comparison with conventional gold nanorods. The deposition of a thin, molecularly imprinted, polydopamine layer on the surface of the nanobones was also demonstrated.

Conclusion. Combining the unique binding selectivity offered by molecularly imprinted polymers and the benefits of using metallic nanostructures as Raman enhancers at liquid interface may lead to sensitive, label-free plasmonic nanosensors with various applications in bioanalysis.

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Synthesis and computational studies of novel polyphenolic derivatives of thiazolidine-2,4-dione. *In vitro* evaluation of the antioxidant and antiradical properties

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In the physiopathology of many diseases, such as diabetes, cancer, atherosclerosis, cardiovascular and neurodegenerative diseases, the oxidative stress has been reported to be an important component. A great interest nowadays is finding from natural sources or developing new compounds that could be useful in conditions for which oxidative stress is suggested to be the root cause or a serious consequence. Various pharmacological activities have been reported for the thiazolidine-2,4-dione derivatives and the phenol moiety is known as a pharmacophore in many naturally occurring and synthetic antioxidants. Twelve derivatives of thiazolidine-2,4-dione with phenolic substituents were synthesized and physicochemically characterized. *In vitro*, the antiradical capacity of the compounds was assessed using two radical scavenging assays (ABTS \cdot^+ and DPPH \cdot) and the antioxidant capacity was assessed through three electron transfer assays (FRAP, TAC and RP). Supplementary a Fe²⁺ chelation assay was performed.

Three polyphenolic compounds presented antiradical and antioxidant activities similar or even better than reference compounds (trolox, ascorbic acid and BHT). The ferrous ion chelation capacity of the newly synthesized compounds was modest.

In order to better understand the differences between compounds, several quantum descriptors were calculated. The energetic level of the frontier orbitals (HOMO and LUMO) partially explained the antioxidant activity, while a better correlation was found with the bond dissociation energy of the phenolic groups.

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Optimization of the drying process for autumn fruits: a study focusing on rosehip (*Rosa canina* L.) and sea buckthorn (*Elaeagnus rhamnoides* (L.) A.Nelson) and their bioactive properties

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Introduction. Nowadays, it is very important to identify the traditional uses of different plants and to create the context in which new cultural or economic value is given to local resources. In this study, two wild fruits traditionally harvested in autumn from Romania were selected in order to evaluate different biological properties. In particular, the properties of these plants can be suitable for possible use in the development of functional foods or for using as potential sources of natural antioxidants. The objectives of this research were to investigate the effects of air temperature on the drying behaviour of the two traditionally used fruits in Romania and to select the best conditions in terms of air temperature and time of drying.

Materials and methods. Fresh fruits were collected manually from different locations situated in Cluj County, Romania and Abruzzo province, Italy. Three different temperature levels (50, 60, and 70°C) were used. Weight change was recorded at 4, 8, 12, 18, 24, 36, and 48 hours during drying, followed by the grounding and extracting of dried fruits in EtOH 70%. The drying process was optimized using Modde 11.0 software. The biological properties exerted by extracts were evaluated in terms of TPC, TFC, antioxidant capacity, antiinflammatory, cytotoxic activity, as well as by inhibition capacity towards some key-enzymes (e.g. glucosidase).

Results. The optimal time with hot air at a temperature of 60°C for *Rosa canina* pseudofruits, resulted from parameters' analysis was 30.4 hours, whereas for *Elaeagnus rhamnoides*, the optimal time required was 24.35 h. The extracts obtained using optimized parameters of drying exerted high values in terms of TPC, TFC, and antioxidant activity, compared to the crude extracts. Moreover, the optimized rosehip extract showed the best α -glucosidase inhibitory activity ($IC_{50} = 0.542 \pm 0.029$ mg/mL). The rosehip and sea buckthorn extracts showed no cytotoxic activity, nor antiinflammatory capacity.

Conclusions. The drying of medicinal plant materials is a process which consists of various physical, chemical, and biological phenomena. They are very important to be understood in order to exert high yields in terms of bioactive compounds. The data presented in this article represents a step-forward in applying the process in industrial-scale.

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PHARMACEUTICAL SPECIALTIES

A quality by design study regarding the formulation and *in vitro* evaluation of orodispersible tablets with loperamide using dynamic compaction analysis

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Introduction. Quality by Design (QbD) concept in drug formulation and development was introduced for a proper product quality. For the orodispersible tablets (ODTs) the tablet disintegration time and mechanical properties have been recognized as critical quality attributes, which must be optimized in the pharmaceutical development phase.

Materials and methods. In order to reach a good balance between their properties, a statistical method was used according to a D-optimal experimental design. The formulation factors used in the design were: the type of the diluent agent, the type and percentage of the disintegrating agent, sweetener, flavor and compression force. The tablets obtained were analyzed in vitro and tableting properties. For the dynamic compaction analysis a new variable was included in the initial experimental design, the compression force, and the mixed powders were compacted at different loads (100, 200, 300 and 400 kg). The experimental design used had 140 formulations.

Results. During this experiment it was observed that the mechanical properties were mainly influenced by the type of diluent agent used and the compression force. The highest values for the friability and disintegration time were noticed for the formulations with sorbitol. The same results were obtained for the tableting properties of the mixed powders. The best results for the determined mechanical and tableting properties were noticed for the formulations in which Ludiflash® was used as a diluent agent. The dissolution profile of the formulations was influenced by the ratio of disintegrant agent and the type of diluent agent used. The formulations with the highest friability values, the ones with sorbitol, had the best dissolution profile, and released 66% of the API at the end of the test.

Conclusion. QbD approach was successfully applied within this study and the ODTs with loperamide that have desired pharmaceutical characteristics may be successfully prepared.

Development of liposomes co-encapsulated with Doxorubicin and Simvastatin for an enhanced therapeutic efficacy in breast cancer

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Introduction. Doxorubicin (DOX) was the first antineoplastic agent incorporated in an industrial liposomal drug product using an ammonium sulphate gradient in order to get a high encapsulation efficiency (EE%). Simvastatin (SIM) is a cholesterol-lowering drug whose antioxidative properties were widely exploited in different types of cancer. The aim of this study was to develop a new long-circulating liposomal (LCL)

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co-formulation with DOX and SIM and to assess its antiproliferative effects on T47D-KBluc breast cancer cells.

Materials and methods. In order to study the influence of the formulation factors and process parameters on LCL's quality attributes a screening study with six variables, namely phospholipids (PL) concentration, DOX and SIM concentration, ammonium sulphate pH solution and incubation time with DOX, was performed. LCL were characterized as regards their size, polydispersity index (PDI), drugs' encapsulated concentration, drugs' EE% and zeta potential. The antiproliferative effects of the drug combination was studied on T47D-KBluc breast cancer cell line.

Results. The EE% for both drugs is highly dependent on the PL and SIM concentration. LCL size and PDI were determined before and after incubation of SIM liposomes with DOX, since it was observed that the incubation process leads to a slow decrease in the LCL size and an increase in the PDI. In vitro preliminary studies demonstrated that the combined administration of SIM and DOX resulted in a strong inhibitory activity on the proliferation of the breast cancer cell line.

Conclusions. The co-administration of DOX and SIM in LCL is a promising approach to inhibit the development of T47D-KBluc breast cancer cells. Further molecular studies should be addressed to reveal the mechanisms underlying the in vitro LCL-SIM-DOX efficacy.

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In-line implementation of a NIR spectroscopic method for real time monitoring of a blending process

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Introduction. Blending represents a critical step in pharmaceutical manufacturing as it influences the product's content uniformity. From an economical perspective avoiding out of specification batches and optimization of processing time are beneficial for the manufacturer. The objective of this study was to implement a real time monitoring tool for the blending of a complex mixture.

Materials and methods. Diffuse reflectance spectra were recorded in the 950-1650 nm region with a 6.2 nm resolution, under static (off-line) and dynamic (in-line) conditions. For in-line experiments a 7 ms acquisition time and integration of 200 spectra was selected. PLS models were developed using spectral data recorded in different setups.

Results. Dynamic acquisition produced higher baseline shift compared to static recording, however pre-processing methods (SNV,SD) efficiently minimized the differences. The increased concentration of paracetamol and ibuprofen was reflected in the performance parameters of PLS models. Both at-line and in-line recorded spectra lead to a good predictive capacity ($Q^2 > 0.9$) with reduced cross-validation errors. For caffeine, higher number of PLS components were fitted to the model, especially under dynamic conditions, as the reduced spectral contribution of this formulation constituent was more prone to be affected by the undesired spectral variability induced by sample dynamics. Static spectral acquisition performed better in terms of Q^2 (> 0.9). The predictive difference of models built using static and dynamic acquisition modes seems

to be API related. The spectral contribution of the target component in relation to other excipients and its robustness to process induced variability was a determining factor.

