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MEDICINE Basic Sciences

Antitumor effects induced by magnetic hyperthermia using functionalized magnetic nanoclusters

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5) Department of Pharmaceutical Physics – Biophysics, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Our study aimed to test the antitumor effects of magnetic hyperthermia using two newly synthesized magnetic nanoclusters (MNC) in vitro on human cell lines: normal dermal fibroblasts and tumor cell lines of melanoma (A375) and colon cancer (CACO2).

Material and methods. $Fe_{3}O_{4}$ magnetic nanoclusters were synthetized by solvothermal method, functionalized with DHBH and characterized by TEM, XPS, FTIR. Biological studies tested cell toxicity, cellular uptake (TEM), apoptosis induction by flow cytometric analysis (annexin/PI staining), mitochondrial potential and caspase (ELISA), oxidative stress by amplex red assay and malondyaldehyde.

Results. MNC were packed into clusters, with well-defined near spherical shapes and size ~ 200 nm, with high value of saturation magnetization. Biological tests showed good MNC biocompatibility. Magnetic hyperthermia decreased viability and increased apoptosis in melanoma and colon cancer cell lines without significant decrease in normal fibroblasts and significantly increased oxidative stress in melanoma cells.

Conclusion. MNC exerted strong and selective antitumor effects against two types of human tumors, following magnetic hyperthermia.

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Iron modulation in experimentally induced cardiac pressure overload

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 Department of Cell and Molecular Biology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania Iron metabolism is implicated in the majority of cardiovascular pathologies, in both acute and chronic settings.

We studied the effects of iron chelation on a rat model of hypertension. Suprarenal abdominal aortic constriction was achieved surgically, with a duration of nine weeks. Deferiprone (100 mg/kg/day), was administered for two weeks. Pressure overload resulted in increased inflammation, fibrotic deposition, oxidative stress, left ventricular hypertrophy, and mitochondrial iron.

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Deferiprone reduced cardiac IL-6, MDA levels, mitochondrial ferritin levels, and hypertrophy, without affecting circulating iron levels or ejection fraction.

Iron molecules pose ambivalent effects in cardiovascular pathology, with beneficial effects of iron redistribution, mainly in the mitochondria.

Medical undergraduate students' perception of their skills in digital literacy

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Introduction. Information and Communications Technology is a mandatory discipline in Romanian high schools. Its curriculum depends on the type of high school studies, for example: theoretical (science or humanities), technical, vocational, or services and economics. Most of the students opting for the Faculty of Medicine are high school graduates coming from humanities high schools, but not exclusively. We aimed to evaluate how the first-year students, from the Romanian section - Medicine program, assessed their digital literacy skills.

Material and methods. We created an online questionnaire regarding the students' perception of general computer use skills, Internet browsing, online information search skills, digital communication skills, and the use of programs from the Microsoft Office package. The eligible participants were first-year students (2022-2023 academic year), Faculty of Medicine, Romanian section, Iuliu Hațieganu University of Medicine and Pharmacy Cluj-Napoca. All eligible participants were invited to self-evaluate their digital literacy skills.

Results. Two hundred and twenty-four students participated. About 90% of respondents declared that they have good skills in overall computer use, but only 55% understand basic computer terminology at an average-expert level. Analyzing the statements about skills at the average-expert level: 85% have knowledge about using the Internet, 83% can use the keyboard well, 93% know how to use an email, 57% consider themselves suitable for computer-assisted training. They claimed to be average-expert-level users of the Microsoft Office suite knowing 90% about Word, 88% about PowerPoint, and 54% about Excel.

Conclusion. Only half of the respondents understood basic computer terminology, despite the fact that the majority of respondents said they had general computer skills. While most respondents were average-expert-level knowledgeable in Word and PowerPoint, only about half of them were proficient in Excel.

Thermosensitive hydrogel-assisted delivery of dexamethasoneloaded second-generation liposomes during cochlear implantation - pilot study

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Corresponding Author: Cristina Maria Blebea e-mail: cristina blebea@yahoo.com **Introduction.** A profound sensorineural hearing loss can be rehabilitated with the help of an advanced hearing device, the cochlear implant. As the criteria for cochlear implantation have expanded in the last years to also include patients with residual hearing, researchers and clinicians try to improve the performance of this prosthesis by protecting the residual hearing. In our experimental pilot study, we aimed to evaluate the potential otoprotective effect of locally administered thermosensitive hydrogel containing microcapsules loaded with dexamethasone (Dex) immediately after cochlear implantation. The evaluation of the potential otoprotective effect of this compound was carried out by determining the hearing thresholds and the histological measurements of the inner ear tissues.

Material and method. The study included seven adult male Rattus norvegicus rats with no signs of otitis media. Both ears were implanted with an analog electrode under general anesthesia under sterile conditions. $30 \ \mu L$ of hydrogel containing microcapsules loaded with dexamethasone concentration 1.5 mg/ml were inserted into the study ear. The contralateral ear was considered as control, and after the same implantation procedure, we applied $30 \ \mu L$ of free Dex solution with a concentration of 1.5 mg/ml. Auditory thresholds were determined preoperatively and seven days postoperatively by brainstem auditory evoked potentials. The histopathological examination was performed after the last hearing test.

Results. The mean auditory thresholds determined postoperatively did not show statistically significant differences for click stimuli or low frequencies. We can interpret this aspect as a lack of cellular toxicity of the compound used in the study. Analyzing each frequency tested individually, only at 32 kHz, the Dex-hydrogel group displayed a significantly lower average hearing threshold shift compared to the Dex group; the difference between the two means was 12.15 dB, a statistically significant difference (Control=95 dB, Dex-hydrogel=82.85 dB, p=0.002, p=<0.05, t-test). As the tested frequencies decrease, so does the degree of protection of auditory thresholds; thus, the differences in the mean thresholds of the two groups are not statistically significant for 24 kHz, 16 kHz, 8 kHz, or click stimuli. Thus, we witness a predominant otoprotective effect on high frequencies. Histological evaluation of the elements of the inner ear does not reveal osteoneogenesis, fibrosis, or rupture of the modiol or basement membrane in any of the groups, but several elements characteristic of an inflammatory reaction. The evaluation of the general degree of inflammation of the cochlear elements does not show statistically significant differences between the two groups.

Conclusion. The use of dexame thas one loaded in hydrogel-embedded microcapsules shows better protection of hearing thresholds at high frequencies in cochlear implanted ears compared to free dexame thas one. The dexame thas one administration vector does not show ototoxicity. If this pattern of protection of hearing thresholds is maintained for longer periods, this form of administration may be useful also in hearing loss caused by chemotherapy or noise exposure, where high frequencies are predominantly affected.

Acknowledgment. This work was supported by the CNCS-UEFISCDI, project number PN-III-P2-2.1-PED-2019-381.

Gut microbiome and hepatocellular carcinoma – new perspectives

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Corresponding Author: Iuliana Nenu e-mail: iuliana.nenu@gmail.com **Introduction.** Despite substantial advances in therapy, the burden of hepatocellular carcinoma (HCC) has increased by 75% in the past three decades. The intestinal microbiome is responsible for inducing resistance to antitumoral drugs. In response to this unmet need, the present study aimed to investigate the role of combining a probiotic (Streptococcus rhamnosus) with regorafenib in improving therapeutic response in an animal HCC model.

Material and methods. Cirrhosis and hepatocellular carcinoma were induced on two-week Swiss male mice using diethylnitrosamine (DEN - 1 mg/kg) one intraperitoneal injection following carbon tetrachloride ($CCl_4 - 0.2 \text{ ml/kg}$) intraperitoneal administration two times per week for six weeks (between weeks 8 and 14). Abdominal ultrasound was performed to validate the presence of liver tumors. Then, the mice were divided into four groups: in the first group (control group), the mice were treated with vehicle, the second group received Regorafenib (Rego) (10 mg/kg one time per day for one week), in the third group probiotic (100 mg/day for one week) was administered, and the last group received the combination of Rego and Pro. Liver tumor and intestinal inflammation, oxidative stress and apoptosis markers, histopathological necrosis rate were assessed.

Results. IL-6 and IL-1 levels from both liver and intestine fragments diminished in the groups treated with probiotic compared to control but statistically insignificant (p>0.05). Similarly, malondialdehyde levels dropped when Pro was added to Rego (p<0.05). Tumor necrosis factor-alpha (TNF- α) and TLR-4 have a decreased levels in the combined regimen (p<0.05) and in the Rego group (p<0.05) when compared to the control group and correlate with the histological findings. Likewise, nuclear factor- κ B (NF- κ B) and IKK α expression decreased in the combined regimen. Intestinal inflammation determined by assessing lipopolysaccharide (LPS) is reduced in the groups where probiotic was administered compared to the control and Rego group (p<0.05).

Conclusion. The combination of Streptococcus rhamnosus probiotic with Regorafenib treatment improves the antitumoral activity of the multikinase inhibitor in animals with experimental HCC and might represent a novel and promising approach.

Acknowledgement. The results of this research were partially funded by the Iuliu Hațieganu University of Medicine and Pharmacy- (Ph.D. study Iuliana Nenu—4322/01.10.2018).

Cardiovascular modifications in experimentally-induced diabetes mellitus treated with *Cornus mas*

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1) Department of Physiology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Several recent studies have proposed natural extracts as treatment for numerous pathological mechanisms like inflammation, oxidative stress, hyperglycemia. These natural extracts can be used as simple solutions or as functionalizing agents for

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Corresponding Author: Daniela-Rodica Mitrea e-mail: rdmitrea@yahoo.co.uk gold nanoparticles (AuNPs), compounds that showed an increased delivery to target organs. Our focus was the cardiovascular system as we aimed to determine the effects of *Cornus mas* L., administered orally, either as a simple solution or as functionalized gold nanoparticles – in diabetic overweight rats.

Material and methods. A high fat diet was given to adult Sprague Dawley female rats for 8 months until their weight increased to 600 ± 20 g. During the last 3 days of the 8th month of the study, diabetes mellitus was induced with streptozocin. Following this, for all hyperglycemic rats, the high fat diet was continued for another month, while they also received the allotted treatment for their randomly assigned group: CMC group carboxymethylcellulose (CMC); Insulin group - insulin; Pioglitazone group - pioglitazone in CMC solution; AuNPsCM group - gold nanoparticles functionalized with *Cornus mas* L. extract (AuNPsCM); *Cornus mas* group - *Cornus mas* L. extract. Oxidative stress and inflammation parameters were evaluated in the aorta and heart samples. The ultrastructural modifications were assessed only in the aorta wall.

Results. *Cornus mas* L. simple solution significantly decreased the malondialdehyde and TNF- α in the heart and aorta wall samples, along with an endothelin-1 decrease in the aorta, while GSH/GSSG ratio was increased in heart homogenate. AuNPsCM, in both aorta and heart, significantly decreased TNF- α and increased iNOS.

Conclusion. Cornus mas L. simple solution decreased the oxidative stress and inflammation in aorta and heart. AuNPsCM had conflicting effects on inflammation, in aorta and heart homogenate.

Antioxidant protection in rats with thyroidectomy

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Corresponding Author: Mădălina Moldovan e-mail: moldov.mm@gmail.com **Introduction.** Thyroidectomy produces oxidative stress that may be decreased by antioxidant treatment. Curcumin and quercetin are natural substances with antioxidant, anti-inflammatory and anti-cancer properties that may re-establish the redox balance after thyroid tissue removal. The study investigated the antioxidant properties of curcumin and quercetin administered each in two different doses in rats with hemithyroidectomy.

Material and methods. Albino Wistar adult male rats with hemithyroidectomy received, for 14 days, antioxidant treatment after they were randomly allocated in the following groups: group CMC - carboxymethyl cellulose (CMC) 1%; Que 20 group - quercetin 20 mg/kg/day; Que 40 group - quercetin 40 mg/kg/day; group Euthyrox - 1.3 µg/kg/day of sodium levothyroxine; Curcumin 15 group - 15 mg/kg/day of curcumin; Curcumin 30 group - received 30 mg/kg/day of curcumin. Oxidative stress was investigated through malondialdehyde, reduced glutathione and oxidised glutathione from blood and from remaining thyroid tissue. Thyroxine and TSH levels were also determined.

Results. In serum, the administered antioxidants significantly decreased lipid peroxidation, with curcumin showing higher protective effects. In the remaining thyroid tissue, quercetin and curcumin in higher doses significantly decreased malondialdehyde and increased antioxidant protection. These antioxidants did not modify the hormone levels.

Conclusion. Quercetin and curcumin, both in serum and in the remaining thyroid tissue, protected against lipid peroxidation and increased the antioxidant protection.

Anti-inflammatory and antioxidant activity of Dichrostachys cinerea fruit extracts in rat-induced chronic inflammation

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Corresponding Author: Raluca Maria Pop e-mail: raluca parlog@yahoo.com **Introduction.** Dichrostachys cinerea (DC) is a terrestrial herbaceous plant that belongs to the Mimosaceae family and is widely spread in Africa and India. It is commonly used in traditional medicine as a natural remedy to treat or prevent various inflammatory diseases because of its anti-inflammatory and antioxidant effects. The aim of this study was to investigate the anti-inflammatory and antioxidant effects of DC fruit extracts effects.

Material and methods. The rat model of chronic inflammation was obtained using complete Freund's adjuvant (CFA). Fruit ethanolic extract was characterized using Liquid Chromatography coupled with Mass Spectrometry (LC-MS). Sixty Wistar-Bratislava rats were divided into 6 groups. The first group was the sham group which included rats with no inflammation while the second group was the control group which included rats with CFA-induced inflammation. Both these groups received normal saline solution. In all other groups, chronic inflammation was induced and the rats were differently treated with sodium diclofenac (7.5 mg/kg) and with three different concentrations of DC fruit ethanolic extracts as follows (207 mg gallic acid equivalents (GAE)/ mL, 105 mg GAE/ mL and 53 mg GAE/mL, respectively). Edema assessment and thermal hyperalgesia tests were performed one day before CFA injection and on days 1, 8, 15, 20, and 30. Plasma levels of interleukin-6 (IL-6), tumor necrosis factor α (TNF- α), and IL-1 β were evaluated. Serum oxidative stress status was also evaluated by measuring nitric oxide (NO), malondialdehyde (MDA), and total thiols (THIOL).

Results. The ethanolic DC extract was rich in polyphenolic compounds like flavan-3-ols, flavone glycosides, and proanthocyanidins. The maximum anti-inflammatory effect was registered on day one after CFA-induced inflammation. The values of IL-1 β and IL-6 pro-inflammatory cytokines and most of the oxidative stress parameters were significantly reduced when compared with the control group, in a dose-dependent manner.

Conclusion. These results revealed the potential anti-inflammatory and antioxidant effects of DC fruit ethanolic extract, some of DC fruit ethanolic extract results being comparable with those of diclofenac.

Acknowledgment. This research was funded by "Bourses de recherche doctorale et postdoctoral « Eugen Ionescu » AUF, grant number 12/2020".

The relationship between paroxonase-1 and atrial fibrillation

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 Department of Pharmacology, Toxicology and Clinical Pharmacology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Human paroxonase-1 (PON-1) is a high-density lipoprotein (HDL)-associated enzyme that inhibits the oxidation of low-density lipoprotein (LDL) and HDL particles. Both PON-1 level and PON-1 arylesterase activity (AREase) have been found to be decreased in patients with atherosclerosis, obesity, or chronic kidney disease. Since oxidative stress plays an important role in atrial fibrillation (AF)

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Corresponding Author: Sabina Istratoaie e-mail: sabina.istratoaie@gmail.com pathogenesis, we hypothesized an association between PON-1 and AF. To the best of our knowledge, previous studies have not evaluated the role of PON-1 in AF.

Material and methods. Sixty seven patients with atrial fibrillation and 59 age- and sex-matched controls were enrolled in the study between December 2019 and December 2020. Serum PON-1 concentration, AREase, total cholesterol (TC), LDL, HDL triglycerides (TG), was measured. Several clinical and imaging parameters were recorded. Multivariate linear regression was used in order to determine which parameters were associated with PON-1 serum concentration and AREase.

Results. Patients with AF presented significantly higher body mass index (BMI) and were more prone to having arterial hypertension, while HDL level was significantly lower in AF patients compared with patients from control group. AF patients had significantly lower serum PON-1 concentration and AREase compared with the patients without AF. Serum PON-1 concentration showed strong inverse correlation with BMI (r=-0.517; p<0.001) and moderate positive correlation with HDL (r=0.242; p<0.006). AREase was strongly correlated with HDL (r=0.333; p<0.001). In multiple regression analysis, AF and BMI were strongly associated with serum PON-1 concentration (B=-0.185, p=0.022 and B=-0.028, p<0.001 respectively).

Conclusion. The study shows a possible association between PON-1 and AF. These preliminary results add information regarding the pivotal role of oxidative stress in the development and perpetuation of AF.

COMT gene and Val158/108Met polymorphism: genotypes and alleles distribution in a sample of 1323 healthy Romanian volunteers

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Corresponding Author: Adina Chis e-mail: achiş@umfcluj.ro **Introduction.** During the last years, numerous genetic association studies have attempted to detect functional gene polymorphisms that contribute to behavior or to the susceptibility for the complex diseases. One of the problems of genetic association studies is the variability in results, which can be explained, in part, by population stratification. One of the most studied polymorphisms in relation to diverse phenotypic associations (various cognitive abilities in healthy individuals and/or people with neuropsychiatric disorders) is the Val158/108Met single nucleotide polymorphism (SNP) in the catechol-O-methyltransferase (COMT) gene; while some studies associate this SNP with major depression or panic disorders, other studies have failed to find any association.

The objective of this study was to describe the distribution, for the first time, of COMT Val108/158Met polymorphism in a large sample of Romanian healthy volunteers.

Material and methods. A sample of N=1323 healthy volunteers were genotyped for the above mentioned SNP. DNA was extracted from buccal epithelial cells or blood and the SNP genotyping was performed using polymerase chain reaction-based restriction fragment length polymorphism assay. To evaluate the genotypes distribution, alleles frequencies and Hardy-Weinberg equilibrium we used χ^2 test run in SPSS.

Results. The distribution of COMT Val108/158Met genotypes in our sample was: 27.9%Val/Val, 48.3% Val/Met and 23.8% Met/Met. The alleles frequency was 52.04% for the Val allele and 47.96% for the Met allele. The genotypes were in Hardy-Weinberg equilibrium ($\chi 2 = 1.39$, p = 0.24).