Conclusions. In the current experimental setup the homogeneity could be reached in terms of ibuprofen and paracetamol only, as the lack of an efficient dispersive contributor to the blending mechanism failed to distribute caffeine correctly.

Environmental protection in the codes of ethics for pharmacists

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Introduction. Many authors, with different backgrounds, are preoccupied by analyzing the meaning of environmental ethics within bioethics and public health ethics. Important international organizations adopted declarative documents proclaiming the importance of respecting the ethical principle of environmental protection in all activities related to human health. At national level, it is the duty of healthcare professional associations to include and develop that principle in their codes of deontology. The aim of this paper is to identify and analyze elements of environmental ethics in codes of deontology for pharmacists.

Material and methods. A documentary research was conducted in order to find codes of deontology for pharmacists from 10 countries: Belgium, Canada, Finland, France, Hungary, Romania, Spain, Switzerland, United Kingdom, and United States. The codes were examined, and their provisions analysed using methods of legal interpretation, then juxtaposed using the comparative method. Considering the need for development of environmental ethics for pharmacists, proposals of deontological regulation were made, that could be taken into account by professional associations.

Results. Explicit provisions on the pharmacists' obligation to participate to environmental protection were found in deontological codes in force in four states: Belgium, Canada, Hungary and Spain. In Romania, such provisions can be found only in a project for a new code, from 2015, not yet adopted by the College of Pharmacists. Those provisions refer, in general, to the ethical duties to assure a proper waste management according to the law and to advise patients in order to prevent environmental contamination with pharmaceuticals or other healthcare products.

Conclusion. To develop the environmental ethics for pharmacists, their codes should include the principle of environmental protection, the expression of environmental values and ideals, and standards of environmental ethics.

Fatty acids profile evaluation of green microalgae *Chlorella sorokiniana* UTEX 2130 using a GC-FID method

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Introduction. Microalgae, in addition to the major planetary role in solar energy conversion and biogeochemical cycles, have a major contribution to a wide range of biotechnological applications, including to photosynthetically valorize CO₂ into

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mono/polyunsaturated fatty acids and other bio-based products. In this research, we determined the profile of fatty acids (as methyl esters) from the culture collection strain *Chlorella sorokiniana* UTEX 2130.

Material and methods. In order to achieve the proposed objectives, a GC-FID method was developed to identify 37 fatty acids, using a Supelco standard. After cell membrane disruption the biomass was subjected to solvent extraction and transesterification. The esters were analyzed by GC-FID using a HP-88 capillary column and helium as carrier gas.

Results. In the series of saturated fatty acids, higher concentrations were recorded for arachidic acid (475.51-589.97 µg/100 mg lyophilisate), followed by myristic acid (122.65-145.7497 µg/100 mg lyophilisate). From the monounsaturated fatty acids series we identified in all the samples oleic (C18:1) and eicosanoic acid (C20:1), higher concentration being observed for the first one (124.2-142.02 µg/100mg lyophilisate). An important class is that of polyunsaturated acids in which we identified and quantified linoleic acid (C18:2 cis, omega 6) and linolenic acid (C18:3 n3, omega 3) in all samples, as major compounds (390.90-394.47, respectively 70.12-80.74 µg /100 mg lyophilisate).

Conclusions. In microalgae samples analyzed we identified and quantified different fatty acids. This research will be used to establish the importance of using low gamma irradiation as a stressor for increasing the amount of fatty acids in microalgae cultivated in different conditions.

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Fused Deposition Modeling Three-Dimensional Printing (FDM-3DP) of channeled tablets with ketoprofen: design, development and pharmaceutical evaluation

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Introduction. Three-dimensional printing (3DP) is a resourceful technology with promising potential in revolutionizing the manner in which medicines are designed, produced and used. Among available 3DP techniques, Fused Deposition Modeling (FDM) gained attention in the pharmaceutical field due to its flexibility, simplicity and low costs. The aim of the present study was obtaining and evaluating a channeled tablet model produced by FDM 3DP, using custom made pharmaceutical polymer-based filaments.

Materials and methods. Ketoprofen was selected as the model active pharmaceutical ingredient (API), while polyvinyl alcohol (PVA) represented the matrix forming polymer with thermoplastic behaviour in which the API was included. Feedstock filaments were obtained by hot melt extrusion (HME) technique, followed by FDM 3DP of the tablets. Assessment of the final product included pharmacotechnical characterization and in vitro dissolution studies.

Results. Results demonstrated the feasibility of higher drug loaded, printable PVA based filaments. Plasticization was achieved by elevated API content, generating

custom made feedstock filaments with proper mechanical and rheological properties. In vitro dissolution testing revealed a complete release of the drug up to 4 h. Humidity was identified as a factor which could impact the quality of the dosage form, subsequently preventive measures are required during preparation and storage.

Conclusion. Production of pharmaceutical dosage forms by HME+FDM represents a novel approach with promising advantages for applications such as personalized medicine manufacturing, creating opportunities to improve safety, efficacy and accessibility of medications. FDM 3DP could be developed as a single platform to adapt dosage forms based on patients' needs, preferences or individual features.

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Effects of alpha-lipoic acid treatment in a rat model of heart failure associated with obesity

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Introduction. As a comorbidity, obesity can influence heart failure (HF) development. Alpha-lipoic acid (AL) is a complex antioxidant that interferes with multiple signaling pathways. The aim of our study was to evaluate the effects of AL treatment in a HF and obesity rat model.

Material and methods. Sprague-Dawley male rats (6 weeks-old) were either included in the control group (n=6) or subjected to abdominal aortic banding (AAB) and divided into 3 groups: standard diet (AAB+SD, n=8), hypercaloric diet (AAB+HD, n=8) and hypercaloric diet and AL treatment (AAB+HD+AL, n=9). For 36 weeks body-weight (BW), systolic blood pressure (SBP), echocardiographic parameters were monitored. Plasma hydroperoxides and renal function were also assessed.

Results. HD induced an increase in BW (~11.5%) in AAB+HD group since week 8 (W8), trend maintained until W36 (~17.83%). The presence of the AAB was confirmed by echocardiography; stenosis was measured to ~37% of the aortic diameter. Also, a decrease in early-to-late filing ratio (E/A ratio) in AAB+HD was observed (1.32 ± 0.05 vs 1.67 ± 0.05) starting with W20, while for AAB+SD, reduction occurred at W28 (1.26 ± 0.12 vs 1.63 ± 0.09). At W36 ejection fraction (EF) was reduced with ~12% in AAB+SD and AAB+HD groups. Regarding renal function, an increase in urine protein and creatinine was noted in AAB rats, without decrease of creatinine clearance, suggesting preservation of renal function. In AAB+HD+AL, treatment reduced BW (~13%) compared to AAB+HD and delayed the onset of diastolic dysfunction, which in this group was observed only at W36: E/A ratio (1.23 ± 0.12 vs 0.81 ± 0.03), E'/A' ratio (1.10 ± 0.12 vs 0.80 ± 0.03), without significant changes to EF. Also, an improvement in SBP and plasma hydroperoxides was registered in the AAB+HD+AL group at W8.

Conclusions. Aortic stenosis induced diastolic dysfunction since W28, process accelerated by HD. AL treatment reduced BW, SBP and plasma hydroperoxides and delayed the onset of diastolic dysfunction.

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Protein corona characterization of a new synthesized class of PEGylated gold nanoparticles

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Introduction. One of the main features that influence the interaction of nanoparticles (NPs) with the biological milieu is their surface chemistry. Biocompatibility of gold nanoparticles (GNPs) can be increased by surface PEGylation resulting in decreased non-specific binding of proteins, enabling them to be perfect candidates as emerging tools for (bio)pharmaceuticals.

Objectives. The aim of this study was to synthesize a new class of PEGylated GNPs and to assess their impact on the protein corona formed in human biospecimen.

Material and methods. Employing a seeding growth approach, GNPs were synthesized via the reduction of HAuCl₄ using polyethylene glycol (1.5 kDa). The morphology of GNPs was characterized by UV-VIS spectroscopy, transmission electron microscopy (TEM), dynamic light scattering (DLS) and differential centrifugal sedimentation (DCS). Cytotoxicity was tested by MTT test on MDA-MB-231 cell line. GNPs were incubated with human serum and plasma and the formed protein corona was analyzed by MS and by an antibody quantum dot (QD-Ab) conjugated mapping method for quantifying selected proteins on the outer layer (i.e. IgG, ApoE, HrpG and C4).