Conclusion. The results from this study extends the efforts to map the allelic distribution of COMT Val158/108Met alleles in populations around the world and emphasizes that population stratification should be controlled for next studies that could report phenotypic associations in DNA samples from different populations.

Auricular acupressure efficiency for reducing dental stress, in patients with anxiety and depression

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Corresponding Author: Ramona-Niculina Jurcău e-mail: ramona_mj@yahoo.com **Introduction.** Auricular acupressure (AA) is a non-invasive method, without side effects, easy to perform and cheap, with calming and relaxing effect, being one of the methods used in reducing stress.

Objective. Evaluation of the efficiency of auricular acupressure in reducing dental stress in people with anxiety and depression.

Methods. Selected patients (men M = 40, female F = 49), evaluated with anxiety and depression, were randomized in the three groups: control (c), without AA (M = 12, F = 14); AA1 which received AA for 1 week (M = 14, F = 16); AA3 which received AA for 3 weeks (M = 14, F = 19). AA wad used three times a day, before dental intervention. Anxiety and depression were evaluated using Beck Anxiety Inventory (BAI) and Hospital Anxiety and Depression Scale (HADS). Stress assessment were: before AA beginning (T1), at the end of first week (T2), immediately pre-intervention (T3), one hour after the dental intervention (T4).

Results. C presented significantly increased scores of BAI and HADS, at T3 and T4, compared to T1. AA1 and AA3 presented significant reduction of BAI and HADS, compared to C, at T3 and T4. The highest differences were at T3 and T4 and between C and AA3, and the lowest between AA1 and AA3. At AA1 and AA3 a significantly higher decrease for HADS compared to BAI scores was found.

Conclusion. For patients with anxiety and depression, dental interventions are an important stress condition. Auricular acupressure has a significant anxiolytic and antidepressant effect, in patients with anxiety and depression, subject to dental interventions. The auricular acupressure anxiolytic and antidepressant effect is more intense after a long-term administration, for 3 weeks. The use of a lasting auricular acupressure is an efficient, economic and non-invasive method of dental stress modulating, in people who have a state of anxiety and depression.

MEDICINE Medical Specialties

Mechanical dispersion and left ventricular global longitudinal strain as predictors of MACE after acute myocardial infarction

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Corresponding Author: Raluca Tomoaia e-mail: raluca.tomoaia@gmail.com **Introduction.** Transthoracic echocardiography can predict the risk of major adverse cardiovascular events (MACE) after acute myocardial infarction (AMI). Traditional parameters including the left ventricular ejection fraction (LVEF) have a proven predictive utility, but novel techniques require further investigation. Our study aimed to determine if STE parameters offer additional prognostic data in the prediction of 1-year MACE in patients admitted with AMI.

Material and methods. This was a prospective bi-centric study that included 68 patients admitted with AMI and preserved or mildly reduced LVEF (>40%). Echocardiography was performed using a Vivid E95 scanner and the automated function-imaging (AFI) tool was used to determine global longitudinal strain (GLS), LV mechanical dispersion (MD) and the LV mass. There was a one-year follow-up period.

Results. The mean age of the patients was of 67 ± 13 years, 53% were male, 66% had STEMI. Mean values for the LVEF, MD, GLS and LV mass were $49 \pm 2.1\%$, 132 \pm 72 ms, $-11 \pm 3.14\%$, and 102 ± 13 g, respectively. Endpoints of 44% (n = 30) were reached after a mean follow-up of 11 ± 3 months. By examining the ROC curves for the prediction of MACE, the Youden index was derived for each of the four variables (MD, GLS, LV mass, LVEF). One year after AMI, survival was predicted by values of > 91 ms for MD (AUC = 0.69, 95%CI = 0.567-0.798, p = 0.002), > -14% for GLS (AUC = 0.67, 95%CI = 0.548-0.781, p = 0.008), and < 43% for LVEF (AUC = 0.684, 95%CI = 0.566-0.791, p = 0.01). LV mass was not associated with the occurrence of MACE (p = 0.33). Logistic regression was used to analyze the relationship between MD, GLS, LVEF and MACE. We found that the OR for the occurrence of MACE increased by 1% (95%CI 1.0024 - 1.0184, p = 0.01) for a one-unit increase in MD, by 0.9% (95%CI 1.0167 - 1.441, p = 0.03) for a one-unit increase in GLS and by 1.5% (95%CI 0.7896 to 0.9717, p = 0.01) for a 10-unit increase in LVEF.

Conclusion. The MD and GLS are promising prognostic predictors of MACE after AMI.

Should ablation be the first choice in atrial flutter management?

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1) Department of Cardiology Rehabilitation, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Radiofrequency (RF) ablation of the cavo-tricuspid isthmus (CTI) is considered an efficient option for the treatment of typical atrial flutter. In the current management for a well tolerated, first episode of atrial flutter RF ablation has a class II indication, level of evidence B. Class I indication is only applied in the case of a well-

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Corresponding Author: Radu Roşu e-mail: rosu.radu1053@gmail.com tolerated atrial flutter recurrence, or of a badly-tolerated episode of flutter. The purpose of this study was to evaluate, in a prospective manner, the acute ablation success rate and recurrence rate of electrical cardioversion, pharmacological cardioversion and atrial overdrive pacing followed by antiarrhythmic therapy, compared to RF ablation alone after a first episode of flutter.

Material and methods.

• Studied population: 99 patients presenting a first episode of atrial flutter, converted to sinus rhythm either by RF ablation, or by electrical cardioversion, pharmacological cardioversion or atrial overdrive pacing + Amiodarone.

• Study type: prospective, non-randomized.

- Inclusion criteria:
- 1. First episode of flutter, with no prior antiarrhythmic treatment.

2. For the group 1 patients, conversion to sinus rhythm using external electrical cardioversion, Amiodarone therapy or atrial overdrive pacing.

3. For the patients undergoing RF ablation (group 2), the participation of the CTI in the flutter circuit, demonstrated by entrainment maneuvers during the electrophysiological study.

• Exclusion criteria:

1. Antiarrhythmic treatment within 5 weeks before the ablation procedure.

2. Recurrent atrial flutter

3. Contraindication to Amiodarone or anticoagulant treatment

4. QTc interval > 460 msec.

5. Documented history of atrial fibrillation

• Follow-up: Performed using clinical exam, ECG and Holter monitoring at 1,

3, 6, 12 months.

Results.

• There were no statistically significant differences between the 2 groups in what concerns the demographic features, associated conditions, cardiovascular risk factors, history of atrial fibrillation and left ventricular function.

• For the patients in group 1, conversion to sinus rhythm was obtained in all cases (100%).

• For the patients in group 2, bidirectional isthmic block was achieved in 37 patients (88.1%), with an average procedure time of 140.2 ± 31.9 minutes and a mean fluoroscopy time of 29 ± 11.3 minutes. There were no major procedure-related complications.

• After a follow-up period of 12 months, the recurrence rate in group 1 was 57.9% (33 patients) and 9.5% in group 2 (4 patients, 3 without bidirectional isthmic block during procedure and 1 with) (p=0.01).

• During the follow-up period, atrial fibrillation was detected in 10.5% of cases (6 patients) in group 1 and 11.9% of cases (5 patients) in group 2 (p=NS).

Conclusion.

• RF ablation should be considered as a therapeutic option in the treatment of a first episode of atrial flutter, due to its superior efficiency in maintaining sinus rhythm and to its low recurrence rate, compared to current first-line therapeutic option.

• This hypothesis should be tested in a prospective study, on a larger population.

Feasibility study of the new assistive VR-enhanced robotic exoskeleton in cardiovascular rehabilitation

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Corresponding Author: Mihaela Mocan e-mail: mihaela.mocan@gmail.com **Introduction.** Early cardiac rehabilitation is essential for patients who undergone through open heart surgery. Existent data concerning this area reveals that patients who benefit from early cardiac rehabilitation post sternotomy have a better functional capacity, a decreased re-admission rate in the hospital and a higher life expectancy when compared with patients who had not benefited of such techniques. In this respect a robotic arm combined with a virtual reality system (CardioVR-ReTone) were designed and tested on healthy volunteers.

Material and methods. 15 healthy volunteers were enrolled to test the feasibility of the robotic system. Eligibility criteria were age >18 years, agreement to participate by signing informed consent. The exclusion criteria were insufficient Romanian-language comprehension, debilitating pathology of upper limb/shoulder, musculoskeletal system that limit exercise capacity. A set of standardized exercises, in accordance with rehabilitations guidelines were explained and applied first without and than with the robot. The volunteers were continuously monitored and feedback from the volunteer regarding pressure or discomfort was continuously recorded. At the end, the volunteers gave their feedback regarding the acceptance and satisfaction level.

Results. Overall, the subjects were satisfied with using the CardioVR-ReTone system. The CardioVR-ReTone proved to be well accepted and the exercises were considered very easy. The observations regarding certain difficulties were used to improve the system.

Conclusion. The CardioVR-reTone system was well tolerated and accepted by the healthy volunteers. Implementing these novel features of the CardioVR-ReTone system, addressability, and efficacy of CR, so problematic in certain situations and especially in cardiac surgery, will be greatly facilitated, being independent of the skills and availability of the rehabilitation therapist.

Are there new biomarkers in active atherosclerosis? – translational medicine from cardiology to angiology

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Corresponding Author: Mirela-Anca Stoia e-mail: mirelastoia@yahoo.com **Introduction.** Atherosclerosis (ATS) involves metabolic, cellular, inflammatory, and immune triggering or transmitting mediators.

Method. Our group studied and found some interesting aspects, which underline the diagnostic and/or prognostic role of some new biomarkers in ATS.

Results. Patients with peripheral arterial disease (PAD) and those with coronary artery disease (CAD), have particular patterns of resistin and leptin, adipocytokines involved in ATS development and in cardiac events (ischemic stroke). Serum leptin levels

were significantly higher, respectively serum levels of resistin were significantly lowers in PAD patients compared to CAD patients. Plasma leptin, but not resistin, TNF- α , and adiponectin, was associated with echocardiographic parameters of cardiac remodeling in CAD patients.

Soluble ST-2 (sST-2), part of interleukin IL-1 receptor family, an immuneinflammatory mechanism of ATS, can be produced by the vascular endothelial cells in hypertensive patients due to the diastolic load. ST2 serum levels are strongly correlated with higher cardiovascular risk in hypertensive patients and are a significant marker of endothelial dysfunction regardless of diastolic dysfunction, and potential predictor for short term poor prognosis.

Visfatin, a relatively new identified endothelial adipokine and a pro-inflammatory mediator in plaque destabilization (through metalloproteinases), fibrosis, and angiogenesis, seems not to be altered in hypertensive patients, but was found high in obese T2DM patients, in which promotes vasoconstriction.

Apelin (13), a new endothelial peptide, similar to adipocytokines, demonstrated a certain protective effect in ATS, revealing a possible new target therapy.

Conclusion. The various adipokines changes suggest different ATS profiles, and are involved in prognosis and evolution of patients with active ATS.

The perioperative management of antithrombotic treatment in pacemaker patients

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Corresponding Author: Dana Pop e-mail: pop67dana@gmail.com **Introduction.** In the setting of antithrombotic classes (both oral anticoagulants – OACs and antiplatelets) widening and treatment recommendations broadening, the perioperative strategies in patients requiring pacemaker implantation have not been definitely stated yet.

Aim. The present study aimed to compare in those patient categories, certain antithrombotic regimes in terms of early hemorrhagic complications.

Method. A number of 44 consecutive patients hospitalized in the Clinical Rehabilitation Hospital Cluj for pacemaker implantation and having the indication for antithrombtic treatment (atrial fibrillation – 18 patients, valvular prosthesis – 10 patients, coronary stent implantation – 14 patients, stable coronary artery disease – 2 patients), were enrolled. Five perioperative strategies were defined (complete OACs interruption, the LMWH bridging strategy, acenocumarol continuation (at the lowes therapeutic INR), DAPT maintenance and aspirin only administration. The resulting five subgroups were compared from 14 days - hemorrhagic complications point of view.

Results. The mean age of study group was 69.8 ± 12.3 years, 65.9% males. The hemorrhagic complications consisted of pocket hematoma formation and small, self-limited pericardial effusion. No hemorrhagic events in the non-OAC subgroup were registered. The DAPT and LMWH strategies recorded the highest hemorrhagic events percentage (75%, p=0.009 and 70%, p=0.05). We noted also hemorrhagic complication in both acenocmrol and aspirin alon groups (40% and 25%) but statistical significance was not reached.

Conclusion. The DAPT and LMWH bridging strategy sems to bring the highest risk for early hemorrhagic complications after pacemaker/defibrillator implantation procedures.

The improvement of sinus node dysfunction one year after the pacemaker implantation

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Corresponding Author: Dana Pop e-mail: pop67dana@yahoo.com **Introduction.** Although the improvement of AV node function after pacemaker implantation is an old issue already proved to occur in up to 30% of the patients, the evolution of sinus node (SN) dysfunction after cardiac pacing has not been established yet.

Aim. The study aimed to follow-up the improvement of sinus node dysfunction along first year after pacemaker implantation.

Method. The study enrolled 51 consecutive patients with sick sinus syndrome admitted along one year in Clinical Rehabilitation Hospital for pacemaker implantation. They were assessed 10 days and one year after the implantation. To establish the improvement of SN function, the percentage of atrial pacing was the parameter taken into account. Afterwards, the influence of pacing indication, associated disease or medication on the improvement of SN dysfunction were assessed.

Results. The mean age of study group was 74.8 years, 49% males. A general 6.56% decreasing in paced beats (41.67% vs 48.23%) at one year follow-up was found. Considering this threshold, 41.8% of the patients were above it and were assumed as patients with improved SN function. Age, gender and medication (as beta-blockers, amiodarone and digoxin) did not influence (in terms of improvement or worsening the SN function). The pacing indication (sinus bradycardia) seems to correlate with further SN improvement (occurred in 50% of the patients with SB, p=0.04), also ischemic heart disease do (improvement occurs in ~ 50% of the patients, p=0.009).

Conclusion. Up to 50% of pacemaker patients improve their sinus node dysfunction one year after the implantation. This seems to depend on underlying ischemic cardiac disease, pacing for sinus bradycardia and, surprisingly, did not correlate with concomitant medication.

The impact of left ventricular hypertrophy on the occurrence of supraventricular tachyarrhythmias

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Corresponding Author: Florina Frîngu e-mail: florina.fringu@yahoo.com **Introduction.** Left ventricular hypertrophy (LVH) has been frequently shown to facilitate both SVTs and ventricular tachycardias (VTs). In studies on hypertensive patients LVH was a strong independent risk factor for atrial fibrillation (AF) and successful regression of LVH also reduces the risk for onset of AF independent of blood-pressure reduction.

Material and methods. The study included patients diagnosed with LVH. They were divided into two groups: The first group consisted of patients diagnosed with HCM, the other group of patients who had left ventricular hypertrophy from secondary causes. Both groups were analysed on the occurrence of SVTs with the goal of finding

out whether a statistically significant difference in the frequency of SVTs exists between those groups. Other variables analysed in this study include the age, cardiac metrics of LVH (Posterior wall thickness (PWT), thickness of the interventricular septum (IVS) and left atrial diameter (LAD)), diastolic function, as well as the presence of other diseases that are often associated with LVH: Aortic stenosis, mitral regurgitation, arterial hypertension, atrioventricular block and ventricular tachycardia.

Results. The mean age of the patients was of 65.1 ± 10.42 , 65% were male, with higher frequency of male patients in both groups. Most patients in both groups (92.5%) had at least grade 1 mitral regurgitation but there was no statistically significant difference in means (p=0.152) and no significant correlation between MR and HCM (p=0.363).

Atrial fibrillation was present in the majority of HCM patients (79.31%) and 45.45% of the patients in the SecLVH group. The chi-squared test showed a correlation with the HCM group (p=0.0394). In the HCM group were 21 (72.41%) cases with ventricular tachycardias while there was only one case (9.09%) in the SecLVH group. Chi-squared test showed that the variables Ventricular tachycardia and HCM were correlated.

Conclusion. AF is significantly more frequent in HCM patients than in secondary LVH patients. Especially patients with an early diagnosis of HCM or those diagnosed with a more severe phenotype should undergo more detailed testing of atrial function and degree of fibrosis using modern imaging techniques if available.

The importance of proteinuria in the diagnosis of restrictive cardiomyopathy

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Corresponding Author: Anca Daniela Fărcaș e-mail: ancafarcas@yahoo.com **Introduction.** The restrictive cardiomyopathies are a heterogeneous group of myocardial diseases. To diagnose each of these is challenging, meaning that diagnosis is frequently delayed. Some clinical signs are suggestive for a specific etiology.

Case presentation. A 62-year-old patient with grade II essential hypertension, atrial fibrillation and chronic kidney disease presents dyspnea, palpitations and fatigue with an onset of 4 days. Electrocardiogram reveals atrial fibrillation with heart rate of 66 bpm and minor RBB, without ischemic changes. The echocardiographic evaluation highlights not only dilated AS, but also other changes suggestive of restrictive cardiomyopathy (dilated RA, LV and RV not dilated with preserved systolic function), medium mitral regurgitation, severe tricuspid regurgitation. Nuclear magnetic resonance imaging confirms the restrictive cardiomyopathy pattern of cardiac damage. Test labs altered renal function (high level of creatinine with proteinuria = 483 mg/24 h), discordant changes with the overall cardiovascular risk of hypertension. The association of kidney damage with restrictive cardiac type leading the suspicion of Fabry disease. We tested the patient enzymatically and the test result confirms the diagnosis ($\dot{\alpha}$ -galactosidase = $0.9 \mu mol/L$) and quantifies the severity of the disease (lyso-GL-3 = 4.1 ng/ml). In this context, the patient begins the enzyme replacement therapy with Fabrazyme, the efficiency of which will be monitored by the level of lyso-GL-3 (the decrease in its level means a favorable evolution).

Conclusion. Once in a while, some common symptoms may lead to both rare and severe diseases and sometimes a patient with proteinuria and restrictive cardiomyopathy can be diagnosed with Fabry disease. Remember, the rare diseases are not just rare, but also underdiagnosed.

A complex pathology can be hidden behind an atrial fibrillation

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Corresponding Author: Florin Petru Anton e-mail: florinantonfr@yahoo.com **Introduction.** Restrictive cardiomyopathy is characterized by the presence of severe diastolic dysfunction, normal or slightly increased ventricular wall thickness and an ejection fraction that is either normal or somewhat decreased, resulting from a various number of possible etiologies, including idiopathic, genetic, inflammatory, infiltrative or toxic.

Case presentation. I present to you the case of a 62-year-old patient from urban environment, who came to the emergency department for palpitations and dyspnea, symptomatology which appeared a few days before admission. Upon presentation, the patient was hemodynamically stable, with a blood pressure of 130/80 mmHg, bilateral basal dullness, arrhythmic heart sounds, hepatomegaly and discrete edema of the lower limbs. ECG findings showed the presence of atrial fibrillation with a high ventricular rate. The patient was subsequently started on anticoagulant and beta-blocker therapy, since the onset of the arrhythmia was not known. Cardiac ultrasound performed in the emergency room revealed the presence of a concentric left ventricular hypertrophy, with preserved left ventricular kinetics, left atrium dilatation and mitral regurgitation stage II. An urgent chest x-ray was performed, which showed the presence of bilateral pleural collections with moderate quantity on the right side. Biologically no pathological changes were detected, except for the increase of NT-pro BNP.

The initial evolution of the patient was favorable, but later he started complaining of abdominal pain, which raised the suspicion of a possible acute cholecystitis. A surgical consultation was requested, recommending a CT scan, which revealed the presence of a massive right pleural collection and possible inflammatory changes in the cholecystic wall. Under the antibiotic treatment prescribed by the general surgeon and after temporarily stopping the anticoagulant therapy, a pleural puncture was performed, with the evacuation of approximately 1500 mL, which turned out to be exudate. Taking into consideration this result in a patient with normal left ventricular ejection fraction and only mild lower limb edema, made further evaluations of possible etiologies necessary. Repeated cardiac ultrasound showed significant changes in the muscular structure, including changes in echogenicity and increased IVS/LVPW values, with the presence of normal ventricular dimensions and dilated atria, raising the suspicion of an infiltrative cardiomyopathy. An abdominal ultrasound was performed, which showed signs of liver stasis and cholecystic wall changes secondary to stasis, excluding the presence of an acute cholecystitis. The cardiac evaluation was completed with the help of strain rate, which also revealed an aspect that advocated for the diagnosis of an infiltrative cardiomyopathy (amyloidosis). Further explorations were needed in order to determine wether this was the case of primary or secondary amyloidosis, which is why the presence of serum amyloid A was measured - raising the suspicion of an inflammatory disease. Furthermore, immunoelectrophoresis of serum and urinary proteins was performed, revealing the presence of free kappa light chains in the blood and lambda light chains in serum, as well as urine. Suspicion of a hematological pathology was raised, which is the reason why a hematological consultation was requested. This established that patient have multiple myeloma.

In **conclusion**, in some cases, atrial fibrillation can be a first manifestation of a much more complex and malignant underlying disease.

Early initiation of angiotensin receptor-neprilysin inhibitor (ARNi) therapy in the setting of acute heart failure related to idiopathic myocarditis

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Acute heart failure (AHF) can be the expression of either new onset or decompensated chronic heart failure (CHF) and it is associated with high morbidity and mortality. We report a case of a previously healthy young female presenting with AHF. After excluding other aetiologies, we suspected an infectious myocarditis, given the patient's occupation as a farm worker. Cardiac magnetic resonance imaging displayed a post-myocarditis dilatative cardiomyopathy aspect, but no causative infectious or systemic inflammatory disease could be evidenced by usual explorations. In this case, the diagnostic work-up includes a series of paraclinical investigations aiming to confirm the diagnosis and to identify a precipitant factor or a coexisting life-threatening condition. The electrocardiogram showed sinus tachycardia, normal QRS axis and left ventricular hypertrophy. Laboratory tests on admission revealed elevated NT-proBNP. Rapid influenza and COVID-19 nasal polymerase chain reaction testings were negative. Chest radiography displayed small pleural effusion with bilateral blunting of the costophrenic angles, increased lung markings indicative of grade I pulmonary hypertension, absence of pulmonary consolidations. Echocardiogram revealed dilated left ventricle with global hypokinesia more severe in the septum and impaired systolic function. There was severe mitral and tricuspid regurgitation, and a small, circumferential pericardial effusion. Novel disease-modifying agents, such as sacubitril/valsartan, demonstrated benefits on cardiovascular morbidity and mortality in CHF, and recently, it showed promising results in AHF after haemodynamic stabilization. In this case, AHF was managed with early initiation of ARNi and the patient presented a rapid clinical and paraclinical improvement, with a stable, event-free course over a period of 9 months. Therefore, we conclude that ARNi treatment started early after stabilization of AHF patients may be of significant short and long term benefit.

Heart failure with mildly reduced ejection fraction: does it really have a better prognosis than heart failure with reduced ejection fraction?

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 Clinical Emergency Military Hospital "Constantin Papilian", Cluj-Napoca, Romania **Introduction.** Heart failure (HF) is a progressive disease with a severe prognosis. Its mortality overpasses that of some tumors and its evolution is marked by reduced functional capacity, frequent hospitalizations, and an altered quality of life. From East European countries there is a shortage of information about these aspects.

Objective. The aim of the study was to analyze the mortality and rehospitalizations of the patients with mildly reduced ejection fraction (HFmrEF) and to compare them with the events occurred in patients with heart failure with reduced (HFrEF) and preserved ejection fraction (HFpEF), respectively, in a county hospital from Romania. Corresponding Author: Cerasela Mihaela Goidescu e-mail: ceraselagoidescusava@gmail.com **Method.** 353 patients consecutively hospitalized for all cause acutely decompensated heart failure were included (age 70 ± 11.2 years, 47% males; HF diagnosed <1 year in 63.7% of patients, more than 5 years in 11.6%) and followed up for 18 months. We noted the re-hospitalizations and all-cause of deaths.

Results. During the 18 months' follow-up, 19.3% patients died and 33.4% were re-hospitalized. The mortality was higher in the HFrEF group (27.1%) as compared with HFmrEF (20.6%) and HFpEF (14.2%) respectively, p=0.03. Also, the mortality rate was significantly higher in the re-hospitalized group as compared with the group that did not require hospital readmission (25.4% vs 16.2%, p=0.04). The ischemic heart disease was the principal cardiopathy (65% of patients), in the surviving group we found significantly higher serum levels of lipids (p<0.01). The body mass index was also significantly increased in the surviving group (p=0.03). A cut-off value <46% for LVEF, a systolic blood pressure <125 mm Hg and diastolic blood pressure <80 mmHg were associated with severe prognosis and increased mortality.

Conclusion. A cut-off value <46% for LVEF, including patients with HFrEF and most of patients with HFmrEF, was associated with increased mortality suggesting that to a large extent, they have the same prognosis.

The long journey of a patient with advanced heart failure between the favorable and secondary effects of pharmacological treatment

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We present the case of a patient, 62 years old, hypertensive, with advanced chronic heart failure (HF), ischemic cardiomyopathy, myocardial infarction treated conservatively, atrial fibrillation with high ventricular rate, moderate mitral regurgitation, moderate pulmonary hypertension, chronic kidney disease (CKD), COPD stage II, chronic viral hepatitis C, colostomy, who presents in emergency with clinical symptoms suggesting an ischemic stroke. Cranial CT and the neurological examination do not show specific elements. Instead, significant hyponatremia (<120 mEq/dL) is detected, a context that can induce clinical manifestations of extreme asthenia, altered state of consciousness, paresthesia, which can mimic a TIA. The patient had several hospitalizations in the Cardiology I department (2021-2022) due to hard-to-reduce congestive cardiac decompensations and low cardiac output, which required sustained treatments, including intensive therapy in the ICU. At each admission, we tried to find a balance in the vicious circle: severe congestive cardiac decompensation (with high need for diuretic infusion), low cardiac output (requiring inotropic drugs) and renal failure (with oligo-anuria and severe electrolyte imbalances). It is the first case of hyponatremia occurring in a patient with HF under treatment with 2 innovative molecules: sacubitril/ valsartan (Entresto) and dapagliflozin (SGLT2 inhibitor), combined with furosemide and spironolactone and whose correction was difficult in the context of cardiac decompensation with the need for iv diuretic and aggravated CKD. This highlighted attention to the need for monitoring natrium along with potassium serum levels and renal function, during the treatment with i-SGLT2, Entresto and diuretics in combination. Innovative medications in the treatment of HF enhanced benefits in morbidity and mortality reduction, but associated with standard therapy, they can have side effects, which must be known and prevented in this category of vulnerable patients.

Blastic plasmacytoid dendritic cell neoplasm - an orphan hematologic malignancy

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Corresponding Author: Liana-Vasilica Străjan e-mail: lianastrajan@yahoo.com **Introduction.** Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare type of hematologic malignancy with an aggressive course, which most frequently manifests as cutaneous lesions with or without bone marrow involvement and leukemic dissemination. Early recognition of BPDCN has been challenging because its clinical features can be heterogeneous and can overlap both lymphoma and leukemia manifestations. There can be a significant delay between the onset of symptoms and diagnosis. The exact incidence is unknown because it is very often misdiagnosed and underreported, but it is thought to occur an estimated 1000 to 1400 cases annually in the US and Europe combined. The average age at diagnosis is 60 to 70 years. There is a male predominance with a male to female ratio of approximately 2.5:1. Currently, there is no standard of care for BPDCN and various approaches have been used including acute myeloid leukemia, acute lymphoblastic leukemia and lymphoma-based regimens with or without stem cell transplantation. Patients diagnosed with BPDCN have a poor prognosis with a median overall survival of approximately 1 year despite the use of combined chemotherapy.

Material and methods. The objective of this paper was to evaluate a 7 case series of patients diagnosed and treated in our clinic in a 5 year period (2017-2022). The group is composed of 5 men and 2 women with an age range of 63 to 75 years old at diagnostic.

Results. Cutaneous involvement was the initial presentation in all patients with deep purple or red-brown macules, plaques or tumors. Cytopenias were also present in all 7 cases indicating bone marrow involvement. The diagnosis was based on a comprehensive analysis of histopathologic, morphologic, immunophenotypic and clinical criteria. The therapeutic approach consists of regimens used for acute lymphoblastic leukemia in the elderly, CEOP, COP, low dose chemotherapy, high dose corticosteroids and palliative chemotherapy.

Conclusion. The efficacy of conventional chemotherapy was limited, with a median survival less than 12 months. One patient was recently diagnosed and is still being treated with acute lymphoblastic leukemia-type regimen used for the elderly, with regression of cutaneous lesions, normalization of hematologic parameters and improvement of symptoms.

Perseverance in the treatment of an arterial thrombosis and saving the lower limb in a patient with a history of neoplasm and acute post-hemorrhagic anemia

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Department of 1st Medical Clinic - Internal Medicine, Cardiology and Gastroenterology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania We present the case of a patient, 58 yrs old, known to have radio-treated and operated osteosarcoma of the right thigh for 8 years, venous thrombosis (DVT) of lower limbs in the antecedents, who presented in emergency for pain and significant edema of the right lower limb. He described black stools a month ago, in the context of chronic NSAID use for pain. Severe hypochromic microcytic anemia is noted (Hb=6.8 g/dL). He is initially hospitalized in the Gastroenterology department, with 2 blood

Corresponding Author: Mirela-Anca Stoia e-mail: mirelastoia@yahoo.com transfusions administered and it is proposed to perform an upper digestive endoscopy, which the patient refused. Vascular doppler ultrasound reveals the absence of color and pulsatile flow at the level of the right posterior tibial artery. The vascular surgery consultation does not confirm critical leg ischemia and recommends monitoring the patient, who is transferred to the Cardiology I department. On admission, the patient complains of intense pain in the leg, amendable under major analgesics. Objectively, altered general condition, significant edema on the right lower limb, cold and marbled teguments, with phlycten, no palpable pulses in the leg anterior tibial (ATA), posterior tibial (PTA) and peroneal (PA) arteries. Echo doppler highlights extrinsic compression through edema, compartment syndrome and thrombosis of the leg arteries. Anticoagulant treatment with IV heparin is promptly initiated, under APTT monitoring. A lower limb angio-CT is performed, which confirms the occlusion of the right ATA, ATP and AP. The surgical consultation recommends compression of the lower limb, with postural drainage. The evolution of the patient was favorable, with the reduction of pain and edema. The particularities of the case are: the occurrence of arterial thrombosis in a patient with karyokinetic antecedents and DVT, with the occlusion of all the leg arteries and the foreshadowing of the evolution towards gangrene of the leg, with its recovery through sustained but risky anticoagulant treatment, due to acute post-hemorrhagic anemia.

Management of leukemia associated thrombosis in patients with thrombocytopenia: a challenging approach

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Corresponding Author: Roxana Schurger-Cimponeriu e-mail: roxanacimponeriu@gmail.com Acute leukemia is a rapidly progressive malignancy characterized by the proliferation of immature white blood cells. It is an aggressive type of blood cancer which represents a medical emergency therefore the treatment needs to begin as soons as possible. It can be classified according to the lineage to myeloid or lymphoid. The most common symptoms include fever, infections, weakness, fatigue bleeding syndrome, enlargement of the spleen or the lymph nodes. Nowadays there are plenty of treatment options which provide good outcome as long as the complications associated to the treatment are being managed properly. Complex cases such a medullary aplasia must be treated by a multidisciplinary team of doctors.

The aim of our case series is to present the management and the outcome of thrombotic events in 5 severly thrombocytopenic patients diagnosed with acute leukemia in our Hematology Department. All the patients were evaluated using blood markers and ultrasound/CT scans depending on the clinical symptoms. Three cases of acute pulmonary embolism and two cases of deep vein thrombosis were diagnosed. The therapeutic decision was made based on multiple factors such as the age, comorbidities, performance status, thrombocyte value and the severity of the thrombotic event.

In conclusion, managing a severe aplasia will always be a challenge. Even though the low platelet count, patients can suffer a thrombosis due to individual factors and due to the hypercoagulable state associated with cancer.

Application of immunohistochemistry to the differential diagnosis of lung adenocarcinoma - case report

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Corresponding Author: Damiana-Maria Vulturar e-mail: damiana_vulturar@yahoo.com **Background.** Pulmonary adenocarcinoma is the most common type of non-small cell lung cancer. The distinction between peripheral lung adenocarcinoma involving the pleura and the pleural epithelial mesothelioma is a diagnostic problem. There is another rare entity named called pseudomesotheliomatous adenocarcinoma.

Clinical case. A 69-year-old female, ex-smoker presented complaints of dyspnea, fatigue, loss of appetite and weight loss. She had no history of chronic pulmonary disease or asbestos exposure. We acknowledge from medical records: cardiac stimulation, cardiac failure, chronic kidney disease. Paraclinical, elevated creatinine, LDH, GGT, NT-proBNP. CT scan revealed intrapulmonary mass in the left superior lobe with the diameter of 36/34 mm in direct contact with the pleura, bilateral pleural effusion, and enlarged mediastinal lymph nodes. Diagnostic thoracentesis was performed with cytology revealing 75% lymphocytes, 10% PMN, 15% mesothelial cells and rare red blood cells and the immunohistochemical staining for the cytobloc was positive for CK-7 and calretinin, markers suggestive for mesothelioma. Lung US-guided biopsy described cylindric atypic cells showing adenoid differentiation. Immunohistochemically, tumor cells were broadly positive for pulmonary adenocarcinoma markers, such as TTF-1, CK-7, Napsin A, but not for CDx2.

Discussion. In adenocarcinoma, the specificity of TTF-1, CEA and CD15 were reported. In malignant mesothelioma, tumor cells are usually positive for calretinin and negative for TTF-1. PMA is uncommonly described and can be easily mistaken for mesothelioma.

Particularity: The aim is to show the differential diagnosis of peripheral adenocarcinoma with pleural involvement versus malignant pleural mesothelioma. The case is challenging regarding the treatment considering her comorbidities.

Conclusion. This report emphasizes an adenocarcinoma with expression of markers of both lung adenocarcinoma and mesothelioma.

Can pneumococcal pneumonia change the evolution of COVID-19 disease? Two case reports

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 Clinical Hospital of Infectious Diseases, Cluj-Napoca, Romania **Introduction.** Bacterial co-infections developed in the respiratory system can lead to higher mortality. Streptococcus pneumoniae is one of the most common causative agent of co-infection among elders with COVID-19 disease which is why pneumococcal vaccination still remain a global public health focus.

Material and methods. Two adult patients were admitted to Hospital for Infectious Diseases Cluj-Napoca for acute respiratory failure related to COVID-19 disease. Both were men, 77 years old, vaccinated against COVID-19 disease (two doses). First patient was known with Chronic Obstructive Pulmonary Disease, with no immunization for pneumoccocal pneumoniae in the past. Clinical and radiological presentation revealed productive cough, bilateral opacities on the thoracic computed

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Corresponding Author: Andrada Ilișiu e-mail: ilișiuandrada@yahoo.com tomography scan. Laboratory findings showed elevated leukocytes and elevated C-Reactive Protein. Bacteriological findings from sputum revealed: Gram positive cocci arranged in diplo and chains, presence of Streptococcus pneumoniae and Hemophilus Influenzae. Antibiotherapy wih Amoxycilin/ Clavulanat was initiated according to the antibiogram, along with low oxygen therapy delivered by Ventury mask. Our second patient had no respiratory disorders. He recently underwent a surgery for a brain tumor. Reported symptoms at admission were: fever, productive cough, dyspnea. The laboratory parameters showed: elevated C-Reactive Protein and Procalcitonin. Blood cultures and Urinary antigen test were positive for Streptococcus pneumoniae and confirmed the pneumococcal pneumonia with bacteremia. The empiric antibiotherapy with Cefalosporine was then changed with Vancomycin according to the antibiogram. He also required low oxygen supply on the cannula interface. Both patients were discharged after ten days of hospitalization with improved clinical condition, no other complications.

Discussion. These clinical cases highlight the importance of recognizing pneumococcal pneumonia as part of the possible clinical onset in patients with Sars-Cov2 infection.

Conclusion. Given the high mortality associated with invasive Streptococcus pneumoniae disease, prevention by immunization in vulnerable elderly patients can avoid complications even regarding COVID-19 disease.

The influence of occupational medicine program in medical students' attitude towards this specialty

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Corresponding Author: Andreea Iulia Socaciu e-mail: andreeaiso@gmail.com **Introduction.** Occupational medicine in Romania is not one of the first choices for residency training programs and there are medical schools with no or just an optional educational program in this specialty for medical students. We tried to estimate the influence of such a program in changing students' attitude towards our specialty.