Results. Narrow sized and fully biocompatible GNPs (15 nm to 80 nm) were synthesized. Similar numbers of proteins were identified in plasma (77) and serum (86) protein corona. Within top 20, the abundances of IgG and C4 were higher in plasma compared to serum. The MS results were confirmed by QD-Ab mapping analysis.

Conclusions. A new synthesized class of PEGylated GNPs was characterized in terms of the formed protein corona. The synthesis resulted in distinct protein corona profile suggesting different immunogenic behavior dependent on the biospecimen used. Based on these findings synthesis and biospecimen chosen for protein corona characterization needs to be considered as an essential pre analytical factor for the production of fully biocompatible and tunable GNPs for medical applications in personalized medicine.

Impact of PEGylation coating on gold nanoparticles serum protein corona

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Introduction. Nanoparticles (NPs) are known to form in biofluids a biomolecular corona conferring them a new identity. One of the most successful strategies capable of minimizing unspecific protein adsorption at the NPs's surface consists of using the stealth properties given by polyethylene glycol (PEG) ligands. Furthermore, the use of different ligand structures can lead to a novel protein corona and therefore a specific

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NP behavior, essential for their use as emerging carriers for (bio)pharmaceuticals.

Objectives. The aim of this study was to assess the impact of the PEGylation method on gold nanoparticles (GNPs) protein corona formed in human serum.

Material and methods. Spherical citrate capped GNP (50 nm) were synthesized and modified by a ligand exchanged process using bifunctional thiolated-PEG-ligands with different functional groups (methoxy, carboxyl). Also, a new direct synthetic method of GNP manufactured with a non-modified PEG (1.5 KDa) ligand as a capping agent was tested. The individually formed serum protein corona was analyzed by MS and by an antibody quantum dot (QD-Ab) conjugated mapping method for quantifying selected proteins on the outer layer (i.e. IgG, clusterin).

Results. Among the 301 proteins identified (predominantly binding proteins), PEG(1.5 KDa) enclosed the lowest protein number (121). Within top 20, clusterin was found in higher abundance in the PEG(1.5 KDa) corona, whereas IgG was not covered. QD-Ab mapping analysis confirmed the MS data.

Conclusion. PEGylation method on GNP surface modification resulted in distinct serum protein corona. For the PEG(1.5KDa) GNPs data showed: a higher abundance of clusterin, suggesting a higher stealth capacity implying a reduced non-specific cellular uptake; and a lower IgG abundance demonstrating a less immunogenic potential. Based on these findings, PEGylation method needs to be considered an important pre analytical factor for GNP production in the (bio)pharmaceutical industry.

Manufacturing of lipid inhalable microparticles via spray drying using Polyglyceryl-3-dibehenate partial ester as lipid-based excipient

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Introduction. The inhalation therapy has rapidly developed in recent years. An advantageous approach in pharmaceutical engineering is the manufacturing of lipid-based Dry Powder Inhalers through Spray Drying (SD). In the present work, the feasibility of polyglycerol fatty acid esters with outstanding stable solid state for the manufacturing of inhalable lipid-microparticles via SD was evaluated.

Materials and methods. Ibuprofen free acid (IBU) and Polyglyceryl-3-dibehenate partial ester (PG3-C22 Partial) were studied. A mass median aerodynamic diameter (MMAD) between 1-5 μm and a geometric diameter of 5-15 μm were pursued. Feed solutions of IBU:PG3-C22 Partial were spray-dried and process parameters were screened. The resulted spray-dried powders were characterized regarding the solid state (via DSC, small and wide angle X-ray scattering and FT-IR), density and particle size distribution. The in vitro inhalability of the particles was assessed using a Next Generation Impactor. Stability tests of the final product were also performed after storing the samples at room temperature and 40°C up to 3 months.

Results. Process yields up to 64% could be achieved. Characterization of the spray-dried powders revealed that the solid state was not altered during the process. Geometric diameters between 3.81 – 11.01 μm and low tapped densities were obtained. All the data revealed stable solid state of the final product as lipid-based formulation. The aerodynamic assessment of the spray-dried powders revealed MMADs between 4.12 – 5.34 μm and a fine particle fraction ranging from 13.08 to 28.61%.

Conclusion. Although optimization of the process is possible, these results showed that manufacturing of inhalable lipid-microparticles is feasible via spray drying.

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Magnetic nanoparticles with high heating power for hyperthermia application

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Introduction. Magnetic hyperthermia (MH) is a promising therapeutic procedure using magnetic nanoparticles (MNPs) to induce the death of cancerous tissue by converting externally supplied magnetic energy into thermal energy. The development of MNPs with increased heating efficiency and selectivity towards the cancerous tissue is the current objective in the MH field.

Materials and methods. The biocompatibility of the synthesized MNPs was investigated on two cancerous cell types (A549, MCF-7) and on normal gingival fibroblasts using two complementary viability assays (Alamar Blue and Neutral Red). The possible interference of the MNPs with the biochemical components of the assays was assessed. The cellular uptake and the potential of the synthesized MNPs to induce selective cellular death on cancerous cells in magnetic field was further explored.

Results. Biocompatibility assays revealed a marginal toxicity that decreased the viability by no more than 20% at the highest tested concentration of 1 mg/mL. The MNPs accumulated at a higher rate in the cancerous cells, in a dose-dependent manner. Exposure to the magnetic field alone did not alter the cellular viability in the tested conditions, while the magnetic field exposure after a 24 h pre-incubation with the MNPs induced cellular death dependent on the cell type, dose and the intensity of the field. A higher toxicity was observed in the cancerous cells, pinpointing the desired selectivity towards cancer cells.

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

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Compatibility studies for the development of a multicomponent pharmaceutical dosage form for ENT use

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Introduction. Acquired neurosensory hearing loss is the most common hearing loss in the modern society. The main factors that cause this condition are: the use of ototoxic drugs, harmful levels of noise and old age. The present study is part of a complex one that aims to obtain capsules with nicergoline, piracetam and dry hawthorn extract, for the treatment of this condition. The active pharmaceutical ingredients (APIs) were chosen based on their therapeutic indications, nicergoline, with vasodilating effect, piracetam, a nootropic drug, dry extract of hawthorn with the role of improving circulation in the brain. On the other hand, a pharmaceutical formulation is considered appropriate when no interactions medicament-medicament or medicament-excipient appears. The objective of this study was to assess the compatibility between the components in the preformulation stage of capsules with nicergoline, piracetam and hawthorn extract by using Differential Scanning Calorimetry (DSC), X-Ray Powder Diffraction (XRPD) and Fourier Transformed Infrared Spectroscopy (FTIR) methods.

Material and methods. Nicergoline, piracetam and dried extract of flowers and fruits of hawthorn were used as APIs and lactose monohydrate, microcrystalline cellulose, sodium starch glycolate, magnesium stearate and polyvinylpyrrolidone K30 as excipients. The individual components and also their 1:1 (m/m) physical mixtures were analyzed using DSC, XRPD and FTIR methods in order to determine the compatibility of the APIs with each other and with excipients, respectively.

Results. Following DSC, XRPD and FTIR results obtained in the preformulation stage, nicergoline, piracetam and dry extract of hawthorn were found to be compatible between them and with the selected excipients.

Conclusion. Based on the results obtained in the preformulation stage, the three APIs as well as the chosen excipients can be further used in the multicomponent capsules formulation stage.

Redox imbalances in a rat model of heart failure

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Introduction. The pathophysiology of heart failure (HF) is not fully understood, causing limitations regarding therapeutic approaches. Obesity, β_3 -adrenergic receptors and redox imbalances were shown to be involved in HF. The purpose of this study was to evaluate: 1) whether diet induced obesity (DIO) and/or overexpression of β_3 -adrenergic receptors in the endothelium (Tg β_3 rats) determine redox imbalances involved in the alteration of diastolic function and 2) the therapeutic potential of alpha-lipoic acid (ALA).

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Materials and methods. The animals (Tgβ3 and WT male rats, n=12/group) were fed with control diet or hypercaloric diet (CD/HD) over a period of 35 weeks (W). Half of the rats from each group (Tgβ3/WT fed with CD/HD) were treated with 50mg/kg of ALA i.p., for the last 14 successive days of each month. During the study, cardiac parameters were assessed by echocardiography. At W35, plasma levels of reduced (GSH) and oxidized (GSSG) glutathione, malondialdehyde (MDA) and homocysteine (Hcy) were assayed by liquid chromatography.

Results. Echocardiographic evaluation confirmed an earlier alteration of diastolic function in HD fed Tgβ3 rats (since 22W). GSH/GSSG ratios were decreased and plasma MDA levels were increased by HD in both Tgβ3 and WT rats, while Hcy levels were increased only in Tgβ3 rats. ALA treatment decreased plasma MDA levels only in HD fed Tgβ3 rats and did not influence GSH/GSSG ratios or Hcy levels. Over-expression of β3-adrenergic receptors in endothelial cells did not influence GSH/GSSG ratios, MDA or Hcy levels.

Conclusions. DIO causes diastolic dysfunction and redox imbalances in WT and Tgβ3 rats. ALA treatment showed limited effects on oxidative stress biomarkers in healthy rats and rats with HF.

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In vitro – *in vivo* characterization of nanoparticulate mucoadhesive polyherbal gel designed for the treatment of periodontitis

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Introduction. Periodontitis is a chronic inflammation of the teeth supporting tissues, involving endogenous collagenolytic enzymes, especially matrix metalloproteinase 8 (MMP-8). Topical application of active principle directly into the periodontal pocket represents a satisfactory approach, presents many advantages and involves the use of a controlled release device with mucoadhesive properties. Phytoconstituents as flavonoids, catechins, saponins, tannins, essential oils can have a high anti-inflammatory and antioxidant potential and they could exert an effect of inhibiting MMP-8 activity at the periodontium level.

Materials and methods. The purpose of this work was to formulate a nanoparticulate mucoadhesive polyherbal gel (NMPH gel), based on *Echinacea purpurea*, *Camelia sinensis*, *Filipendula ulmaria* and *Calendula officinalis* extracts and to evaluate *in vivo* efficacy regarding clinical parameters, histopathology and immunologic profiles (serum and salivary levels of MMP-8). The designed NMPH gel formulation consisting of Carbopol 940 and Kolliphor P407 was prepared (the extracts being incorporated in the same ratio) and evaluated regarding the rheological properties and *in vitro* adhesive capacity (assessed by measuring the time of detachment of the sample from a synthetic membrane). The total polyphenolic content of the polyherbal extract was estimated using Folin-Ciocalteu reagent and the content of epigallocatechin-3-gallate was analysed by HPLC coupled with Mass Spectrometry. The *in vivo* testing of the NMPH gel was performed using an experimental model of induced periodontitis

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in rats, by placing the ligatures around the inferior incisor.

Results. The studied NMPH gel showed rheological and *in vitro* adhesion properties suitable for application in the periodontal pocket that can provide adherence to the gum for a prolonged period of time, ensuring an increased concentration in total polyphenols at this level. The experimental results showed that topical application of designed NMPH gel reduced the local inflammatory response induced by periodontitis, led to clinically and histopathologically healing of gingival lesions and determined a decrease in serum and salivary levels of MMP-8.

Conclusions. The results suggest that the prepared NMPH gel may be favorable for topical application in periodontal therapy.

Protective effects of walnut (*Juglans regia* L.) and walnut septum extract in D-galactose-treated rats

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Introduction. Aging is a multifactorial physiological process not yet fully elucidated. A murine model, in which high doses of D-galactose (D-gal), a monosaccharide commonly found in milk and its by-products, are chronically administered for the artificial induction of senescence, was used in this study of anti-aging therapeutic interventions. D-gal can generate free radicals, increase oxidative stress, chronic inflammation, and the incidence of age-related diseases. The objective of our study was to examine the influence of a diet supplemented with walnut kernels (WK) or with a polyphenolic-rich walnut septum extract (WSE), on several biomarkers of senescence in D-gal treated rats.

Materials and methods. Young 3-month old Wistar rats were randomly divided into four groups of 8 animals each: Control group and D-gal – received standard pelleted food; D-gal + WK – received daily a diet with 9% WK; D-gal + WSE – received daily the equivalent volume of WSE corresponding to 9% WK, based on determined total phenolic content. Except for the control group, all animals were subcutaneously injected with D-gal at a dose of 400 mg/kg body weight dissolved in normal saline (0.9% sodium chloride) solution three times per week, while the rats in the control group were subcutaneously injected with 0.9% normal saline at equal volumes. After 56 days of treatment, all rats were sacrificed and several specific biochemical, hematological, anthropometric parameters were evaluated, particular oxidative stress biomarkers and histopathological changes in liver and brain were assessed.

Results. The results showed that walnut-enhanced diets, as well as septum extract, could improve body weight, liver and brain indices and normalize oxidation in aging rats. The antioxidant cellular status measured by TEAC, DPPH, and FRAP assays presented an upsurge in D-gal + WK and D-gal + WSE groups compared to D-gal group. The imbalance between the generation and removal of reactive oxygen species and advanced glycation end products was improved in the two mentioned groups compared to model. Also, D-gal increased acetylcholinesterase (AChE) activity in rat brain, a cholinergic system dysfunction and a source of memory and cognitive deficits, but the addition of WK and WSE inhibited AChE activity in D-gal treated rats.

Conclusions. The results of our study demonstrate that walnuts or septum extract can protect against liver and brain damages in D-gal-induced aging rats which may positively influence some aging-associated problems and beneficially affect age-related diseases. The mechanisms might include a reduction in cellular oxidative stress and inhibition of acetylcholinesterase activity coupled with restoration of acetylcholine content. However, other specific molecular mechanisms of action remain to be further investigated.

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 that improves the glycaemic 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. A new test formulation with dapagliflozin was developed and its pharmacokinetics was assessed in comparison with an authorized reference product under fasting condition.

Materials and methods. The single-dose study was designed as crossover, open, balanced, randomized clinical trial, 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. The subjects were administered either test or reference drug product with 240 mL of 20% glucose solution in water at ambient temperature. The wash-out between study periods was 7 days. During each study-period, 46 blood samples were taken. For determination of dapagliflozin plasma concentrations a validated HPLC method was used, coupled with mass spectrometry. Non-compartmental pharmacokinetic analysis was performed using Phoenix® WinNonlin® version 6.3. The calculated pharmacokinetic parameters were AUC_{0-t} , $AUC_{0-\infty}$, C_{max} , T_{max} , K_{el} and $T_{1/2}$. 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 result obtained for $\ln(C_{max})$ was 105.17% (96.07% – 115.12%), for $\ln(AUC_{0-t})$ was 103.15% (101.04% – 105.30%) and for $\ln(AUC_{0-\infty})$ was 102.09% (99.90% - 104.33%). The mean T_{max} values for dapagliflozin under fasting condition from the test formulation was 1.64 hours and 1.80 hours from the reference formulation, respectively.

Conclusions. 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.

DENTAL MEDICINE

Maxillary transversal deficiency assessment

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Introduction. The transversal anomalies appear early and are very frequently met in clinical practice, being well related to the functional environment. The common symptom is the maxillary transverse deficiency estimated at approximately 8-18% in mixed denture (Raberin). The evaluation of maxillary deficiency is made beginning with the history of the dentomaxillary malocclusions, functional assessment, facial and intraoral examination and continuing with the complementary investigations (dental casts, postero-anterior cephalometry, CBCT).

The purpose of our study is to assess the maxillary transversal deficiency using different methods mentioned in the literature.

Material and method. We randomly analyzed a group of 46 patients presented in Orthodontic and Dentofacial Orthopedics Clinic, Cluj-Napoca. We conducted a dimensional analysis of dental casts by assessing the maxillary width (Index Pont, McNamara method, Howe et al).

Results. The results obtained for every dental casts were statistically compared.

Conclusions. The application of these quantification methods is relevant for the assessment of the severity of maxillary transversal deficiency and treatment approach in clinical practice.

Pilot study regarding dental erosion in everyday practice

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Introduction. This study aimed to determine dental erosion incidence and severity in a regular everyday dental practice.

Material and methods. The study included 140 patients, aged 21 to 72 years old, and was conducted in 2018. One trained clinician performed anamnesis, clinical examination and BEWE index determination. Dental erosions were diagnosed, the severity of dental tissue loss was evaluated with BEWE index and location was noted.

Results. 22 patients aged between 27 and 61 years old were diagnosed with dental erosion. 3 patients presented BEWE index more than 14. Investigations regarding diet showed presence of high consumption of acidulated beverages in 12 patients diagnosed with dental erosions. Medium BEWE score in patients diagnosed with dental erosions was 11, compared with the rest of 118 patients with medium BEWE score 4. Most frequent localization of dental erosion was on the palatal and cervical dental surfaces.