Material and methods. We used the 18 items questionnaire developed by Smits and Verbeek and published in Occupational Medicine Journal in 2015, which was applied in its original form (English version) on 141 fourth-year medical students before and after their educational program in occupational medicine. Data was collected in a Microsoft Excel Datasheet and analyzed using statistical functions (average, sum, standard deviation, t-test paired samples, and 0.05 statistical significance threshold was used). Items were collapsed in three scales according to the authors (a career in occupational medicine -6 items, occupational medicine as an interesting specialty -11 items and role and position of the occupational physician -1 item).

Results. For the first scale the mean score before was 17.35 and 16.87 after the educational program (0.48 difference and p=0.082). The second scale had a mean score before of 42.97 points and 43.78 after (0.81 difference and p=0.010), and the third scale, 3.39 before and 3.58 after (difference of 0.19 and p=0.048).

Conclusion. Results showed us scores which are comparable with the ones described in the original paper. In our research the educational program didn't reveal a positive effect in students' attitude regarding choosing a career in occupational medicine (the score decreased but not statistically significant). A positive response was noticed in changing their attitude about occupational medicine as a specialty (higher score after and statistically significant) and in the awareness of the necessity of independence of the occupational physician from the employer.

A challenging case of endocrine hypertension in a young patient

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Corresponding Author: Oana Stănoiu-Pînzariu e-mail: oana pinzariu@yahoo.com **Introduction.** Primary aldosteronism (PA) is an underdiagnosed cause of hypertension, determined by aldosterone hypersecretion.

Case report. A 40-year-old patient is referred to the Endocrinology Department with suspicion of endocrine hypertension. The patient had elevated blood pressure (BP) values for 3 years, despite the triple combination of antihypertensive drugs. Biochemistry (including sodium and potassium levels) was within normal limits. The hormonal profile showed FT4, TSH, 24-h urinary metanephrine, and normetanephrine within normal limits. Basal cortisol was slightly increased (30.8 μ g/dl) but suppressed after administration of 1 mg of Dexamethasone (1.7 μ g/dl). Plasma aldosterone was within normal limits (13.4 ng/ml) but with suppressed direct renin (<0.5 uUI/l). The aldosterone/renin ratio was high (26.8). After 50 mg Captopril administration, aldosterone decreased by only 17% (11.12 ng/ml) of the basal value, and renin remained suppressed. Captopril test certified the aldosterone hypersecretion. Abdominal CT scan showed normal-appearing adrenal glands. The clinical, hormonal, and imaging aspects established the diagnosis of PA through bilateral idiopathic hyperplasia. The patient received monotherapy with Eplerenone 25 mg/day, obtaining the normalization of BP.

Conclusion. Normokalemia, normal plasma aldosterone, and normal appearance of the adrenal glands on CT scan do not exclude PA. In this situation, performing a dynamic test is imperative.

A rare case of atypical parathyroid adenoma

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Corresponding Author: Oana Stănoiu-Pînzariu e-mail: oana_pinzariu@yahoo.com **Introduction.** Atypical parathyroid adenoma (APA) represents a type of parathyroid neoplasm with uncertain malignant potential and is responsible for < 1% of cases of primary hyperparathyroidism (PHPT). This type of tumor has atypical histopathological features different from those in parathyroid adenoma or carcinoma. The preoperative distinction between APA and parathyroid carcinoma is often difficult.

Case report. A 70-year-old patient was diagnosed with asymptomatic PHPT by detecting hypercalcemia (ionized calcium=6.67 mg/dl, total calcium=12.86 mg/dl) on routine blood tests. Parathyroid hormone (PTH) was high (503.1 pg/ml). Cervical ultrasound, corroborated with parathyroid SPECT/CT revealed a right inferior parathyroid adenoma (3 cm), for which surgical excision was performed. The histopathological examination established the diagnosis of APA. The postoperative evolution was favorable (ionized calcium=4.75 mg/dl, total calcium=9.21 mg/dl, PTH=82.8 pg/ml). Neck, chest, and abdominal computed tomography (CT) scan did not show recurrences or local or distant lymph nodes.

Conclusion. Although the patient was asymptomatic, follow-up is necessary, considering the unpredictable nature of APA.

From dysmorphophobia to secondary amenorrhea

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Corresponding Author: Oana Stănoiu-Pînzariu e-mail: oana pinzariu@yahoo.com **Introduction.** Secondary amenorrhea is a common feature of anorexia nervosa. It is due to a severe food restriction that generates inhibition of the gonadotropin-releasing hormone (GnRH) pulse generator system.

Case report. A 21-year-old female complained of secondary amenorrhea, significant weight loss (16 kg in the last year), dysmorphophobia, and easy crying. In addition, the patient performed excessive physical exercises and self-administered purgatives. The clinical examination revealed underweight (BMI=16.2 kg/m2), gaunt face, hypotension (90/70 mmHg), and heart rate of 56 b/min. The hormonal profile showed the presence of hypogonadotropic hypogonadism (estradiol=12.5 pg/ml, FSH=0.40 mUI/ml, LH<0.2 mUI/ml). The GnRH stimulation test was negative. The pituitary MRI ruled out an organic pituitary disease. The psychiatric examination established the diagnosis of anorexia nervosa and instituted treatment with sertraline 50 mg/day and lorazepam 1 mg/day. In addition, a hypercaloric diet and combined estrogen-progestin therapy (21 days/month) were recommended.

Conclusion. The early identification of dysmorphophobia and the institution of psychiatric treatment would significantly contribute to maintaining body weight and avoiding the onset of secondary amenorrhea.

Power spectral density changes in chronic pain

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Corresponding Author: Livia Popa e-mail: livintz@yahoo.com **Introduction.** The complex integration of pain experience at the cerebral level can be explained through different mechanisms, such as the synchronization observed in different frequency bands. Various regions of interest, like the primary and secondary somatosensory cortexes, the anterior cingulate cortex or insula, can be considered part of an integrated network of cortical areas, labeled the "pain matrix", involved in the generation of nociceptive stimuli.

Material and methods. 81 EEGs recorded in chronic pain patients are currently analyzed through quantitative electroencephalography (QEEG) methods. Recordings were performed in both eyes open and eyes closed conditions. Three different cognitive tasks have been applied during the recording, testing the reaction speed, attention, and working memory. Preprocessing, artifact rejection, and spectral analysis were performed with the BrainVision Analyser 2.1 software (BVA). Post-processing data were exported from BVA to Microsoft Excel.

Results. Nine patients were analyzed since the beginning of the process. Since chronic pain was associated with an increment in theta oscillations in previous studies, we restricted our analysis to this frequency range. We investigated whether cognitive tasks were associated with location-specific power changes in the theta frequency band. We found task-positive power increases in the frontal and occipital areas (Fz, FC1, FC2, Oz, O1, O2).

Conclusion. Our partial results overlap with other research in which an increment in theta oscillations was described as the most common EEG-related marker in chronic pain (integrated into complex disorders such as thalamocortical dysrhythmia). Further directions in the ongoing study are: exploring the changes in functional connectivity associated with chronic pain, searching the correlation between clinical scales scores and functional connectivity parameters, identifying EEG-based biomarkers of chronic pain.



Insights into a rare association: Gaucher disease & Parkinsonian syndromes

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Corresponding Author: Livia Popa e-mail: livintz@yahoo.com **Introduction.** Gaucher disease (GD), the inherited deficiency of glucocerebrosidase (GCase. E.C.3.2.1.45), is a rare disorder primarily affecting cells of the reticuloendothelial lineage. Lysosomes within macrophages become engorged with the undigested substrates glucocerebroside and glucosylsphingosine, giving rise to the characteristic-appearing "Gaucher cell". Parkinson's disease (PD), the second most common neurodegenerative disorder, is influenced by genetic and environmental factors. Mutations in the GBA1 gene, which encodes for the lysosomal enzyme glucocerebrosidase, represent the most prevalent genetic risk factor for PD and other Lewy body disorders that has been discovered so far.

Material and methods. The current work is an updated review of the literature on the connection between GD and parkinsonism, which is focused on the role of lysosomes in neurodegenerative disorders.

Results. Synucleinopathies and GBA1 mutations are related. Glucocerebrosidase levels and oligomeric α -synuclein levels were found to be inversely correlated. In GD patients, parkinsonian symptoms began at a relatively young age and the disease progressed more quickly, causing cognitive impairment. Around 25% of patients had a family history of PD. Unilateral tremor and bradykinesia are the most common presenting features, although gait abnormalities and postural instability are also relatively frequent. Levodopa responsiveness is largely positive. Rapid-eye-movement (REM) sleep disorder, impaired olfaction, depression, and anxiety have been reported. It has been suggested that the extent of cognitive impairment is related to mutation severity.

Conclusion. GD may be correlated with parkinsonism due to mutations in the GBA1 gene and the alteration in the autophagosomal/lysosomal pathway. Further research utilizing methods from cell biology, neuropathology, and genetics is required to more clearly identify the mechanisms underlying GBA-associated parkinsonism.

New developments in dementia research

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Material and methods. In this presentation, we discuss recent advances in comprehending the clinical evolution and treatment of Alzheimer's disease, with updates regarding clinical trials still in progress.

Results. Developing new tests for early detection and new medications for treating dementia is a slow process. This situation could be especially disappointing for people with Alzheimer's and their families waiting for new treatment options.

Conclusion. Despite the fact that we have no new drugs for dementia in the last 15 years, we are hoping for some progress with different treatments and other breakthroughs.

New trends regarding personality disorders

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Material and methods. This presentation is based on the review of recent literature, performed in order to understand the new changes in diagnostic guidelines. We examined similarities and differences between these two systems in terms of personality disorders.

Results. Currently the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) abandons the multiaxial system, therefore we can consider that personality disorders partially lose their specificity, but also it proposes an associated approach between the categorical and the dimensional model. ICD-11 exclusively adopts the dimensional approach for personality disorders based on individual differences that are better captured, as well as features that are below the threshold, with better temporal stability, an aspect that gives the clinician the freedom to focus on the disorder itself.

Conclusion. In just a short period of time, estimated at about 100 years, the symptoms and manifestations of personality disorders have changed, but on the other hand, we cannot consider that the evolution of individuals could change radically in such a short period of time.

The importance of ADHD and autism diagnosis in adult patients

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Material and methods. For this presentation, we used PubMed in order to find studies which were published in the last 5 years. The key words were: ADHD, autism, adults.

Results. The studies show that 4.4 % of adult patients were diagnosed with ADHD, and very often this condition was missed because it has similar symptoms with other psychiatric disorders, including personality disorders. Children who were diagnosed with autism are lost when they turn 18, and they also will be misdiagnosed.

Conclusion. It is very important to diagnose these two diseases in adult patients, in order to give them a proper therapeutic management, and to increase the quality of life.

Alcohol dependence - a financial burden for the mental health system

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Corresponding Author: Cătălina-Angela Crișan e-mail: ccrisan2004@yahoo.com **Introduction.** Chronic alcohol dependence is a psychiatric condition associated with significant morbidity and mortality and with a major impact on patients' quality of life. The disorder represents a major burden on the healthcare system through the associated direct and indirect costs and associated psychiatric comorbidities.

Material and methods. We analyzed the number of admissions in the Psychiatric Clinic of the Emergency County Hospital Cluj-Napoca during last year and made correlations between hospitalization costs and psychiatric or somatic comorbidities for patients with alcohol dependence.

Results. Of the total hospitalizations in the last year, 60.1% were represented by patients with a primary or secondary diagnosis of chronic alcohol addiction, with psychotic disorders and personality disorders in the second and third place. The most affected age group was 45-54 years old (33%). Hospitalization costs were significantly higher in patients with associated psychiatric and somatic comorbidities (p=0.001).

Conclusion. Patients with chronic alcohol dependence have increased rates of comorbidities, which lead to a marked decrease in productivity and quality of life. Anti-stigmatization, prevention and specific national programs for patients with this pathology are necessary measures that can lead to the early identification of patients at risk, increasing the quality of life and their socio-professional reintegration.

Bipolar disorder - a constant major diagnosis challenge

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Material and method. Systematic review of the literature.

Results. Worldwide, 45 million people are diagnosed with BD. Epidemiological studies reported a lifetime prevalence of de 1% for BD type 1. The prevalence rates vary among countries and regions due to several factors such as ethnical and cultural, diagnosis criteria and research methods. The incidence is similar for both genders and age group 18-29 years old is the most affected. Annual costs associated with bipolar disorder are estimated to 45 billion dollars.

Conclusion. Bipolar disorder is one of the main causes of disability worldwide and it is associated with high rates of premature death caused both by suicide and medical comorbidities.

Gender dysphoria

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Corresponding Author: Ramona Vinași e-mail: ramonavinasi@yahoo.com **Introduction.** Gender dysphoria, gender identity disorder or transsexualism is a psychological condition that requires care and multiple health professionals; endocrinologists, surgeons and psychiatrists are just some of the professionals needed to address these situations.

Gender identity defines the extent to which each person identifies themselves as male, female or a combination of the two. It is the internal reference, built over time, which allows individuals to organize a sense of self and behave socially according to the perception of their own sex and gender. Gender identity determines the way people experience their gender and contributes to their sense of identity, singularity and of belonging.

The Diagnostic and Statistical Manual of Mental Disorders (DSM-5), the term gender identity disorder has been replaced by the term gender dysphoria. The International Classification of Diseases (ICD 10) mentions five different forms of GID, using, once again, the term transsexualism to refer to one of these forms.

In 1869, there was a phenomenon described as "conträre sexual empfinding" which included some aspects of transsexualism. In 1931, there was a reference with regards to the first patient who had an anatomic sex change performed.

Studies of the epidemiology of transsexualism are scarce or null in most countries. The best estimate of the prevalence of GID or transsexualism comes from Europe, with a prevalence of 1 in 30,000 men and 1 in 100,000 women. The majority of clinical centers report three to five male patients for every female patient.

Material and methods. Review of the literature.

Results. People with gender dysphoria suffer from high levels of stigmatization, discrimination and victimization, contributing to negative self-image and increased rates of other mental health disorders. Transgender individuals are at higher risk of victimization and hate crimes than the general public. Suicide rates are also markedly higher compared to the general population. Transgender individuals also face challenging in accessing appropriate health care and insurance coverage of related services.

Conclusion. While gender dysphoria is a frequent diagnosis in our professional and social field, there is little research about the subject and there is a lack of precise information about the prevalence of this diagnosis. In addition, there is a lack of guidelines to approach these patients. This situation causes the treatment to be performed in a partial manner, without taking into account that the proper approach includes at least a couple of health professionals who are in charge of guiding, informing and assessing the patient's physical and psychological condition. It is our duty as health professionals to promote a multidisciplinary approach which allows gender dysphoria patients to improve their quality of life and decrease their present symptomatology.

Cannabis lessons learned

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Material and methods. A PubMed search using the keywords "marijuana" OR "cannabis" AND "legalization OR decriminalization" was performed.

Results. The legalization of cannabinoids for medical purposes is limited to a few indications, the most notable being cachexia from HIV/AIDS, neuropathic pain, emetic syndrome associated with chemotherapy, spasticity from multiple sclerosis, epilepsy resistant to treatment. In terms of recreational use, it was observed that in the countries where marijuana has been legalized there is a higher rate of substance use disorder, but in these states the use was higher before legalization.

Conclusion. The prevalence of marijuana use disorders has not increased due to legalization, but this policy has raised other health issues which include the acute effects of cannabis intoxication on the ability to drive, accidental intoxications in children, the relationship between cannabis use and opioid use, and last but not least the relationship, which has been shown to be causal, between cannabis use and schizophrenia.

Assessing post-stroke depression via quantitative electroencephalography

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Corresponding Author: Livia Popa e-mail: livintz@yahoo.com **Introduction.** Depression is one of the neuropsychiatric conditions that patients experience the most frequently after a stroke. The pathophysiology of poststroke depression (PSD) is complicated and is impacted by different biological and psychological factors. Between three and six months following the ischemic event, depression showed a noticeable surge.

Quantitative electroencephalography (QEEG) parameters together with neuropsychological testing are useful tools for assessing depression in post-stroke patients.

Material and methods. The current research, a secondary data analysis of a phase IV trial involving the role of N-Pep 12 in stroke rehabilitation, focused on exploring the relationship between QEEG indicators, namely the DTABR values (delta+theta)/(alpha+beta), and the HADS-D (Hospital Anxiety and Depression Scaledepression) subscale scores in stroke survivors. The QEEG indices were measured in four brain areas based on the electrode montage: Frontal Standard, Frontal Extended, Temporo-Parietal, and Global.

Results. Two significant correlations between DTABR values and the HADS-D scores were found during statistical analysis: a negative correlation in the Frontal Extended Region (following the pattern of earlier studies that linked increased right frontal activity with unpleasant emotions) and a positive correlation in the Global Area
(all 32 electrodes), indicating that overall brain activity directly synchronizes with depressive symptoms in stroke patients.

Conclusion. Despite its exploratory nature, the current study could provide valuable information on the relationship between the shifting of frequency bands in the power spectrum (using the DTABR to assess the predominance of either slow or fast waves) and the HADS-D subscale scores in a small sample of stroke survivors.

Factors that influence the hospital length of stay in patients with ischemic stroke

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Corresponding Author: Anca Guțu e-mail: anca.gutu@yahoo.com **Introduction.** Ischemic stroke is currently one of the most important public health problems worldwide and the hospital length of stay is a major indicator of the economic burden of this disease. Thus, the aim of this study was to analyze the factors that influence the hospital length of stay in patients with ischemic stroke.

Material and methods. This was a descriptive, observational, and retrospective study, in which were included 520 patients with ischemic stroke admitted in the Neurology Department of the County Emergency Clinical Hospital Cluj-Napoca. The data were collected from the RES-Q database and analyzed using non-parametric tests. We verified the hypothesis that there was a significant correlation between gender, age, presence of atrial fibrillation, hypertension, dyslipidemia, smoking, and stroke severity, and the length of stay.

Results. The median hospital length of stay was higher in women than in men (8 days vs. 7 days, respectively, p=0.027), and in hypertensive patients than in patients with normal blood pressure (8 days vs. 7 days, respectively, p=0.003). In addition, there was a statistically significant correlation between stroke severity and length of stay (p=0.004), but not between age and length of stay (p=0.668). The median length of stay was the same (7 days) in patients with and without atrial fibrillation (p=0.644). Moreover, even though the median length of stay was higher in dyslipidemic patients than in patients without dyslipidemia (8 days vs. 7 days), and in smokers compared to non-smokers (8 days vs. 7 days), this difference did not have any statistical significance (p=0.147 and p=0.546, respectively).