Conclusions. Etiology of dental erosion is multifactorial, most severe cases were associated with high consumption of acidulated beverages. Males presented a higher risk of dental erosion than females. The relative high percentage found (15.7%) of patients with dental erosions, requests more preventive measures in order to avoid expensive prosthetic treatment in advanced dental tissue loss.

Evaluation of odontal and periodontal parameters in direct class II restorations

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Introduction. The aim of this preliminary study was to evaluate the clinical performance of class II direct restorations from odontal and periodontal point of view. An ormocer (Admira Fusion®, Voco) which is the first purely ceramic – based restorative material, containing silica oxide based fillers and resin matrix without classic monomers was used in this study for direct restorations.

Material and methods. Twelve patients with class II carious lesions were included in this study. Twelve medium and deep direct fillings have been performed using the proximal wall restoration technique in association with Palodent V3 Matrix System (Dentsply). Four periodontal parameters were evaluated i.e. plaque index, bleeding index, probing depth and attachment loss. The clinical performance of the restorations was appreciated using the modified US Public Health Service criteria, regarding marginal adaptation, marginal discoloration, surface texture, abrasion, postoperative sensitivity and secondary caries. The odontal and periodontal parameters were followed up at four different times, day of the restorations, fourteen days, one month and three months after the procedure.

Results. It was observed a decreasing trend of plaque and bleeding indices. For the most of the restorations the probing depth was stable. After three months of follow up no significant changes were observed regarding marginal adaptation, marginal discoloration, surface texture, abrasion, postoperative sensitivity and secondary caries.

Conclusion. This preliminary study showed good clinical behavior of the class II restorations, realized by the proximal wall technique from odontal and periodontal point of view.

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Patients' perspective regarding the treatment of a tooth with chronic apical periodontitis

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Introduction. The therapeutic decision in dentistry is a complex cognitive process that implies taking several factors into consideration. The purpose of this study was to analyze the factors affecting the patient in choosing a therapy in case of a tooth (either anterior or posterior) with chronic apical periodontitis.

Material and methods. This survey included questions about treatment options for various scenarios presented, concerning anterior or posterior teeth with apical periodontitis, but it also included questions about the factors that might influence the patient's decision regarding the treatment, for the same pathology; the survey also included general questions regarding age, gender, monthly income, etc. After

descriptive statistical analysis was performed, preferences rates were subjected to Chi-square test (including McNemar test for significance). Statistically significant differences were considered when $p \leq 0.05$.

Results. Patients who participated in this study preferred the classical endodontic treatment and keeping the tooth on the dental arch. For the anterior tooth, the respondents preferred the apicoectomy. Regarding the role that patients prefer to play in the decision making process, only 19.2% of respondents wanted to have an active role.

Conclusion. Patients preferred mostly to keep the tooth on the dental arch, mainly with non-surgical endodontic treatment or with apicoectomy. Nonsurgical endodontic treatment was preferred in case of a posterior tooth. Regarding the role that patients preferred to have in the decision-making stage, we observed a predominantly passive role for survey participants.

High Frequency Ultrasonographic (HFU) assessment of Advanced Glycation End Products (AGEs) in soft tissues correlated with biological fluids. Preliminary results

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Introduction. Advanced Glycation End Products (AGEs), are mainly food derived, UV exposure, cigar smoking and are associated with oxidative stress, subclinical chronic inflammation, cellular and tissue premature aging by binding collagen fibers. Their assessment can be performed in biological fluids and tissues using quantitative and semiquantitative assays techniques. The purpose of this study was to evaluate AGEs (Carboxymethyllysine- CML) in biological fluids (saliva, urine) and sun-exposed skin using High Frequency Ultrasonography (HFU) and electrochemical sensor evaluations.

Material and method. The present pilot study is a cross-sectional analytical, observational and prospective investigation. For the included subjects (N=20) urine and stimulated saliva samples were harvested (by chewing cotton swabs before and after mechanical removal of dental plaque). Screen-printed electrodes were used for electrochemical tests of CML. Tissular accumulation of CML was indirectly assessed by HFU device. The evaluation was performed at sun-exposed tissue, assessing tissue's depth (thickness), pixels (px) count and density.

Results. Quantitative CML assessment showed that the mechanical dental plaque removal lead to a strong decrease in salivary CML evaluation showed inhomogeneous skin layer distribution regarding thickness, density and pixel count. Statistical analysis showed strong correlations between CML levels in tested fluids and both epidermal depth and pixel count.

Conclusion. CML could be considered a biomarker in the diagnose of chronic subclinical inflammation. HFU could be a diagnostic tool for monitoring general/oral cavity inflammatory pathology and diet-related disease.

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Removal of calcium hydroxide from root canals using three different methods of irrigation

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Introduction. Calcium Hydroxide is frequently used as a temporary dressing of the root canals. The removal of the calcium hydroxide before the final obturation is a key factor in the success of the treatment. The aim of the present study was to compare three different irrigation methods for calcium hydroxide removal.

Material and methods. The root canals of 18 monoradicular extracted teeth were prepared using Revo-S (Micro-Mega, France) and irrigated with sodium hypochlorite. The roots were split longitudinally with a disk and the halves were reassembled into the initial position using a wire and wax. In the root canals was placed calcium hydroxide followed by storing them in a humid medium for 7 days. This group of teeth was used for verifying the efficacy of 3 irrigation methods in removing calcium hydroxide: conventional irrigation, with ultrasonic activation, using the EndoUltra device and the irrigation using the self-adjusting file (SAF). After this step, the roots were dismantled and the efficacy of the calcium hydroxide removal was evaluated in the three thirds (apical, medial and coronal) using scores from 0 to 3.

Results. In the statistical processing of the data it was used the "T-Test" ($p=0.05$). It was found a significant difference between the SAF and the conventional groups, and between the ultrasound and the conventional groups. No difference was found between SAF and ultrasound groups.

Conclusions. No irrigation method managed to completely remove the calcium hydroxide from the root canals, but SAF and passive ultrasonic irrigation proved to be better.

Therapeutic attitude in partial edentulous elderly patients with pemphigus vulgaris

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Introduction. Elderly patients requiring masticatory rehabilitation often suffer from autoimmune disease which is more frequently in this group of age. Pemphigus vulgaris is an autoimmune disorder that involves the appearance of blisters, resulting in painful wounds on the skin and mucous membranes that will not heal. This disease limits the treatment options, when the oral mucosa of the edentulous crest is involved and it is also a contraindication for implant treatment.

Material and methods. Our case report includes a Romanian female patient from Cluj-Napoca, 84 years, diagnosed with pemphigus vulgaris. The patient presented masticatory disorders due to maxillary and mandibular partial edentulous status. The patient was under treatment for the last 3 years and we observed a relative stagnation of the evolution of the autoimmune disease.

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Results. In the 3rd and 4th quadrants the lesions of pemphigus on the jugal and crest mucosa were painful and the final decision was to rehabilitate the maxillary arch only, where the disease didn't affect the crestal mucosa. The upper arch was completely restored with a removable partial denture and a metal-ceramic bridge.

Conclusion. In this case we chose the prosthetic solution in order to achieve masticatory comfort and improve life quality. Periodical survey should be established in patients with pemphigus vulgaris in order to manage the disease evolution.

The psychological effect of orthodontic treatment

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Introduction. Despite the widespread expectation that orthodontic treatment improves psychological well-being and self-esteem, there is little objective evidence to support this. Therefore it is important to set out a study to claim the hypothesis that the psychological beings of patients are improving after the treatment.

Material and methods. We have created a closed answer questionnaire assessing the self-esteem and attentiveness of dental care before and after, in patients who underwent orthodontic treatment after 18 years of age. The questionnaire was designed with 9 closed answered questions using the Likert scale (5, 4, 3, 2, 1) being; strongly agree, agree, neither agree or disagree, disagree, strongly disagree. One question was left as an open answered question; this was to give a better insight on how the orthodontic treatment has affected the participant's life quality. Due to the Likert scale, and multiple answers to each question, the data collected are known as ordinal data. In order to get a P value less than 0.05, a chi-square test was conducted. The open answered question underwent sentimental analysis. As the data obtained was nominal, the median Likert scale answer (i.e. 'agree' is 4 on the Likert scale) was calculated by using the estimated equal distribution scale.

Results. The majority of participants were satisfied with the orthodontic treatment they received. For all the questions the median Likert score was 3.72-4.60, representing a continuous random variable assumption in the 5 point scale for these questions falls into category 4 'agree'. Based on open question 7a, a positive correlation between the increase in quality of life and receiving orthodontic treatment was found.

Conclusion. A positive correlation was found between orthodontic treatment and an increase in self-esteem and self-worth.

Additively manufactured secondary cranioplasty for a post-stroke epileptic patient

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Introduction. Post-stroke and post-traumatic epilepsy is a common complication and a frequent cause of hospital admission. These patients require appropriate multidisciplinary management and support. The aim of the paper is to present a viable and long-term solution for cranial reconstructions in craniotomized patients suffering from epileptic seizures.

Material and methods. A 61-year-old post stroke epileptic male, treated with an initial polymethylmethacrylate (PMMA) right parietal cranioplasty plate was referred to the department of Cranio-Maxillofacial surgery. He complained of mobile plate fragments, local discomfort and cranial asymmetry after head trauma during an epileptic seizure. Clinical examination and computer tomography revealed a comminuted PMMA plate fracture with displacement. Based on the CT, a new titanium, lightweight, five-point fixation cranial plate with a mechanically resistant biomimetic design was produced by 3D planning and printing techniques and the fractured PMMA plate was replaced.

Results. The results were assessed by clinical and imaging investigations and showed good symmetry with easy closure of the soft tissues, good marginal adaptation and excellent five-point fixation with an expected high impact resistance, considering the mechanical properties of titanium. No immediate or late postoperative complications were to be noted during follow-up.

Conclusion. Titanium cranioplasty is a feasible long-term skull reconstruction option for patients suffering from seizures and should be the primary option when compared to PMMA. Polyetheretherketone (PEEK) is also a modern, high impact resistant material used in cranioplasties. However, both titanium and PEEK cranioplasties have high production costs even for developing countries and future affordable materials and design methods should be investigated.

Imaging of the minor salivary glands tumors

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Introduction. Minor salivary gland tumors are relatively rare, but their imaging diagnosis is important because most are known as malignancies. The aim of this study is to evaluate the clinical-imaging characteristics of patients with minor salivary gland neoplasms and to make correlations with the tumor localization and their histopathological form.

Material and methods. A retrospective study of cases diagnosed as benign and malignant neoplasms of the minor salivary glands was performed. The data were collected from the medical records of patients at Oral and Cranio-Maxillofacial Surgery I, Oral and Cranio-Maxillofacial Surgery II, Oto-Rhino-Laryngology (E.N.T) Cluj-Napoca, over a period of 3 years. The study included all cases with histopathological diagnoses

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of salivary gland neoplasms (benign or malignant) located in the minor salivary glands. The sample was made up of 69 cases.

Results. Our study showed a 54.2% prevalence of the pleomorphic adenoma from all the benign tumors and a 38.2% prevalence of the adenoid cystic carcinoma from the malignant ones. The palate (42.1%) was the most common location of benign tumors and oral mucosa (33.3%) was the most common site for malignant tumor. The most frequent location of tumors, both benign and malignant, was the oral mucosa. In our study, females (38.4%) were more affected by benign tumors of minor salivary glands and men (26.6%) are affected by malignant tumors. In our study, CT was the most common method of examination followed by CBCT, IRM and panoramic x-ray. Perineural invasion is common in adenoid cystic carcinoma. MRI helped us to identify the extent of tumors in the deep spaces with perineural invasion and CT helped us to observe the bone invasion.

Conclusion. Pleomorphic adenoma was the most common tumor in minor salivary glands. The oral mucosa was the most common location of both benign and malignant tumors. CT and MRI are complementary examinations in the diagnosis and treatment of MSG tumors.

Periodontal status screening in a group of oropharyngeal cancer patients

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Introduction. Periodontitis is a chronic inflammatory disease associated with several systemic diseases. Of growing interest is the involvement of periodontitis in the oral cancer development. However, scientific data regarding the underlying biological mechanism that link periodontitis to cancer are inconsistent. The aim of this study was to assess the periodontal status of oral cancer patients and their behaviors towards oral health.

Material and methods. A number of 36 patients with oral and oropharyngeal cancer were recruited for this study from the Cranio-Maxillofacial Surgery Department. Patients information were collected by means of a questionnaire and from patient's medical files. All dentate patients underwent a full mouth periodontal examination according to the international protocols.

Results. Patients were predominantly men, with an average age of 61 years. Among participants more than a quarter was completely or subtotal edentulous. Participants were current or former heavy long time smokers with an average of over 20 years of smoking. The periodontal examination revealed an average IHI of 85% and BOP of 65%. All dentate patients had numerous missing teeth, deep periodontal pockets and extensive attachment loss.

Conclusion. Patients recruited for this study had extremely poor periodontal status. The majority of participants were current or former heavy long time smokers. Smoking is a recognized risk factor in cancer development but it is also significantly associated with periodontitis severity due to its immunomodulatory effects and alteration of the oral microbiome. Therefore local chronic inflammation and the vast array of periodontopathogenic bacteria might contribute to oropharyngeal cancer development and progression. Future research is needed to certify this hypothesis.

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Pilot study regarding the effects of full-mouth caries treatment on saliva volume and buffer capacity in children

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Introduction. This study aimed to determine the effect of one-stage full mouth restorations on saliva buffer capacity in children with high carioreceptivity.

Material and methods. This study included 15 patients, aged 7 to 13 years old, with a mean DMF-S index of 7.5. A written informed consent was obtained from the legal representatives. Three previously trained clinicians (kappa index for inter-examiner correlation = 0.80) performed anamnesis, clinical examination according to International Caries Detection and Assessment System and collected socio-demographic data. Standard at rest and stimulated saliva samples were collected at 2 times: at the beginning of the study and respectively one week later. The buffer capacity was evaluated by using chair-side kits.

Results. A statistically significant increase was observed in the buffer capacity after one week following the treatment of existing cavitary carious lesions (ICDAS \geq 3), compared to baseline values ($P < 0.05$). One-stage full-mouth restoration has significantly reduced the number of patients with a low-buffer capacity, from 40% (baseline) down to 20%.

Conclusion. The one-stage treatment of deep caries can increase the saliva volume and buffer capacity, improving also the rehydration time. Further studies should be performed on larger number of patients in order to confirm these findings.

Protocol of extractions procedures under bisphosphonate therapy – animal model study

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Introduction. Osteoporosis is a bone cellular disorder being characterized by decreased bone mass and bone tissue integrity, leading to fragility and decreased bone hardness. Bisphosphonates are the most commonly used medication for the treatment of osteoporosis in postmenopausal women. The aim of present study is to assess the risk of maxillary bone necrosis occurrence after dental extractions procedures under bisphosphonate therapy.

Material and method. This study was conducted on 30 female Wistar rats with an average age of 8 weeks. Osteoporosis was induced by bilateral ovariectomy and treated for 2 weeks (before dental extractions) with, bisphosphonates: Ibandronic acid and Denosumab). Sedation for dental extraction was performed by intraperitoneal anesthesia. The syndesmotomy and the extraction of the upper central incisor were performed and resorbable suture thread 5.0 was used. Postoperative, the animals were kept in a stable and clean environment. After two weeks, histopathological examinations of the postextractional bone site were performed.

Results. Histopathological examination revealed the presence in the postextractional bone site of the following aspects: severe bone osteonecrosis, severe

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bone resorption, increased number of osteoclasts, presence of a severe inflammation with degenerated and intact neutrophils, discrete or moderate granulation tissue.

Conclusions. Bisphosphonates are useful for the treatment of osteoporosis, but their administration can have a secondary effect necrosis of the maxillary bones. Working protocols are needed for oral surgical procedures that need to be constantly updated according to the new results obtained from the fundamental and clinical demands.

Characteristics of translucency for three different flowable giomers

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Introduction. The main complain of patients today, when addressing dental professionals, is aesthetics. The big variety of dental materials, gives dental practitioners the opportunity to choose the best solutions. The choice for direct restorations in the aesthetic area takes into account mainly the optical properties of selected materials.

Objective. The purpose of this study was to compare the translucency parameter of three different flowable giomers (Beautifil F02, F00 and F03), in A2 color.

Materials and method. A number of 63 samples (21 for each material, diameter 10 mm, thickness 1 mm) were prepared using a round mold (Smile Line, CH). On the free surface a Miller strip was applied, the photo polymerization was done for 20 seconds.