Conclusion. The hospital length of stay in patients with ischemic stroke is influenced by gender, presence of hypertension and stroke severity.

The principles of dialectical-behavioral psychotherapy in the treatment of borderline personality disorder

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Introduction. Borderline personality disorder (BPD) affects approximately 6% of the general population, representing a major public health problem through numerous psychiatric comorbidities and multiple suicide attempts. One of the most studied types

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Corresponding Author: Maria Bonea e-mail: maria.bonea@yahoo.com of psychotherapy in BPD is dialectical-behavioral psychotherapy (Dialectical Behavior Therapy - DBT).

Material and methods. This presentation is based on the review of recent literature, for one of the most studied types of psychotherapy in BPD, that is DBT.

Results. The patient simultaneously benefits from individual psychotherapy, group psychotherapy, for the teaching of mindfulness skills, emotional regulation, interpersonal efficiency and distress tolerance, as well as telephone counseling. It is considered that working with patients with BPD is extremely demanding for the psychotherapist, who is obliged to be part of a consulting team, together with other psychotherapists.

Conclusion. DBT is eminently a behavioral psychotherapy, the rules are being exposed to the patient from the very beginning. However, DBT starts from the premise that, at any moment, the patient does only what he can, the only situation in which he is excluded from psychotherapy is for the absence of 4 consecutive sessions. DBT is based on the balance between acceptance and change, it reduces the rate of self-harming behaviors, suicide attempts, decreases the rate of admissions to psychiatric wards and increases the quality of life.

Schizophrenia in mass-media: a rhetoric of stigma

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Corresponding Author: Cosmin Moga e-mail: moga cosmin 33@yahoo.com **Introduction.** In this presentation, we aim to highlight the methods and mechanism of stigmatizing the schizophrenia diagnosis in mass-media

Methods. Several meta-analyses and articles about the use of the concept of schizophrenia in Anglo-saxon, French and East-Asian media were analyzed and reported.

Results. The ways of stigmatizing schizophrenia in the three mass-media cultural spaces vary in content but converge towards a bifactorial structure around the "schizophrenic" descriptor: it's association with violence and its metaphorical decontextualization.

Conclusion. Stigmatization of schizophrenia in the mass-media is a constant phenomenon with minor variations over time. Correct information about the medical reality of the concept and anti-stigma towards target populations can counteract the amplitude of stigma for schizophrenia patients in mass-media.

The evolution of the anxiety concept

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Department of Psychiatry and Pediatric Psychiatry, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The importance of the concept of anxiety as a major influencer over the contemporary life is increasingly recognized, reflected by literature publications, arts, science, religion and also in many other areas of our culture. Research on anxiety has dramatically increased over the past decades.

Material and methods. This presentation reviews the evolution of anxiety as an important construct and tries to set a conceptual frame of reference that identifies the

Corresponding Author: Ioana Micluția e-mail: ioanamiclu@yahoo.com major roles and interests as a causative agent for diverse consequences.

Results. Anxiety is found as a possible explanation in many contemporary theories of personality, a cause for symptoms such as insomnia, psychosomatic manifestations, major depression, alienation of individuals in urban areas. Also, it has various connections with different biological substrates, such as immunological, neuroendocrine, or inflammatory systems, and multiple behavioral explanations represented by coping strategies, social anxiety, phobias.

Conclusion. Understanding the basic nature of anxiety as a complex response, with further investigations of the associative networks that link cognitive and physiological components of anxiety would have a positive effect for the treatment of patients suffering from anxiety disorders.

The impact of spirituality in heart failure patients in palliative care

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Corresponding Author: Georgiana Delia Ciuca e-mail: deliaciuca@gmail.com **Introduction.** Palliative care is provided to patients suffering from oncological diseases, but also to those with life-threatening chronic conditions in advanced stages such as HIV/AIDS, chronic lung diseases, neurodegenerative neurological diseases, cardiac diseases (congenital heart defects, congestive heart failure NYHA III and IV). The defining element of palliative care is the integration of the psycho-socio-spiritual dimension of the patient into the medical process. The trajectory of congestive heart failure involves a slow deterioration of the patient with each new exacerbation. The unpredictability of these exacerbations can lead to both self-conscious anxiety and existential questions frequently asked by these patients. The spiritual experience focuses on the symptomatology of heart failure patients in palliative care.

The present study represents the observation of the impact of spirituality on quality of life in heart failure patients in palliative care, as evidenced in the published literature between 2017 - 2022.

Material and methods. To highlight the search strategy we used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart. To retrieve the articles we used the PubMed database together with a manual search in the Google search engine, entering the keywords "spiritual" AND "heart failure".

Results. Of the 15 studies, six were conducted in the United States, six in Iran, one in Turkey, one in the United Kingdom and one in Spain. Thirteen of the studies analyzed are quantitative (seven correlational, five randomized clinical trials and one cross-sectional study), one study is qualitative and one study is mixed.

Of these, 3 studies showed a significant increase in spiritual well-being following the intervention, with a direct positive impact on QOL, in 11 studies - spirituality has an important role in increasing the quality of life of HF patients, 3 studies - highlighted the existence of an influence of spirituality on physical health.

Conclusion. Patients who had a high level of spirituality or religiosity showed both a better quality of life and lower levels of anxiety and depression. Equally important as holistic care is the person providing the care, whose presence greatly influences the patient's well-being.

Linking clinical specialties with cell biology in monogenic diseases affected by lyonization process: learning from Ornithine transcarbamylase deficiency

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Corresponding Author: Romana Vulturar e-mail: romanavulturar@gmail.com **Introduction.** The urea cycle is the body's primary tool for the disposal of excess nitrogen, and dysfunction in urea production results in hyperammonemia (HA). This cycle is starting in the hepatocyte's mitochondria and is ending in the cytoplasm. There are several clinically relevant disorders, the most common being ornithine transcarbamylase deficiency (OTCD), the gene being on the X chromosome.

Methods. A comprehensive review on Pubmed articles published in the last decade regarding OTCD was conducted, focusing on genetics, clinical and therapeutic data.

Results. OTCD affects the urea cycle and ammonia can accumulate and reach toxic levels, the brain being the most affected. When it occurs as a neonatal-onset disease (in males), usually results in severe HA, encephalopathy with coma in the first week of life. Unfortunately, in our country, OTCD is not part of the routine neonatal screening and by the time the neonates with OTCD come to the medical attention they typically have severe encephalopathy, respiratory alkalosis, seizures and hypothermia.

The diagnosis of OTCD is established by metabolic investigations and molecular testing.

Conclusions. Female carriers of OTC deficiency form a particular subgroup due to the variable individual inactivation of the X-chromosome hosting the mutant OTC (lyonization phenomenon); thus, some are asymptomatic, others report symptoms over many years that are likely explained by recurrent undiagnosed HA. Patients with complete enzyme deficiency, with very low protein tolerance or frequent metabolic crises despite treatment, should undergo liver transplantation as soon as it is possible and safe (>3 months of age and/or >5 kg bw). Until then, aggressive conservative measures must be employed to preserve mental function. Treatment requires a low-protein diet. To avoid dietary deficiencies, vitamins, essential amino acids, and trace elements should be monitored and supplemented as needed. In addition, most patients will require nitrogen-scavenging drugs: oral sodium benzoate/ sodium phenylbutyrate. Oral glycerol phenylbutyrate (Ravicti) is a more palatable alternative to standard preparations. At the moment, there are other therapies under investigation: gene therapy which implies the delivery of an OTC gene with an adeno-associated virus, or lipid nanoparticle.

Neonatal outcomes in preterm infants under 28 weeks of gestation from mothers with chorioamnionitis

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Corresponding Author: Gabriela Zaharie e-mail: gabrielazaharie1966@gmail.com **Background and aims.** Chorioamnionitis is associated with up to 40% of cases of early-onset neonatal sepsis. Aside from the risk of fetal sepsis, the fetal inflammatory response may induce cerebral white matter injury, intraventricular hemorrhage, and periventricular leukomalacia.

The aim of the study is to evaluate the morbidity and mortality at the prematures from mothers with chorioamnionitis (group A) compare with the group of premature from mothers without (group B).

Material and methods. The study is performed on 152 premature infants < 28 weeks of gestation (wks) admitted in a III-rd level unit, Cluj-Napoca, Romania; from those, 15 premature babies (group A) were from mothers with chorioamnionitis. We evaluate the incidence of early complications: respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), early sepsis, and late complications: periventricular leukomalacia (PVL) bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP) and mortality. Statistical analysis was done with the IBM SPSS V25 program. All the patients had the informed consent signed.

Results. The subgroups are homogenous. The Gestational Age was 25.714 ± 1.49 weeks, group A versus 25.713 ± 1.25 wks group B. Group A had a weight of 748.571±174.08 g vs 772.181±130.364 g (p<0.5). The incidence of chorioamnionitis was 9.86% in our study. The Apgar Score at 1/5/10 minutes was without significant statistical differences. All the prematures developed RDS but the FiO₂ was significant higher only in the first day in group A 58.71±19.07% vs $45.27\pm17.41\%$ (p=0.009). Early sepsis had incidence of 42.76%. No significant differences in the incidence of early or late complications. We observed a mild inverse correlation between the duration of premature rupture of membranes (PROM) and the degree of IVH (r=-0.31). The mortality was not influenced by chorioamnionitis of the mothers. Statistically significant relationship, Chi-squared p=0.001 was found concerning the relative risk of death after pulmonary hemorrhage: 2.349 [1.360-3.884] times higher in the group from chorioamnionitis.

Conclusion. The relative risk of death by pulmonary hemorrhage was 2.34 times increased in chorioamnionitis group. In our study, early and late complications in the premature babies <28 weeks was not influenced by the mother's chorioamnionitis.

Perinatal factors influence on Cerebral Fractional Tissue Oxygen Extraction (cFTOE) and the Cerebral Oxygen Saturation (crSaO2) of preterm neonates. Single center study

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Corresponding Author: Melinda Mátyás e-mail: melimatyas@yahoo.com **Introduction.** Near-infrared spectroscopy (NIRS) is a non-invasive method of monitoring brain oxygenation, easily performed at point of care. Regional cerebral oxygen saturation (crSaO₂) and the cerebral fractional tissue oxygen extraction (cFTOE) evaluated by NIRS provide more accurate information on brain oxygenation than the blood oxygen saturation measured by pulse oximetry. We evaluated the effect of perinatal conditions on cerebral oxygenation of preterm newborns.

Material and methods. We conducted a longitudinal study. Were enrolled 48 preterm newborns <34 weeks of gestation who underwent NIRS monitorisation during the first 72 h of life. crSaO₂ was measured and cFTOE was calculated for each patient.

Results. Episodes of apnoea, frequent condition of preterms proved to influence the cerebral oxygen saturation of the study group (p = 0.0026). One-way ANOVA showed no significant main effect of intraventricular hemorrhage (IVH) severity on crSaO₂ and cFTOE (p > 0.05); there was a tendency toward statistical significance concerning the difference between the means of crSaO₂ (p = 0.083) and cFTOE (p = 0.098). Patients with intraventricular hemorrhage (IVH) had a lower mean of crSaO₂ and a higher mean of cFTOE ($59.67 \pm 10.37\%$ vs. $64.92 \pm 10.16\%$ for crSaO₂; 0.37 ± 0.11 vs. 0.32 ± 0.11 for cFTOE) compared to those with no IVH. Significantly lower values of crSaO₂ and higher values of cFTOE were found in neonates receiving inotropic treatment (p < 0.0001). No significant association between the maternal hypertension treatment and the cerebral oxygenation of preterms was found.

Conclusion. In our study, we found a decreased cerebral oxygen saturation of preterms with apnea episodes, IVH and inotrope treatment.

Maternal SARS-COV-2 infection effect on neonatal outcome

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2) Department of Medical Informatics and Biostatistics, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The SARS-COV-2 infection affected the pregnant women during the pandemics. Immunological particularity of this population and the increased need for medical assistance put this population in a high-risk category for SARS-COV-2 infection. The aim of our study was to analyze the impact of maternal SARS-COV-2 infection on neonatal outcome.

Material and methods. We conducted a prospective, longitudinal study in the Neonatology Department of 1st Obstetrics Clinic, Cluj-Napoca. Ninety neonates of 32 to 42 weeks of gestation, born to mothers with positive RT-PCR test were enrolled in the study. Each neonate was evaluated by clinical and laboratory exam. A follow up questionnaire with 10 questions about mothers' symptoms, immunity after COVID,

Corresponding Author: Melinda Mátyás e-mail: melimatyas@yahoo.com hospital stay impact and breastfeeding of their child at follow up was done.

Results. All newborns enrolled had negative RT-PCR test at birth. We have no vertical transmission of SARS-COV-2 infection. No symptoms characteristic for SARS-COV-2 infection were found at enrolled neonates.

Mothers anosmia and ageusia was associated with a higher value of WBC, lymphocytes (p=0.06; p=0.04) of neonates and also higher ASAT value (p=0.08).

Maternal and children Ig G was studied. From 73 (82%) responders, twelve mothers checked the Ig G value after the infection, with positive test on 9 cases. Of newborns, 14 were tested and 2 (14.3%) had + Ig G test.

At 57.3% of mothers breastfeeding was started after discharge. Only 41.57% continue to breastfeed the child at the follow up visit. The experience related to the hospital stay was negative in 40 (43.95%) cases. Mothers were emotionally affected by separation of newborn and unable to breastfeed. 16 (18%) were non respondent to the follow up questionnaire.

Conclusion. None of the children enrolled in the study had SARS-COV-2 infection neither at birth nor first 3 months. Only few (n=2) neonates had IgG passage from the mother. Breastfeeding was started at more than half of newborns after discharge. More than half of respondent related negative experience during their hospital stay due to the separation from their children.

Linking clinical specialties with cell biology in monogenic diseases affecting the brain: learning from Niemann-Pick disease type C

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5) Cognitive Neuroscience Laboratory, Department of Psychology, Babeş-Bolyai University, Cluj-Napoca, Romania **Introduction.** Niemann-Pick type C disease (NPCD) is a rare, recessive disorder characterised by a progressive neurovisceral picture, affecting the intralysosomal and late-endosomal pathways of endocytosed cholesterol.

Methods. A comprehensive review on Pubmed articles published in last two decades regarding NPCD was conducted, focusing on genetics, clinical and therapeutic data.

Results. Most of the patients had neurological signs and different age onset: early-infantile (5% of patients), late-infantile, juvenile-onset (classic NPCD, 50–60% of cases), and adult-onset. Common neurological signs were: cognitive impairment (>70%), ataxia, vertical supranuclear gaze palsy etc. About 95% of patients have mutations in NPC1 (a lysosomal membrane protein), the rest in NPC2 (a soluble lysosomal glycoprotein). In adult-onset forms, patients presented psychosis, cognitive decline, dystonia, isolated splenomegaly.

Conclusions. NPCD is heterogeneous, and may present even isolated psychiatric signs arising in adolescence/ adulthood in a previously non-symptomatic patient. Large-scale clinical data collection may generate increased natural history knowledge. A classification by the type of neurological signs (rather than age at onset) is supported, due to correlations between age at neurological onset and course of disease. Elevated biomarkers have limitations, the diagnosis requires analysis of NPC1/NPC2 genes. In few cases (with inconclusive genetic testing) the filipin test is the best functional test. The therapy focuses often on symptomatic drugs (antiepileptics etc). To date, the approved drug is Miglustat, a substrate inhibitor that passes the encephalic barrier,

Corresponding Author: Romana Vulturar e-mail: romanavulturar@gmail.com decreasing NPCD progression, mainly in late-onset cases. Encouraging results are obtained with a pharmacological oral chaperone (arimoclomol), with intrathecal/ I,V. adm. of 2-hydroxypropyl- β -cyclodextrin, or with oral adm. of N-acetyl-L-leucine. Besides, there is a rationale for stem cell therapy in NPC2 patients. The management of metabolic rare diseases has consisted in diet, supportive therapy, but recent progress in molecular sciences showed that other therapy options become available: enzyme /coenzyme replacement therapy, removal of harmful substances, cell/ organ transplantation, and sometimes even gene therapy.

The importance of early diagnosis and treatment in biliary atresia outcome

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Corresponding Author: Claudia Simu e-mail: claudia.sirbe@yahoo.com **Introduction.** Biliary atresia (BA) is a very rare disorder characterized by the destruction of the extrahepatic bile duct. It represents an important cause of cholestatic hepatitis and the leading indication for children's liver transplantation (LT). Without surgery, BA can be fatal. Two types of surgery are used to treat this condition, Kasai portoenterostomy (KP) in early-diagnosed patients and liver transplant (LT).

Methods. We performed a retrospective study including children with BA diagnosed and followed up from November 2010 to October 2022. We have analyzed the clinical manifestations, surgical treatment (KP and/or LT), evolution, and outcome.

Results. BA was diagnosed in 41 children (15 males, 36.58%) with age at diagnosis or presentation between 1 week and 6 months. The first presentation in our hospital was before the age of 3 months in 27 patients (65.85%), all with cholestasis and acholic stools. KP was performed in 27 patients, with favorable evolution in 10 cases (37.04%) and unsuccessful in 17 (62.96%). Among those with unsuccessful KP, one child died immediately postoperatively, and 16 patients progressed to cirrhosis and required LT. The diagnosis was delayed in 14 patients (34.15%), and KP was not performed, with children already showing signs of cirrhosis at admission. Eighteen patients (43.90% of the total) were referred for LT in different European LT centers. Twelve patients with LT had a favorable long-term evolution; three died during the pre-LT period, two died immediately post-LT secondary to infections and one after a few years post-LT. After LT, all children received immunosuppressive therapy with tacrolimus or cyclosporin. Currently, the oldest child in our cohort is 15 years after LT and on minimum doses of tacrolimus.

Conclusion. Our study highlights the importance of early recognition of BA, as timely diagnosis and surgical intervention can significantly improve the prognosis of these children. For some infants with BA, the KP can be lifesaving, mainly for those without LT possibilities.

A possible evolutive pattern following Kasai portoenterostomy for biliary atresia

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Corresponding Author: Alina Grama e-mail: gramaalina16@yahoo.com **Background.** Biliary atresia (BA) is a progressive fibro-obliterative disease of the bile ducts and represents the leading indication for pediatric liver transplantation (LT). The first step in managing BA is the Kasai portoenterostomy, aiming for full biliary flow recovery, most likely obtained if the surgery is performed in the first 45 days of life. Otherwise, the infant is exposed to early cirrhosis development.