Color was measured according to the CIEDE2000 scale relative to the standard illuminant D65 over a white tile and a black tile, using a spectroradiometer (Spectra Shade). For each specimen, the color measurement was repeated three times. The relative translucency parameter RTP00 was calculated with the DE00 formula and it is the difference between the $L^*a^*b^*$ parameters of the samples over a white and a black background (L^* luminosity parameter, a^* chromatic parameter on the red-green scale and b^* on the yellow-blue scale).

Results. The relative translucency parameter RTP00 varied between 28.46 and 32.02 for F00 material, between 28.76 and 32.94 for F02 material and between 28.05 and 33.46 for F03 material.

RTP varied significantly between F00 and F02 (p -value=0.00), with a 95% probability F02 Beautifil flow has a greater translucency than F00 Beautifil flow plus.

RTP between F00 and F03 varied significantly (p -valued=0.01), with a 95% probability F03 has a greater translucency than F00. RTP did not differ significantly (p -value=0.4) between F02 and F03 materials.

Conclusions. Optical properties of the recently introduced giomers are variable; their translucency has to be selected with care in the restoration of anterior teeth.

Interactive methods of teaching ethics to students in dental medicine: the role-play

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Introduction. Before starting to teach a topic, whatever it may be, any teacher should think about the mechanisms of thinking that they need to mobilize in order to achieve their goal: receiving the message and passing on the knowledge. Teaching Bioethics to students in Dental Medicine is a major challenge: how to motivate them and how to show them the place and purpose of this discipline between other curricula subjects.

Material and methods. We will describe the interactive methods to teach in the university, especially to students in Dental Medicine. The role-play is a very good tool to put students in complex situations, to ask them to simulate a case, by playing roles, and to provide arguments sustaining their point of view. In the end the group work together on analyzing the presentation and to detect ethical issues related to the case.

Results. Our role-play method contains three steps: the preparation, the presentation of the role-play and the analysis. The ethical issues related to the case and the conflicts between principles, values and interests are incorporated in the role-play by any character. After analyzing the case and alternative solutions, we summarize the ethical key-points and issues related to the case and make the conclusion.

Conclusion. We believe that bioethics topics should be taught using new forms, adapted to the new generations of students, communicating their meaning and using the same language. This is the reason why we will present and argue in favor of using the role play in teaching Ethics to students Dental Medicine.

Acknowledgements. Our method was inspired and developed with our students, during courses of Bioethics and Ethics and Integrity in Academia within Faculty of Dental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania.

Clinical indications and radiation doses of cone beam computed tomography in orthodontics

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Introduction. Cone beam computed tomography (CBCT) is considered a low dose radiological examination, but it exposes patients to higher radiation doses compared to conventional radiographic imaging. Orthodontic treatment is started at young ages, when the detrimental health effects associated with ionizing radiation exposures are more important because of the higher radiosensitivity and longer lifespan. The aim of our study was to review the main indications of CBCT in orthodontics and to evaluate the radiation doses and potential risks of CBCT irradiation in pediatric patients.

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Material and methods. We searched PubMed for publications in English language. The articles published in the last 10 years were selected. For the analysis of radiation doses, the information that specified the CBCT device, the exposure technique, the type of the phantom and the dosimeters were included.

Results. Even though CBCT provides a detailed image of the anatomical truth, the routine use of CBCT for all orthodontic patients is currently not supported by strong evidence. The conclusion of several guidelines was to prescribe necessary radiographs only after individual case examination and only if justified for an improved diagnosis, treatment planning and treatment outcome. Regarding radiation doses, these vary widely, depending on the type of the CBCT machine and the exposure factors. There is a need of studies regarding irradiation dose optimization that consider patient factors, such as gender or age, image quality and acceptable dose levels in controlled settings.

Conclusion. The effects of ionizing radiation in pediatric patients following CBCT exposures and the cumulative risk of radiation should be further investigated. By assessing the benefits and risks of CBCT based on up-to-date literature, our study aimed to discuss the use of CBCT in orthodontics and to highlight the responsibility of the orthodontist towards a moderate use of CBCT in daily practice.

Anxiety and awake bruxism among young adults

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Introduction. Awake bruxism is a potential risk for oral hard tissue damage, temporomandibular disorders and failure of dental restorations. The literature encloses in a multifactorial etiology for this behavior, with multiple hypotheses, regarding the central etiology. Identifying the determinants of awake bruxism among teenagers will enable development of preventive interventions for those at risk. The aim of this study was to determine the association between anxiety and awake bruxism in healthy young adults.

Material and methods. Two hundred and ten healthy subjects, aged below 25 years, males and females, had to answered a personalized questionnaire. The questionnaire had two parts: the first part evaluated the presence of self-reported (SR) awake bruxism, oral habits, facial pain and masticatory disturbances; the second part analyzed the anxiety levels of the general state of the subject. The data was analyzed using MedCalc Software version 17.4 program, with statistical significance at $p < 0.05$.

Results. The frequency of awake bruxism was 15.2%. We noticed a higher score for TMJ pain ($p = 0.05$) and masticatory disturbances in subjects with awake bruxism. The anxiety level score was significantly higher in subjects with awake bruxism ($p = 0.012$). In subjects with bruxism, the score for anxiety were significantly higher in the females compared to males.

Conclusions. This study indicates a scientifically proven correlation between awake bruxism and TMJ pain. The studies performed until now, including the present one, showed that psychological factors with focus on anxiety could be considered increasing factors of the awake bruxism.

New biomembranes for guided bone regeneration

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Introduction. In guided bone regeneration (GBR), a surgical procedure for promoting new bone formation, a barrier membrane is used to block the proliferation of regenerated connective tissue or to provide direct drug delivery and mechanical support. GBR membranes are based on a variety of polymers and can be prepared by using different methods, like electrospinning.

Materials and methods. PCL-biomembranes loaded with 0, 5; 1 and 2 wt % of GEN and 0; 5; 10; 15 wt % of n-HAP were obtained through electrospinning and dried under vacuum for 48 h before testing. The morphology of the electrospun biomembranes was examined by scanning electron microscopy (SEM). The antibacterial effect was evaluated on different bacterial strains: *P. Aeruginosa* (PMG 6395), *S. Aureus* (ATCC 6538), *S. Mutans* (ATCC 25175), *E. Coli* (ATCC 2592) by disk diffusion assay. The cytotoxicity was evaluated by running the MTT assay at 24 h on human adherent keratinocytes.

Results. The agar disk diffusion assay showed a clear inhibition zone, which was increasing with the higher content of GEN. All biomembranes showed good biocompatibility. The SEM images showed an increasing diameter of the electrospun fibers of the biomembranes with the increasing content of n-HAP.

Conclusions. The antimicrobial activity of the GEN/n-HAP loaded biomembranes depended on the GEN quantity. The biomembranes with the highest GEN content showed the largest inhibition zone. The biocompatibility was higher for the biomembranes with increased n-HAP content. The developed electrospun GEN/n-HAP loaded biomembranes could be promising third-generation biomembranes for GBR.

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Bruxism and dental occlusion correlations

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Introduction. This study aims to describe the bruxism as a health phenomenon and to analyze the parameters that can influence it, based on a case-control distribution. The objectives were to observe the differences of the incidence of bruxism correlated with general factors (stress, snoring, presence of obstructive sleep apnea syndrome); with local factors (premature contacts; occlusal interferences, joint impingement, vicious habits); and evaluation of the post-therapeutic evolution.

Material and methods. A number of 100 patients (51 women and 49 men) were analyzed. Subjects were divided into two groups: the case group (50 subjects)

and the control group (50 subjects). Personalized questionnaires were used for data capturing. Statistical analysis was performed.

Results. Bruxism was positively correlated with the incidence of premature contacts / interferences ($Hi2 = 23.4$; $OR = 8.1$), with joint damage: joint pain ($Hi2 = 36.95$; $OR = 18.85$), joint fatigue ($Hi2 = 46.31$; $OR = 27.98$), joint noises ($Hi2 = 46.31$; $OR = 27.98$); with stress and snoring ($Hi2 = 13.07$; $OR = 5.25$). Patients underwent treatment with occlusal splints. The reduction of joint pain (80%), the increase of the masticatory efficiency (83%) and the reduction of the incidence of snoring (60%) were observed.

Conclusions. From a clinical point of view, the study shows that the effects of bruxism can be corrected and controlled therapeutically. Most of the subjects reported the improvement of the quality of life with treatment.

Radio-opaque and radio-lucent lesions of the mandible – ortopanthomographic analysis

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Aim. To analyze on orthopantomography (panoramic) radiographs the space occupying mandibular lesions, both radiopaque and radiolucent ones, according to different parameters, in order to establish a presumptive diagnosis.

Material and methods. The study reviewed retrospectively 988 panoramic radiographs, performed in a 9 month period, mean age of the patients 42.5 [16-81]. The images were analyzed by 2 different examiners, a 6th year Dental Medicine student and a radiologist.

Results. 94 panoramic radiographs (9.5%) presented radio-opaque or radiolucent space occupying lesions in the mandible. From this lot, the majority, 84%, were radiolucent images, 15% were sclerotic lesions and 1% showed mixed pattern. Odontogenic lesions were found in 88.3% of the cases only 11.7 being non-odontogenic. As lucent images the most common diagnosis was radicular cyst (30.85%) with a male:woman ratio of 2.22:1, mostly in people aged between 30-50. Second most frequent diagnosis was the periapical granuloma (29.79%) followed by residual cyst in 17.02% with a male:woman ratio of 1.28:1. Other diagnosis were dentigerous cyst, odontogenic keratocysts and sarcoma. Opaque lesions presented as cementoma, odontomas or sclerotic islands. Many of the morphological features of the lesions such as border, cortical expansion, homogeneity, periosteal reaction, provided the accurate diagnosis.

Conclusion. A good quality panoramic radiography can still offer sufficient imaging features when considering space occupying lesions in the mandible, for the practitioner to reach a presumptive diagnosis and to correctly manage the patient.

CBCT assessment of maxillo-facial bone tumors in pediatric population

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Aim. To detect and assess by using CBCT, the maxillofacial bones space occupying lesions in the pediatric population, as well as to establish correlations between the imaging characteristics and the histopathology result.

Material and method. The study group included retrospective CBCT examination of 27 patients admitted in the Maxillofacial Surgery II in Cluj-Napoca in two years interval. Several features were assessed by using individualized CBCT reconstructions: density, contour, location, the relationship with nearby teeth and structures, e.g.

Results. There were 2 patients' age under 10, 9 patients between the ages of 11 and 14 years and 16 adolescents, aged over 15. Only 6 lesions were hyperdense ones the majority being hypo-dense, with cystic aspect on CBCT. 70% of the lesions were located in the mandible, the rest at maxillary bone or sinus. 74% of the lesions presented the sharp contour, results revealing benign etiology, 3 lesions being malignant ones. CBCT offered important information regarding the characteristics of the lesions, and their relationship, few lesions presenting atypical features, an example being an odontogenic keratocyst with multilocular presentation.

Conclusion. In children and adolescent lesions detected in the maxilla and mandible were mostly benign, but malignancy was still present. CBCT examinations allowed the analysis of the three-dimensional characteristics bone lesions, allowing careful evaluation of the anatomical elements.

Gingival mesenchymal stem cell behavior under platelet-rich fibrin stimulation – preliminary results

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Introduction. Periodontal regeneration is an inconsistent outcome in the treatment of infrabony defects. Proper stimulation of mesenchymal stem cells (MSCs) could lead to promising results. Platelet-rich fibrin (PRF) is an autologous product which contains multiple growth factors. The current in vitro study aimed to investigate the behavior of gingival MSCs (gMSCs) cultured in media supplemented with PRF.

Material and methods. MSCs isolated from healthy gingival tissue, were grown in standard media and characterized. For PRF preparation, tubes of 10 ml of blood were collected without anticoagulants and centrifuged. The experimental culture media were prepared as follows: 5% and 10% PRF by adding the corresponding PRF volume to the standard medium, 10% PRF-FCS (fetal calf serum) by replacing the FCS from the standard medium with PRF. The media were changed every 3 days. The morphology of gMSCs was analyzed via optical microscopy. At 72 h and 7 days, a proliferation assay was performed.

Results. After 72 h, the highest proliferation was in the gMCSs from the control group, with 10% PRF group showing significantly lower results. After 7 days, 5% PRF group showed significantly higher proliferation, whereas the proliferation in 10% PRF and 10% PRF-FCS groups was significantly lower. The optical microscopy images showed the cells maintained their stem cell morphology through the entire experiment. The contact inhibition appeared: cell population was influenced by the availability of space provided by PRF components.

Conclusion. In general, PRF supplemented media induced lower cell viability. Only 5% PRF, after 7 days of culture, induced significantly better results. The microscopy morphological aspects support these results. Higher concentrations of platelet concentrates could negatively influence cell proliferation.

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Treatment of mandibular condylar fractures in pediatric patients

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Introduction. Mandibular fractures in children are relatively rare, being a particular kind of pathology, as they take place within a rapidly growing organism. Most often the mandibular fractures involve the condyle by indirect trauma. The choice between the conservative treatment or the surgical one is still debated in the literature considering the particularities of the pediatric patient. Given the condyle role in the jaw development, these fractures can lead to severe complications. Hence, the treatment must be differentiated according to multiple factors, such as the degree of condylar displacement or mouth opening, the level and number of fractures, the contact between fragments and the state of dentition.

Material and methods. We present a review of the most recent publications that were selected based on keywords entered in the PubMed database. We will also present the case of a 14 year old female patient with a right condylar fracture with severe medial displacement of the condylar head associated with major functional impairments. The patient was surgically treated (open reduction and internal fixation) by transparotid approach. Postoperatively an elastic intermaxillary fixation was applied for two weeks.

Results. Most of the pediatric condylar fractures can be treated conservatively with a good clinical outcome. The surgical treatment is reserved for fractures with severe medial displacement of the condylar head associated with significant functional impairment, in cases of loss of ramus height and for the bilateral condylar fractures. Following the surgical treatment applied in our case we obtained a complete restoration of the functional disorders in a short healing time with a low morbidity.

Conclusion. Improved functional results after surgical treatment of severely displaced condylar fractures are reported in pediatric and adult patients. In selected cases of pediatric condylar fractures, the surgical treatment should be considered.

Cavernous hemangioma of the temporalis muscle. A case report and current data from the literature

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Introduction. Hemangiomas are benign vascular neoplasms that usually develop in the skin or subcutaneous tissue with only 1% of all cases occurring in the muscles. In the head and neck region, the masseter is the most frequently affected, whereas intra-muscular hemangiomas of the temporalis muscle are extremely rare.

Materials and methods. We have searched the current literature data using the PubMed as the main engine with the following terms: “hemangioma”; “intramuscular”; “temporalis”; “muscle”. No time limit was applied. We would also like to present a case report from our daily practice.

Results. There are 29 cases mentioned in the literature. No sex predilection was found and the maximum incidence is in the third decade. It presents as a slow-growing mass with distinct margins, mobility and do not exhibit any of the vascular signs. CT is useful but MRI is the method of choice in defining the vascular nature of the tumor. Surgical excision with safety margins is recommended, as it allows a histological evaluation and it reduces the local recurrence rate. Other nonsurgical treatments include embolization, radiation, injection of sclerosing agents or corticosteroids and electrocoagulation. In our case a 3 years old female patient with a history of 1 year of painfully swelling in the right temporal area was referred. CT and MRI examinations revealed a cystic tumor with septa and vessels measuring 4.7/3.5/2.8 cm. The patient underwent surgical treatment with histopathological report of cavernous hemangioma. Due to the careful closure of the temporal fascia, no hollowing effect was observed. No recurrence reported until this date.

Conclusion. Combined with radiologic findings, cavernous hemangiomas should be suspected when the mass occurs in the temporal region even in the very young patients. The surgical treatment is the most common choice but it should be individualized for each patient.

Influence of dental office stress on two biometric variables

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Introduction. In this study, we intended to observe if the stress in the dental office has an influence on the oxygen saturation and on the heart rate in children. In addition, we want to identify the situation that can favor a higher heart rate and a variation in the oxygen saturation.

Material and methods. The heart rate and the peripheral oxygen saturation, before, during and after the clinical appointment in the dental office, were determined

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on a sample of 30 children from 4 to 15 years, who addressed the Department of Pedodontics of the University of Medicine and Pharmacy of Cluj-Napoca. It was used the pulse oximeter MeasuPro OX100 for measure the parameters in the waiting room, during the treatment and after the treatment, a questionnaire and a Visual Facial Anxiety Scale.

Results. The heart rate was increased in patients less than 8 years old, in case of consultation without specific reason, in case of pain, when the high-speed handpiece or even micromotor were used. The peripheral oxygen saturation did not undergo any statistically significant difference at different times of the consultation in the dental office.

Conclusion. Knowing the factors that cause the most stress in the young patients will help the dentist to take the best measures to avoid or reduce them, so that the patients remain relaxed and compliant during the treatment.