Case report. We report the case of a three-month-old female infant who was referred to our clinic for post-operative surveillance. She had been diagnosed with BA at 2.5 months and had undergone the Kasai portoenterostomy soon after. At the three-month post-operative evaluation, she was still jaundiced, malnourished, weighing 5700 grams (2nd percentile for age), with a total bilirubin of 8.56 mg/dl and direct bilirubin of 5.13 mg/dl. Albumin and cholinesterase levels were low, and INR was elevated. Transient elastography showed increased liver stiffness, equivalent to cirrhosis. The infant later presented repeated episodes of variceal bleeding complicated by sepsis and severe thrombocytopenia. Considering the severe persistent growth failure and decompensated cirrhosis, the patient was referred for living-related LT in a foreign center.

Conclusion. As the leading indication for LT in children, efforts should be made to early diagnose the BA and perform the Kasai procedure. It is well-known that most patients eventually require LT, even with optimized management. However, late diagnosis and surgery are associated with early cirrhosis development, and LT involves significant risks during the first year of life.

Portal cavernoma – a cause of non-cirrhotic portal hypertension in children

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Corresponding Author: Alina Grama e-mail: gramaalina16@yahoo.com **Background.** Portal vein thrombosis (PVT) and subsequent cavernous transformation of the portal vein (i.e. portal cavernoma) is a significant cause of portal hypertension (PHT) in children. The risk factors include umbilical vein catheterization (UVC), abdominal surgery, omphalitis, sepsis, dehydration, thrombophilia, and vascular malformations. Although acute PVT is usually asymptomatic, the development of PHT may lead to severe complications, such as gastrointestinal (GI) bleeding, hypersplenism, ascites, cholangiopathy or cardiopulmonary disease.

Case report. We report the case of an 8-year-old boy diagnosed with PVT and PHT at the age of 2 months. He was born preterm at 31 weeks (due to large uterine leiomyoma), weighing 990 grams, with an Apgar score of 6/7. He was admitted to the neonatal intensive care unit, required UVC and developed neonatal sepsis. Further investigations revealed associated protein S deficiency. He was followed up in our clinic and received prophylaxis with nonselective beta blockers. The first episode of GI bleeding occurred at age 5, and endoscopic band ligation was performed. Three years later, he

had another episode of GI bleeding triggered by a respiratory infection. Clinically, he was lethargic, with skin pallor, splenomegaly, and melena. Laboratory tests showed moderate posthemorrhagic anemia, thrombocytopenia, and increased inflammation markers, with normal liver parameters. Treatment consisted of endoscopic ligation of esophageal varices, octreotide infusion, proton-pump inhibitors and antibiotics. The evolution was favorable, and the boy was discharged after 4 days.

Conclusion. Our patient had multiple risk factors for developing PVT. Despite early diagnosis and prophylactic measures (medical and endoscopic), he continued to present recurrent GI bleeding episodes. To improve these patients' long-term outcomes, research is needed to find medical therapies to manage pediatric PVT better, or a surgical shunt must be performed but with known possible long-term complications.

Treatment and prognosis of autoimmune hepatitis in children

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Corresponding Author: Alina Grama e-mail: gramaalina16@yahoo.com **Introduction and objectives.** Autoimmune hepatitis (AIH) is a chronic liver disease with an increasing incidence characterized by immune-mediated hepatocyte injury resulting in inflammation, liver failure and fibrosis. Our study provides new information regarding the presentation, natural history, treatment, and prognosis of children with AIH.

Material and methods. This retrospective study included 30 hospitalized children with AIH, followed up in our clinic over a six-year period (between February 2016 and February 2022). All included patients met the International Autoimmune Hepatitis Group simplified diagnostic criteria (IAIHG criteria). We have analyzed the clinical presentation at diagnosis, biological and immunological changes, treatment, and evolution of the patients.

Results. Children with AIH were aged between 4 months to 17 years and 8 months (mean age of 6.5 years). There were 19 girls (63.3%) and 11 boys (36.6%). Most patients had an acute onset with nausea and vomiting, abdominal pain, hepato- and/or -splenomegaly, jaundice, dark urine, and pale stools. Sixteen patients did not develop jaundice. All patients had elevated liver enzymes and most patients (22 children, 73.3%) had increased immunoglobulin G (IgG) levels. Partial immunoglobulin A (Ig A) deficiency was found in 4 children (40% of type 2 AIH patients). There were 20 patients with type 1 AIH with positive antibodies against smooth muscle (SMA) and antinuclear antibodies (ANA), and 10 patients with type 2 AIH with anti-liver cytosol type 1 (anti-LC-1) and anti-liver kidney microsome type 1 (anti-LKM-1) antibodies. All patients received prednisone from diagnosis. Fifteen patients received azathioprine in combination to steroid therapy. Liver enzymes values normalized in 18 patients. Complete remission was achieved in 10 patients. Most children had a favorable prognosis, but five patients presented cirrhosis. Two children died due to complications of autoimmune cirrhosis.

Conclusion. The prognosis of children with AIH treated with immediate immunosuppressive therapy is favorable, with good long-term survival rates. Understanding the pathogenetic mechanisms of this disease could help those patients that do not respond to standard immunosuppression, avoid drug side effects, and prevent possible relapse after liver transplantation.

Complications after liver transplantation in a child with deoxyguanosine kinase deficiency

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Corresponding Author: Claudia Simu e-mail: claudia.sirbe@yahoo.com **Introduction.** Deoxyguanosine Kinase (DGUOK) deficiency is a very rare disorder characterized by liver dysfunction, neurologic manifestations and metabolic disorders secondary to severely reduced mitochondrial DNA content due to DGUOK deficiency.

Case report. We are presenting the case of a 6 months-old female diagnosed with DGUOK deficiency who developed acute liver failure. At 9 months, she underwent living-related liver transplantation (LT) in Cliniques Universitaires St Luc, Bruxelles, with an initial favorable evolution under immunosuppression therapy with tacrolimus. Four months after LT, she was admitted to our hospital for two prolonged bacterial and rotavirus enteritis episodes. She developed severe renal acidosis type IV, secondary to the high tacrolimus level, requiring dose reduction and fludrocortisone therapy. Meantime, both parents became infected with SARS-CoV-2, but the patient showed no clinical or serological signs of infection. Her condition deteriorated progressively, with significant weight loss, with a total refusal of food, so we started feeding on the nasogastric tube. The neurological evaluation did not reveal any suggestive signs of the progression of the underlying disease. A slight increase in transaminases and cholestasis enzymes was detected, and the abdominal ultrasound revealed four hypoechoic lesions, granuloma-like (three on the liver and one on the spleen). The Epstein-Barr and Cytomegalovirus infections were proven, most likely developing post-transplant lymphoproliferative disease (PTLD). We referred her again to the transplant center at 1 year and 4 months, where tacrolimus dose reduction was continued, and methylprednisolone and Ganciclovir were started. Two months later, her clinical features and laboratory parameters improved considerably.

Conclusion. This case highlights the unpredictable evolution of children with LT. Without any neurological signs of disease progression, she developed complications secondary to immunosuppressive therapy received post-LT. The possible neurological impairment of the mitochondrial disease is the basis of controversies regarding the indication of LT in these patients. Only a few cases of DGUOK deficiency that underwent LT have been reported worldwide, with low survival for over five years.

Conjuctivitis or ataxia-telangiectasia? - a diagnostic trap

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Corresponding Author: Diana-Alexandra Borcau e-mail: dianaborcau@gmail.com **Introduction.** Ataxia-telangiectasia is a rare disorder, with autosomal recessive inheritance. It is caused by ATM gene's mutation, gene encoding the protein ATM. These protein coordinates DNA repair. Secondary to the altereted response to DNA damage, oculo-cutaneous telangiectasia, immunodeficiency, cerebellar degeneration with progressive cerebellar ataxia, cancer susceptibility and radiation sensitivity appear.

Case report. We report the case of a 15-year-old boy with no significant family and personal medical history, who was first referred to our department at the age of 6 for progressive ataxic gait. He had a normal neurological and motor development,



walking independently at 13 months and even being able to ride tricycle at 3 years.

At the age of 1, the mother firstly observed the ocular telangiectasia, being considered as a sign of conjuctivitis. Two years later ataxic gain appeared. No modifications were found on the cerebral MRI.

At admission, at the age of 6, he presented ocular telangiectasia, cutaneous telangiectasia on the neck, failure to thrive, a language delay and ataxic gait. The laboratory exams revealed humoral immune deficiency with low IgA, IgG2 and IgG4, a low percentage of lymphocyte B on immunophenotyping and a high level of alpha-fetoprotein. The cerebral MRI at that moment revealed cerebellar atrophy.

Genetic tests, performed afterward, identified two pathogenetic mutations: c.1564_1565 del (p.Glu.5221efs*43) and c2250G>A (Silent), which confirmed the diagnosis of Ataxia Telangiectasia.

In evolution, his ataxia fell into decline, the telangiectasias accentuated and dysarthria appeared. The MRI confirmed progression of the cerebellar atrophy. Alpha-fetoprotein was in continuous accession. All these facts confirm the progression of the disease.

Conclusion. Ataxia-telangiectasia is an insufficient known disease with an infaust prognosis in the presence of continuous evolution of the lesions. There is no treatment known to stop the neurodegeneration.

Liver steatosis does not influence significantly the prognosis and mortality of patients with moderate and severe COVID-19

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Corresponding Author: Rareș Crăciun e-mail: rares.c.craciun@gmail.com **Introduction.** Liver involvement in Coronavirus Disease 19 (COVID19) has been widely documented. However, data regarding liver-related prognosis is scarce and heterogeneous. The current study aims to evaluate the role of liver steatosis on the prognosis of hospitalized COVID19 patients.

Method. We conducted a retrospective cohort study to investigate the impact of CT-documented liver steatosis on mortality and admission on intensive care unit (ICU) in patients with moderate and severe COVID19, with no prior liver disease history.

Results. 370 consecutive patients were included, of which 289 patients (72.9%) had abnormal liver biochemistry on admission. Of the whole study group, 124 (37,4%) had liver steatosis. Comparing patients with and without steatosis, no significant associations were found for hospital stay (p=0.11), ICU admission (p=0.23), or survival (p=0.56). The severity of COVID19 infections assessed through CT scan (TSS score) did not differ significantly depending on the presence of steatosis (p=0.95).

Conclusion. On our study group, the presence of steatosis was not a significant prognostic feature in patients with moderate and severe forms of COVID19.

An unusual case of hepatic cytolysis

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Corresponding Author: Bianca Jurjiu e-mail: bianca.jurjiu@gmail.com **Introduction.** Immune mediated necrotizing myopathy (IMNM) is a type of idiopathic inflammatory myopathy characterized by proximal muscle weakness, often rapidly progression and disabling. Most IMNM are associated with anti-SRP and anti-HMGCR antibodies (80%).

Case presentation. A 76 year old patient presents with proximal muscle weakness and weight loss (11 kg in 2 months). The disease onset was marked by dyspeptic syndrome and elevated liver enzymes, which is why the pacient was initially evaluated in a gastroenterology unit. An extensive etiologic set of analysis was performed to exclude an infectious or autoimmune cause for the hepatic cytolysis, which were all negative, but the analysis revealed important muscle cytolysis and inflammatory syndrome. Based on these initial results the pacient was referred to the rheumatology unit. Immunological tests showed positive antinuclear antibodies (ANA) 1:1280 – cytoplasmic polar/Golgi like, extended myositis specific antibody (MSA) panel was negative, and the anti-HMGCR antibodies were positive in high titer. The electroneuromyographic study revealed an active myogenic pathway, and the muscle biopsy showed myofibrilar necrosis, reduced inflammatory infiltrate and no perifascicular atrophy. The interruption of treatment with lipid lowering drugs and the initiation of therapy with Prednisone (0.5 mg/kg/daily) and Azathioprine 100 mg/daily led to a clinical and paraclinical favorable outcome.

Discussion. The difficulty and delay in establishing the diagnosis were due to the clinical and biological manifestations that suggested a liver disease, only later in the course of the disease the pacient developed muscle weakness affecting predominantly the lower limbs.

Conclusion. Lipid lowering drugs with important hepatic cytolysis should draw the attention towards testing for anti-HMGCR antibodies, in order to confirm an IMNM diagnosis.

Persistence of the inflammatory syndrome in a patient with rheumatoid arthritis treated with biological agents – a hidden issue

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2) County Emergency Clinical Hospital, Rheumatology department, Cluj-Napoca, Romania **Introduction.** The safety of biological therapy in the treatment of inflammatory rheumatic diseases represents a great challenge, both from the point of view of possible adverse reactions post-administration, as well as the flare of pre-existing conditions or the development of new pathologies. Therefore, rigorous and frequent infectious and tumour screening is of imperative importance.

Objectives. This study aims to emphasize the need to complete investigations in the case of persistence of the inflammatory syndrome, discordant with the clinical condition, in patients with rheumatoid arthritis (RA treated with biological therapies.

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Corresponding Author: Flavia-Bianca Mararu-Nicoară e-mail: flavia_buda@yahoo.com **Material and method.** A 57-year-old patient with seropositive RA, on biological treatment, who presented marked inflammatory syndrome.

Discussion. The patient diagnosed with seropositive PR since 2005, on combined treatment with leflunomide and rituximab (started in 2007 as part of a clinical trial) was monitored in another rheumatology service and referred to the Cluj Rheumatology Clinic – outpatient unit to complete the infusion treatment (8 cycles). The overall good clinical condition, but with the persistence of the inflammatory syndrome and elevated values of alkaline phosphatase (>7xVN) drew our attention. The patient was asymptomatic at the time of the hospital admission. Investigations revealed a G3 T3N0M1 bronchopulmonary adenocarcinoma with bone secondary lesions, which required a complex oncological approach.

Conclusion. Our study shows the importance of evaluating the biological activity in the case of rheumatoid arthritis with persistent inflammatory syndrome. Moreover, we show the need for exclusion of other pathologies especially in cases of conflicting clinical conditions.

Interplay between autoimmunity, immunodeficiency and infections in ANCA-associated vasculitis

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Corresponding Author: Cristina Pamfil e-mail: cristinapamfil.umfcluj@gmail.com **Background.** Common variable immunodeficiency (CVID) is the most frequent primary antibody deficiency in adults; heterogeneous clinical manifestations of this disorder delay the diagnosis by approximately 6-7 years from symptom onset. Autoimmunity is present in up to 30% of patients with CVID.

Case report. We present the case of a 55-year-old woman diagnosed with pANCApositive microscopic polyangiitis. The patient's medical history was notable for recurrent urinary tract infections and an episode of shingles 15 years ago. The disease onset was sudden in May 2021, with acute polyradiculoneuritis and alveolar hemorrhage; later, the patient developed rapid progressive glomerulonephritis with chronic kidney disease KDIGO G4. The patient underwent induction treatment with IV cyclophosphamide and glucocorticoids. During therapy, the patient developed multidrug-resistant urinary tract infections and severe and recurrent shingles. Thus, CVID was suspected and confirmed by hypogammaglobulinemia (IgG: 5.73 g/L; biological reference range: 7-16 g/L) and peripheral lymphocyte subset analysis, which revealed B lymphocyte CD19+ deficiency and a significant decrease in the count of natural killer cells. Substitution therapy with subcutaneous immunoglobulins led to the resolution of recurrent infections while the patient continued immunosuppressive therapy.

Discussion. In ANCA-associated vasculitis, infections are triggers of disease relapses. Cyclophosphamide and rituximab are employed for the remission induction and maintenance therapy of ANCA-associated vasculitis at the cost of high infectious risk. Associated immunodeficiencies further augment this risk. Importantly, immunosuppressed and immunodeficient patients have poor responses to protein- and polysaccharide-based vaccines.

Conclusion. Mitigating the risk of infections in ANCA-associated vasculitis is mandatory; a screening of immunodeficiency should be considered in patients with a history of recurrent infections prior to therapy.

Scleroderma renal crisis – not always easy to identify, but certainly difficult to treat

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Corresponding Author: Evelyn Futo e-mail: evelyn.evy14@gmail.com **Objectives.** Emphasizing the severity and the difficulty of treating scleroderma renal crisis (SRC), a pathology that is associated with an unfavorable prognosis and requires, in addition to numerous therapeutic resources, a good interdisciplinary collaboration.

Material and method. Presentation of a complex clinical case of SRC, identified late and the therapeutic difficulties that appeared.

Discussion. A 56-year-old patient, diagnosed with diffuse cutaneous systemic scleroderma (anti-Scl70 antibodies positive) and seropositive rheumatoid arthritis (RA), in the records of Cluj-Napoca Rheumatology Clinic since September 2021, presents repeatedly to the ER complaining of nausea, vomiting, epigastric pains and elevated blood pressure. Patient is given diuretic medication with a temporary reduction in blood pressure. At the second presentation within a few days, BP>210 mmHg and a marked nitrogen retention syndrome are detected. The symptoms are interpreted as being in the context of a mixed ARF (self-medication with NSAIDs, dehydration). The clinical condition deteriorates markedly, with elevated blood urea nitrogen. The patient comes as scheduled to the rheumatology department, where SRC is identified. The hydroelectrolytic rebalancing proved insufficient, after collaboration with the nephrology department, it was decided to include the patient in the hemodialysis program. The therapeutic approach was also made difficult by the subsequent infection with SARS COV2.

Conclusion. Rapid deterioration of renal function, accompanied by malignant hypertension in a patient with recently diagnosed diffuse cutaneous systemic scleroderma, requires increased awareness to identify renal crises and appropriate, multidisciplinary therapeutic approach.

The impact of anti-Ro antibodies in pregnant patients with Systemic Lupus Erythematosus and Sjögren's Syndrome

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Introduction. The presence of anti-Ro antibodies in female patients diagnosed with systemic lupus erythematosus (SLE) and primary Sjögren syndrome (SS) in their fertile years raises concern among the medical team due to the risk of neonatal lupus in their newborns (NB).

The aim of this study was to determine whether there are differences between the outcome of anti-Ro positive pregnancies in SLE and SS.

Material and methods. A retrospective observational study carried out in a Rheumatology tertiary center. Anti-Ro positive female SLE and SS patients were included. Clinical, immunological and pregnancy parameters were recorded, as well as maternal risk factors.

Results. Eleven anti-Ro positive SLE patients and 10 anti Ro-positive SS patients

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Corresponding Author: Daisy Ana Maria Vaida-Voevod e-mail: daisy.vaida.voevod@gmail.com were included and had 13 and 12 pregnancies, respectively.

The majority of both SLE and SS patients had moderate anti-Ro antibody titers (<200 U/ml) before as well as during pregnancy: 6 (46.5%) and 8 (61.53%) in SLE, 5 (41.6%) and 7 (58.3%) in SS.

More preterm NB and stillbirths were encountered in SLE mothers, both groups encountered 1 pregnancy loss, and cesarean delivery outweighed vaginal ones in both SLE and SS patients.

There were 4 (33.33%) NB with cutaneous neonatal lupus all from SS mothers, 3 of whom used HCQ before and/or during pregnancy; and there were 5 NB with complete fetal atrioventricular block (AVB), 3 (25%) from SS mothers and 2 (15.38%) from SLE mothers. Two NB died (both from SLE mothers) and 3 NB (all from SS mothers) needed pacemaker implantation. From the latter, 1 developed pacemaker cardiomyopathy and 1 developed sepsis.

Conclusion. Neonatal lupus seems to be more prevalent in anti-Ro positive SS patients than SLE patients, even though no difference was seen in anti-Ro titer between the two diseases. Fetal cardiac arrhythmia may lead to SS diagnosis. Dexamethasone did not improve the outcome of the fetal AVB.

Lysinuric protein intolerance (LPI): a multi-organ metabolic disease evolving with hyperammonemia

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Corresponding Author: Romana Vulturar e-mail: romanavulturar@gmail.com **Introduction.** Lysinuric protein intolerance (LPI) is an autosomal recessive disease, caused by mutations in the SLC7A7 gene, with defective transport of lysine, arginine and ornithine in the basolateral membrane of epithelial cells from the small intestine, proximal renal tubules, and in the plasma membrane of monocytes and macrophages. These disturbances can cause considerable multisystem damage, primarily affecting the immune system, with a predisposition to inflammatory diseases, hematological abnormalities, hepatosplenomegaly, osteoporosis, kidney failure, and neurological impairments.

Methods. A comprehensive review on PubMed articles published in last decade regarding LPI was conducted, focusing on genetics, diagnosis and therapy.

Results. The natural history of LPI still remains incompletely characterized. Hyperammonemia (HA) may present as refusal to eat, vomiting, stupor and even coma, and can be misdiagnosed as food protein-induced enterocolitis syndrome. The diagnosis LPI may be complicated, is based on the combination of increased urinary excretion and low plasma concentrations of the cationic amino acids, especially lysine, or molecular tests. If plasma amino acid concentrations are very low, owing to very limited protein intake, urinary cationic amino acid excretion may be within the normal range. Postprandial orotic aciduria is always seen in untreated patients. The rare cases of acute HA in LPI patients should be treated as in other urea cycle defects. Oral glycerol phenylbutyrate (Ravicti) is a more palatable alternative to standard preparations.

Conclusion. The clinical heterogeneity of LPI is obvious in adult patients. Some are of moderately short stature, and may have marked hepatomegaly with/ without splenomegaly. Two-thirds have exhibited osteopenia, but pathological fractures seldom occur in appropriately treated patients. Mental capacity varies from normal to moderate impairment, depending on the previous history of HA. The treatment should prevent HA (with a low-protein diet, L-citrulline supplementation and nitrogen-scavenging drugs) and to provide a sufficient supply of protein and essential amino acids for normal metabolism and growth. However, LPI should be regarded as a severe multisystemic disease that can be treated.

Linking clinical specialties with cell biology in monogenic treatable diseases: learning from Wilson disease

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Corresponding Author: Romana Vulturar e-mail: romanavulturar@gmail.com **Introduction.** Wilson disease (WD) is an inherited autosomal recessive disorder caused by mutations in ATP7B gene and, if left untreated, will cause a deadly accumulation of copper in the liver, brain, and other systems (renal, cardiovascular and musculoskeletal).

Methods. A comprehensive review on PubMed articles published in last decade regarding WD was conducted, focusing on molecular genetics, and clinical and therapeutic data.

Results. The global prevalence for WD is 1/10000 - 1/30000 and, being mostly diagnosed between 5-35 years old, the clinical features may not always point to a rapid diagnosis. The primary defect in WD is a defect of a protein from the trans-Golgi network, ATP7B, an adenosine triphosphatase (ATPase), which is responsible for the excretion of copper and for the incorporation into ceruloplasmin. Wilson disease is one of the disorders that, with prompt and correct treatment, can be well managed. ATP7B is highly homologous to ATP7A, the protein defective in Menkes disease.

Conclusion. WD is a heterogeneous disorder, almost 800 mutations in ATP7B gene have been described to date. Interestingly, the calculated genetic prevalence of WD is at 1:7000 (at least 5 times higher than the disorder frequency in population). Some of this difference might be due to missed diagnoses of WD, to incomplete penetrance or to the suboptimal performance of computer programs that predict whether a variant is diseasecausing or not. A number of patients exhibit severe liver disease, others redistribute copper to the brain (basal ganglia), causing neurological disease with dysarthria and diminished control of movements, tremors, rigidity and swallowing problems, and ophthalmologic (Keyser-Fischer ring). A frequent early sign is a deterioration in the quality of handwriting. In some patients psychiatric symptoms predominate, ranging from behavioral disturbances to psychosis. Copper excess exerts its hepatic toxicity by generating free radicals that oxidize the mitochondrial membranes, resulting in their swelling and loss of oxidative phosphorylation capacity. The prognosis is excellent for patients who start treatment before severe tissue damage has occurred. The treatment for WD includes D-penicillamine (binds to copper), zinc, trientine (also binds to copper) and ammonium tetrathiomolybdate.

MEDICINE Surgical Specialties

The keystone perforator island flap in reconstructive surgery

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Corresponding Author: Tímea Helga Virág e-mail: viragthelga@gmail.com **Introduction.** Surgery is the first choice of treatment for chronic, relapsing, intractable Hidradenitis Suppurativa presenting at late stages. The aim of this study is to investigate the effectiveness of keystone perforator island flap for the reconstruction of axillary, inguinal and sacrococcygeal soft tissue defects in Hidradenitis Suppurativa. It is accepted that wide local excision and local coverage is the crucial treatment to prevent recurrence of the disease.

Material and methods. All patients presenting for surgical treatment of hidradenitis suppurativa between 2014 and 2019 were identified from the hospital database. Only patients with hidradenitis suppurativa confined to the axillary, inguinal and sacrococcygeal regions in Hurley grade II and III were included. We performed descriptive analysis of demographic data, comorbidities, topographic distribution of lesions, Hurley scoring, size of defect, specific type of reconstruction, complications, follow-up period, recurrences.

Results. 21 patients with localized axillary, inguinal or sacrococcygeal hidradenitis suppurativa were identified, and 22 KPIF was performed. All keystone perforator island flaps survived giving a durable cover to the affected regions. There were no complications. Functional and aesthetic results were satisfactory and there were no recurrences.

Conclusion. These findings confirm that the keystone perforator island flap procedure can be effective for immediate defect reconstruction after wide local excision of advanced hidradenitis suppurativa of the axillary, inguinal and sacrococcygeal regions and provides excellent aesthetic results.

Surgical management of a patient with necroziting scleritis

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Corresponding Author: Sorin Simion Macarie e-mail: sorimaca@yahoo.com **Introduction.** Necrotizing scleritis is a severe eye disease which can lead to dramatic ocular complications, including perforation of the sclera and, subsequently, functional or/and anatomical loss of the affected eye. Adequate treatment can prevent this evolution.

Material and methods. Case report of a 74 year female patient with necrotizing scleritis of the right eye with very important thinning of the sclera and major perforation risk. Patient is suffering from rheumatoid arthritis, this condition leading to immunological disorders determining scleral involvement. We decided to prevent scleral perforation by tectonic enforcement of the sclera. This was achieved with tendinous tissue collected from the patient and sutured at the level of scleral thinning.

Results. Sclera was reinforced and perforation was prevented. Visual function was preserved. We noticed no complications.

Conclusion. This method allows the prevention of scleral perforation and functional and anatomical conservation of the eye in severe situations.

Recurrent Dermatofibrosarcoma Protuberans of the forearm. Case presentation and review of literature

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Corresponding Author: David Andras e-mail: dr.andrasdavid@gmail.com **Introduction.** Dermatofibrosarcoma protuberans (DFSP) is a rare histologic subtype of sarcoma, arising from the dermal fibroblast. This superficial sarcoma spreads in the dermis and subcutaneous tissue, representing a diagnostic and therapeutic challenge. The standard of care is primary surgery with wide local excision and because of the high risk of local recurrence. The aim of this poster is to present the multidisciplinary approach to the management of recurrent DFSP incorporating the expertise of a general surgeon, plastic surgeon, pathologist and compare it to the literature. Although we want to raise awareness in the medical society that sarcoma is an aggressive rare disease but not a forgotten cancer.

Case presentation. We present the case of 41 year old male patient who was referred with recurrent DFSP to our institution. The patient underwent two surgical procedures in a lower ranked Hospital in Romania, for a supposed diagnosis of forearm abscess between Sept 2021 - February 2022. The patient suffered from a third local multifocal relapse in June 2022, which was confirmed for DFSP through biopsy and forearm contrast enhanced MRI. After multidisciplinary team discussion, we performed wide local excision and intra-operative pathologic assessment of the resection margins. En bloc resection of the tumor with a clinical resection margin of 5 cm in all directions of the skin was performed. Completing the deep resection margin required sacrifice of antebrachial fascia, the flexor carpi radialis muscle and tendon, radial artery.

Pathological report and CD34 staining confirmed complete excision of the tumor with free margins up to 3.2cm. Although we must underline the presence of the invasion of the tendon of flexor carpi radialis muscle, which was completely excised en bloc with the resection specimen. Internal saphenous vein was grafted from the right calf in order to reconstruct the radial artery. The reconstruction of the forearm was done using an antero-lateral myofascial flap of the thigh with a flow through flap vascular reconstruction technique.

Conclusion. Dermatofibrosarcoma protuberans has an indolent but locally infiltrative behavior. Invasion of the surrounding tissues like fascia, muscle and bone suggests the need for a multidisciplinary team approach. Surgical excision should be as wide as possible considering up to 5 cm resection margin followed by complex reconstructions to achieve relapse free survival.

The incidence of laparoscopic approach for the surgical treatment of acute appendicitis. A Romanian multicenter prospective study

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2) The Collaborative Group for the Study of Acute Appendicitis

Corresponding Author: Vasile Bințințan e-mail: vasile.bintintan@umfcluj.ro **Introduction.** Due to lack of a nationwide registry of minimally-invasive operated patients, the real incidence of the laparoscopic approach for treatment of acute appendicitis in Romanian hospitals is not known. The aim of this study is to shed a light on this issue.

Material and method. A national multicenter study prospective study was conducted during a 6-month period, form 15 May to 15 November and included hospitals of all categories: 6 university hospitals, 9 county hospitals, 6 municipal hospitals and 1 private hospital. Inclusion criteria for the hospitals was the willingness to record data in a prospective manner. All patients with acute appendicitis operated both open and laparoscopic were enrolled in the study.

Results. 588 patients were included in total, of which 562 adults, 6 pregnant women and 20 minors aged between 9 and 17 years. Of these, 274 (46.6%) were operated laparoscopically while 313 patients (53.2%) were operated with an open of which 294 with McBurney incision (50%), 19 (3.2%) with Jalaguer incision and 1 (0.2%) oblique inguinal incision. The incidence of laparoscopic appendectomy was 100% in the private hospital, 72,3% in university hospitals, 37.3% in county hospitals and 29.5% in city hospitals. The overall conversion rate was 6.93%. The wound infection rate was significantly higher in the open vs the laparoscopic group (7.9% vs 2.4%). The average postoperative hospital stay was also significantly lower in the laparoscopic group (4 vs 6 days, respectively).

Conclusion. In this sample of 22 hospitals that cover the entire diversity of Romanian hospitals, the incidence of laparoscopic appendectomy aims towards 50% and is higher than expected. Probably there is a selection bias, probably younger, enthusiastic surgeons were more eager to take part in a prospective trial. However, it shows a trend in Romanian surgery toward modernization that is clearly led by the new, young generation of surgeons now used with minimally-invasive surgery from their training as residents.

The effect of platelet-rich plasma injection on short term vocal outcomes following phonosurgery

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Introduction. The efficiency and optimal voice rest period following phonosurgery remains debatable. Platelet-rich plasma (PRP) is a safe and cheap alternative to many bioactive agents being studied on animal models and is already



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Corresponding Author: Magdalena Chirilă e-mail: magdalena.chirila@gmail.com in use in many medical areas. We investigate the short-term effects of PRP and voice rest on voice outcomes following phonosurgery as an alternative to voice rest alone.

Material and methods. A prospective single-blinded pilot study was conducted. Sixteen patients with a diagnosis of vocal fold cyst and polyps were included, forming equal groups (PRP and voice rest vs. voice rest alone). Voice analysis was carried out on the preoperative day, day three, and week three following surgery. The measured parameters were fundamental frequency (F0), noise–signal ratio (NSR), harmonic poverty (HP), attack alteration (AL), pitch instability (PI), and amplitude instability (AI). VHI (Voice Handicap Index)-30 questionnaires were carried out before surgery and three weeks following surgery to assess the impact of subjective voice change on quality of life. PRP was obtained using commercial kits with separator gel.

Results. An average 3.68-fold increase in platelets was obtained in the PRP. All voice parameters improved on day three and week three following surgery. Statistical significance was noted only in the fundamental frequency of male patients (p = 0.048) in favor of the PRP-voice rest group. In addition, the VHI-30 questionnaire results between preoperative and postoperative assessments showed statistically significant differences in total VHI score (p = 0.02) as well as the physical (p = 0.05) and emotional (p = 0.02) scale in favor of the PRP-voice rest group.

Conclusion. PRP presents short term safety in patients who undergo phonosurgery, although long term outcomes are unknown. PRP and voice rest are superior to voice rest alone when considering subjective assessment of the voice. When analyzing acoustic parameters, PRP and voice rest are not superior to voice rest alone.

Jet-Ventilation: a new perspective in the conservative treatment of iatrogenic traheo-bronchial injuries

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Corresponding Author: Ioana Medeea Tiţu e-mail: medeea.titu@gmail.com **Introduction.** Iatrogenic tracheobronchial injuries are very rare. The major causes are orotracheal intubation and percutaneous tracheostomy. Therapeutic management is still controversial, with emergency surgical treatment showing a high mortality of 71%. We report a case of an iatrogenic tracheobronchial lesion after emergency orotracheal intubation treated conservatively.

Case presentation. A 53-year old woman was operated for thyroid carcinoma (total thyroidectomy). Five hours later, acute respiratory failure of unknown cause occurred and emergency orotracheal intubation was mandatory. Subsequently, bilateral massive pneumothorax, pneumomediastinum and extensive subcutaneous emphysema developed. A CT scan revealed the tip of the tracheal tube in the mediastinum. Emergency bilateral pleurotomy was performed. Bronchoscopy detected a large injury of the posterior part of distal trachea and right main bronchus. As emergency measure a left sided tracheal tube was placed. As hypoxemia persisted, jet ventilation was started on the right lung followed by rapid normalization of the blood gases. About 24 hours later, the clinical improvement allowed a switch to spontaneous breathing. After bronchoscopic control showing the lesion covered by mediastinal tissue the patient

was safely extubated. The further evolution was uneventful with discharge at day 5. The 1 month follow-up CT scan showed complete recovery of the tracheal lumen.

Discussion. HFJV (Twin Stream, Carl Reiner Breathing Engineering, Bronchoscopy program, Mode CAT-1 Lumen) is a form of mechanical ventilation that combines very high respiratory rates (>60 breaths/minute) with tidal volumes smaller than the volume of anatomic dead space. Jet parameters were titrated according to patient's status.

Conclusion. Conservative management of iatrogenic tracheobronchial injuries by spontaneous breathing or orotracheal intubation with overlapping the injury should be the main treatment option. Various types of ventilations including HFJV can help in normalizing the gas exchange and stabilize the patient.

Sternum repair for sternal dehiscence after median sternotomy using the ClawTM Fixation System: case report

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Corresponding Author: Ioana Medeea Tiţu e-mail: medeea.titu@gmail.com **Introduction.** Full median sternotomy is still the most used surgical approach in cardiac surgery with early sternotomy complications representing a major cause of morbidity (incidence 0.5% - 8.4%). The most common technique to repair a sternal dehiscence is the Robicsek technique, but in case of its failure the subsequent repair can become very problematic. We report a case of sternum repair for sternal dehiscence after full median sternotomy, using ClawTM Fixation System.

Case presentation. A 73-year-old woman with a history of percutaneous transluminal coronary stenting in the left anterior descending artery, coronary artery by-pass graft surgery (CABG) for triple vessel disease via median sternotomy and repair of a sternal dehiscence using the Robicsek procedure, complained of abnormal motions of the sternum, chest pain at rest, decreased exercise tolerance and significant decrease in quality of life. Physical examination revealed mobility during spontaneous breathing, increased by motion and chest pain by palpation. Chest X-ray showed multiple ruptures of the sternal wires. Ultimately, the patient was diagnosed with recurrence of the sternal dehiscence. Due to the proximity of the mammaria interna graft to the posterior sternal aspect we used for sternal fixation a non-circular technique (osteosynthesis with ClawTM Fixation System). The immediate and long term sternal stability was very good (clinical and radiologic follow-up 1 month postoperative).

Discussions. Multiple surgical techniques are used to repair sternal dehiscence after median sternotomy, but none of them can be considered the gold-standard. We chose the sternal claw plate procedure because of the fragmented sternum, with high mobility, and also to protect the CABG crossing right behind the sternum.

Conclusion. The ClawTM Fixation System ensures an efficient closure, achieving rigid fixation without bone penetration. It is also quick and easy to use, made from pure titanium or titanium alloy and ideal for osteoporotic bone or poor bone quality.

Endoscopic surgical management of recurrent intractable epistaxis

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Corresponding Author: Sever Pop e-mail: sever.pop@umfcluj.ro **Introduction.** Epistaxis is one of the most common ENT emergencies. Most patients are successfully treated by various types of nasal packing. However, recurrent, intractable posterior epistaxis remains challenging, characterized by repeated unsuccessful anterior and posterior packings, prolonged hospitalization and increased costs. Endoscopic sphenopalatine artery cauterization is a safe and reliable option for managing these patients.

Material and methods. The authors performed a retrospective review of the patients who underwent endoscopic sphenopalatine artery cauterization in our department between 2016 and 2021.

Results. Twenty-nine patients were included in this study. All of them have been previously managed by repeated unsuccessful nasal packings. The success rate was 89.65% (26 from 29). A revision endoscopic procedure was required for three patients. To control the bleeding, an additional fat plugin of the ethmoid cells was performed in two patients and an external carotid artery ligation in one patient. Mean hospitalization was 6.1 days. No serious complications have been recorded.

Conclusion. Endoscopic sphenopalatine artery cauterizations is a safe and effective surgical procedure for controlling bleeding in intractable posterior epistaxis.

The use of phytotherapy in hepatocellular carcinoma - a systematic review

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3) Department of Family Medicine, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Hepatocellular carcinoma (HCC) is one of the most common malignant tumors and the second most frequent cause of cancer-related death worldwide. Hepatocellular carcinoma acts as the most common type of primary liver neoplasm.

The aim of this review is to identify whether phytotherapy has an effect over the treatment of hepatocellular carcinoma or if it's suitable as a combination with chemotherapy.

Material and methods. A systematic review was performed in order to offer current information over the use of phytotherapy in hepatocellular carcinoma. We conducted an electronic search of articles published in English in peer reviewed journals between 2012 - 2022. The research process took place in October 2022. A combination of the following search terms was used: phytotherapy and hepatocellular carcinoma.

Corresponding Author: Paula Pop e-mail: cristinapaulapop10@yahoo.com **Results.** After keywords were associated, 302 articles were found. After the exclusion of articles which did not meet the necessary criteria for our study, there were 77 articles eligible for abstract evaluation, from which the following were discarded: two case report, one systematic review, 36 *in vitro* studies and nine studies which discussed other pathologies or with no regard to phytotherapy. The remaining 29 articles encompassed 27 *in vivo* studies of phytotherapy in hepatocellular carcinoma and two randomized control trials. These articles were included in the final analysis. This selection process is illustrated in the Prisma Flow Diagram.

Amongst the evaluated articles, two of them researched the effect of phytotherapy over human subjects in two randomized control trials, while the other 27 articles illustrated the outcomes of phytotherapy over hepatocellular carcinoma cells and murine specimens. The outcomes of these articles were divided into the following categories: molecular effects and clinical and paraclinical issues.

Conclusion. All in all, regardless of the use of only one herb or a mixture of medicinal herbs, phytotherapy has proven its usefulness in hepatocellular carcinoma, mostly through the following mechanisms: anti-inflammatory effect, suppressed malignant cell proliferation, inhibiting angiogenesis, stimulating apoptosis and even sensitizing cells to chemotherapy.

Acknowledgement. This systematic review is part of the PhD research project entitled "Perspectives in the diagnosis and treatment of Hepatocellular carcinoma" and was conducted with the support of Iuliu Hațieganu University of Medicine and Pharmacy.

PHARMACY Fundamental Research

Influence of extraction techniques and parameters on the phytochemical profile and biological activities *Trifolium pratense* L. extracts

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Corresponding Author: Octavia Dorina Gligor e-mail: gligor.octavia@umfcluj.ro **Introduction.** The purpose of this study was to gain an insight into the manner several extraction processes (both classical as well as innovative) affected bioactive compound yield, and subsequently assessing some of their biological activities.

Material and methods. Several red clover (*Trifolium pratense* L.) extracts were performed, using maceration, Soxhlet extraction, turboextraction, and ultrasound-assisted extraction, and a combination of the last two. The resulting extracts were analyzed for total phenolic and flavonoid content. The extracts presenting the best results were subjected to a phytochemical assessment by way of HPLC-MS analysis. After a final sorting based on the extracts' phytochemical profile, the samples were assessed for their antimicrobial activity, anti-inflammatory activity, and oxidative stress reduction potential using animal inflammation model.

Results. The Soxhlet extraction yielded the most satisfactory results both qualitatively and quantitatively. The ultrasound-assisted extraction offered comparable yields. The extracts showed a high potential against Gram-negative bacteria and induced a modest antioxidant effect on experimental inflammation model in Wistar rats.

Conclusion. The Soxhlet extract presented biological activity considering the results of the phytochemical profile of the other extracts. Therefore, red clover could also constitute a medicinal herbal species with interest towards complementary therapies, demonstrating safety and efficacy for antioxidant and antimicrobial activities

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Label-free aptamer-based biosensor for the detection of peanut allergy-inducing protein Ara h1

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Corresponding Author: Magdolna Casian e-mail: magdolna.casian@elearn.umfcluj.ro **Introduction.** Ara h1 is one of the major allergens found in peanuts that can trigger an immunological response in more than 50% of the allergic population, representing the first leading cause of anaphylactic fatalities worldwide. Taking into consideration the ongoing demand for analytical strategies for on-site sensitive detection of food allergens, this poster presents a strategy for the determination of the presence of Ara h1 protein in food products by enabling an electrochemical approach based on DNA strands.

Material and methods. The screen-printed gold electrodes were modified with p-aminothiophenol (p-ATP) and Ara h1 specific aptamer (Apt) by multi-pulse amperometry



(the applied potential was switched between +0.5 V and -0.2 V vs. Ag+ with a 10 ms pulse duration for different amounts of time), followed by the incubation with Ara h1 protein on the surface of the working electrode, at room temperature.

Results. Several strategies were addressed to diminish the protein fouling at the electrode surface and obtain the optimal sensing parameters. Each step of modification was optimized accordingly, with respect to the concentration and deposition time of p-ATP and Apt and incubation time of the protein. The currently obtained sensing platform showed a LOD of 21.24 nM.

Conclusions. Further optimization methods of the sensing platform to lower the detection limit are envisioned, as well as interference studies and real sample analysis. This work could be a starting point for aptamer based electrochemical detection platforms which target multiple allergens from food samples.

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Direct electrochemical detection of kynurenic acid – application of nanocomposite materials for wearable sensor design

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Corresponding Author: Maria-Bianca Irimeş e-mail: maria.bi.irimes@elearn.umfcluj.ro **Introduction.** Kynurenic acid (KA) is one of the active metabolites of tryptophan and it presents important biological properties such as neuroprotective and antiinflammatory function. It has been observed that KA is present in various biological fluids and its levels changes in some chronic diseases. Electrochemical methods represent a better approach for the analysis of biological samples due to their many advantages, such as high sensitivity and specificity, suitability for miniaturization, and in situ analysis.

The main purpose of the study was to design a platform for KA sensitive and direct electrochemical detection in biological samples with prospects for biomedical applications in the diagnosis and monitoring of patients.

Materials and methods. The planar carbon electrodes were in-lab printed by using conductive and insulating inks. KA prepared in phosphate buffer saline was tested by differential pulse voltammetry. To increase the sensibility of the method the surface of the working electrode was modified with graphene oxide, which was further electrochemically reduced and the detection of KA was performed as previously mentioned.

Results. The electrochemical behavior of KA was analyzed regarding the influence of electrode material, pH, electrolyte solution, and scan rate. Analytical parameters such as detection limit, limit of quantification, and sensitivity for KA were also determined.

Conclusion. The elaborated sensor allows KA direct detection and it can be further developed for medical applications.

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Electrochemical sensor based on screen-printed electrodes modified with nanomaterials for the sensitive detection of PQS in Pseudomonas

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Corresponding Author: Denisa Căpățînă e-mail: DENISA.ELEN.CAPATINA@elearn. umfcluj.ro **Introduction.** Infections caused by Pseudomonas aeruginosa are associated with a high mortality rate due to its ability to develop multidrug resistance and form biofilms. With antibiotic resistance on the rise, it is crucial to develop new methods to identify infections caused by P. aeruginosa. There are new detection methods targeting representative structures, such as quorum sensing (QS) molecules. QS is a form of cell-to-cell communication between bacteria, that plays a key role in determining virulence and biofilm formation. The most representative QS molecule for P. aeruginosa is PQS. The quantification of this molecule in biological fluids could provide important information about the infection with P. aeruginosa. Screen-printed electrodes (SPEs) have been largely applied for the field detection of a wide range of analytes in different biological samples. The possibility of modifying the SPEs with nanomaterials offers benefits to the detection method, increasing the sensitivity due to their good conductivity and large surface area. In this study, we developed a sensitive and specific electrochemical sensor based on carbon nanotubes (CNT)-modified SPE for the rapid and sensitive detection of PQS in P. aeruginosa.

Materials and methods. Several electrode materials, different electrolytes and pH, and two different electrochemical techniques were tested.

Results. The highest and most reproducible signal was obtained by differential pulse voltammetry using CNT-SPE and H2SO4 0.5 M as the electrolyte. The method allowed the sensitive and selective detection of PQS, with a limit of detection (LOD) of 50 nM. The sensor showed good results in detecting PQS in real samples.

Conclusion. A sensitive and selective sensor for the detection of PQS in P. aeruginosa was developed, being a promising tool for on-field detection.

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Electrochemical aptasensor based on ONS-23 aptamer for the detection of Campylobacter jejuni

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1) Department of Analytical Chemistry and Instrumental Analysis, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Campylobacter jejuni is a dangerous bacterium with high pathogeny. Reports show that in 2017, Campylobacter was the most common gastrointestinal bacterial pathogen in humans in Europe.

Conventional detection (culture on agar plates) takes a few days and the complementary methods (PCR, mass-spectrometry) are laborious and expensive.

In this context, biosensors and biomimetic-based strategies have emerged as promising alternatives, by offering rapid, selective and easy to use portable platforms for



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Corresponding Author: Alexandra Canciu e-mail: alexandra.canciu@elearn.umfcluj.ro the detection of various pathogens. One example, is the employment of aptamers (APTs) in the construction of electrochemical sensors. APTs are short single-stranded DNA/RNA oligonucleotides that act as ligands with enhanced properties compared to antibodies. Our work focused on the use an APT for the development of an electrochemical sensor for C. jejuni.

Material and methods. For the aptasensor elaboration, gold nanoparticles were electrodeposited onto the carbon-based screen-printed electrodes to allow the binding of the thiolated APT (ONS-23). The C. jejuni-binding APT was immobilized via multipulse amperometry and afterwards, using the same approach, a blocking step with mercaptohexanol, was performed. For the final detection, the platform was incubated with dilutions of C. jejuni cells. A portable potentiostat was used for the electrochemical measurements.

Results. The APT was successfully immobilized and allowed the electrochemical detection of the bacteria.

Conclusion. The approach showed promising results for further development of portable sensors suitable for on-site detection and surveillance of C. jejuni.

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Design of innovative nanostructured platforms for the electrochemical detection of gluten

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Corresponding Author: Alexandra Pusta e-mail: alexandra.pusta@umfcluj.ro **Introduction.** Gluten is the generic name for the proteins found in wheat, rye, barley and oats. It can be found in many types of foods, even in products where it is not expected and it is considered an allergen because many people are intolerant to this compound. Therefore, the detection of gluten in food is of particular and practical importance. The aim of the study was to design a nanostructured platform for the rapid, sensitive and selective detection of gluten in foods with prospects for applications in food industry.

Materials and methods. The first approach was related to the direct electrochemical detection of gluten on in-house printed carbon electrodes. Two different platforms were used: bare printed electrodes and printed electrodes functionalized with gold nanoparticles (AuNPs). The platform was tested using different pH conditions.

The second approach refers to the development, optimization and characterization of an aptasensor for the selective and sensitive detection of gluten. The same printed platform functionalized with AuNPs was used and a specific aptamer for Gliadin 4 (an important component of gluten) was immobilized through stable thiol-gold bonds.

Results. The results obtained using the direct detection method on real samples of wheat flour were promising, but the recovery rates for spiked samples were quite low, justifying the need for a more complex experimental approach, involving components that aim to increase the selectivity for the detection of the target analyte. The optimized aptasensor has been shown to be sensitive and selective for the target analyte, even in real samples of wheat flour.

Conclusion. The developed aptasensor demonstrated selectivity and sensitivity for the target, which recommends it for applications for food quality control, to prevent some serious health complications such as food allergies and celiac disease.

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Aptasensors for the diagnosis of Pseudomonas aeruginosa infection through quorum sensing molecules detection

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Corresponding Author: Teodora Lupoi e-mail: teodora.lupoi@elearn.umfcluj.ro Infection with P. aeruginosa represents an important issue of the medical system because of its high mortality rate. To optimize the treatment, early diagnosis is required, an unaccomplished demand by the standard bacterial culture method. Electrochemical sensors can overcome this drawback and are a cheaper and simpler alternative. In this study, an electrochemical biosensor was developed for P. aeruginosa detection using N-3-oxo-dodecanoyl L-homoserine lactone (3O-C12-HSL) and cyclic dimeric guanosine monophosphate (c-di-GMP).

The support platform was a portable carbon screen printed electrode (C-SPE) modified with gold nanoparticles (AuNPs). Biomimetic elements represented by thiol functionalized aptamers, specific for each quorum sensing molecule, were integrated into the sensing platform to increase the specificity of the method. The electrochemical characterization methods were differential pulse voltammetry (DPV) and electrochemical impedance spectroscopy (EIS) using [Fe(CN)6]3-/4- as a redox probe. The aptasensors detected the analytes from biological and real culture samples with good recoveries.

The signal increased logarithmically with the concentration of the 3-O-C12-HSL solution, obtaining a range of detection from 0.5 to 30 μ M. The aptasensor exhibited good selectivity for 3-O-C12-HSL and good recoveries in spiked urine and beef nutrient broth samples. The results obtained with this developed aptasensor correlated well with the number of bacterial colonies and are an indicator of its practical use.

The analytical method using the developed aptasensor can detect 3-O-C12-HSL, has good sensitivity and specificity and is a potential early diagnosis tool.

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Optimization of electrochemical (EC) activation methods of gold screen-printed electrodes for EC-SERS detection of thiabendazole and propranolol

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Corresponding Author: Petrică Ionuț Leva e-mail: petreleva@gmail.com **Introduction.** The discovery of surface enhanced Raman scattering (SERS) from an electrochemical (EC)-SERS experiment is known as a historic breakthrough. In the last few years several important developments have been made towards quantitative analysis, Raman spectroelectrochemistry representing now a promising alternative to conventional trace analytical methods.

Material and methods. A portable Raman spectrometer and a potentiostat were used for measurements. Commercially available gold screen-printed electrodes (AuSPEs) were used after an optimized EC activation of SERS features. For this, several roughening procedures (cyclic voltammetry, double-step chronoamperometry, fast chronoamperometry) and conditions (KCl with or without added HAuCl₄) were compared. Thiabendazole, propranolol and p-aminothiophenol were chosen as model molecules.

Results. Among EC methods, the double-step chronoamperometric procedure in 0.1M KCl proved to generate nanostructures in only one minute on the AuSPEs, being the most suitable for SERS detection of propranolol. An applied potential (-0.9 V vs. Ag/AgCl) increases the SERS signal of propranolol allowing its detection down to the μ M range. Furthermore, propranolol could be preconcentrated at the surface of the electrode. The detection of propranolol proved itself capable of offering quantitative data, therefore a calibration curve was developed and all the samples used constituted of spiked tap water.

Conclusion. The EC methods for activation of low-cost screen-printed electrodes offer a convenient, accessible, and ready-to-use alternative to commercially available SERS substrates. EC roughening procedures of AuSPEs were successfully optimized for the detection of thiabendazole and propranolol. By manipulating the surface charge through polarization, a higher enhancement of the Raman signal was observed for these molecules. The EC-SERS detection method is suitable for simple, fast and selective detection of residual thiabendazole and propranolol from relevant matrices. Also the quantification of propranolole was achieved, being able to build a calibration curve with an accuracy factor. Also the analysis of a real tap water sample spiked with a known concentration of propranolol was performed, with a good percentage of 89.2% recovery.

Acknowledgement. The research leading to these results has received funding from the NO Grants 2014-2021, under Project contract no. 32/2020, also by PN-III-P2-2.1-PED-2019-5473.
SERS labelled magnetoplasmonic nanoparticles for biomedical applications

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Corresponding Author: Constantin Mihai Lucaciu e-mail: clucaciu@umfcluj.ro **Introduction.** The combination of magnetic and plasmonic properties in one nanocomposite can provide new multifunctional nanomaterials with unique multimodal properties opening up great prospects for the application of these nanomaterials in biosensing, drug targeting, bioassays, diagnostic, photothermal, and photodynamic therapy, and other medical applications. However, for medical applications, these hybrid nanoplatform should possess controlled physicochemical properties and biocompatibility.

Material and methods. We used a seed-mediated growth method to obtain core-shell $ZnxFe_3-xO_4$ (a) Au magnetoplasmonic nanoparticles (NPs). The cores are composed of zinc ferrites close to the superparamagnetic state of 16 nm diameter, the zinc substitution aiming at increasing their magnetic moments. The surface of the cores was coated with amino groups for binding small-size (2-3 nm) negatively charged Au seeds. A continuous gold layer was further grown using an iterative method and a mild reduction of gold ions. Thiolated cyclodextrins were coated between these iteration steps and used as spacers for the inclusion of surface-enhanced Raman scattering (SERS) labels between the gold layers.

Results. The Zn substitution in the crystal structure of iron oxides lead to an increase in their magnetic moment, surpassing the magnetization saturation of bulk magnetite. The negatively charged Au seeds were attached to the aminopropyl tetra ethoxy silane (APTES) coated magnetic nanoparticles by electrostatic interaction. The reduction steps were performed in chloroauric acid using hydroxylamine and sodium citrate. Depending on the amount of precursors the thickness of the shell could be increased up to 20 nm. We notice that the resulting hybrids' magnetic performance decreased as the plasmonic shell's thickness increased. We also were able to cap the NPs with thiolated beta-cyclodextrin, used as a spacer to include rhodamine 6 G a SERS label between the gold layers. The resulting hybrid NPs possess both magnetic and plasmonic properties and have an intense label SERS signal.

Conclusion. The seed-growth method seems to be a reliable technique in the fabrication of nanomaterials with multimodal properties. Depending on the application the magnetic and/or plasmonic properties could be controlled by a proper choice of synthesis parameters.

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Antioxidant activities of some new thiazolyl-chalcones and thiazolyl-pyrazolines - in vitro evaluation

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Introduction. There is increasing experimental, clinical, and epidemiological evidence highlighting an involvement of free radicals and reactive oxygen species (ROS) in a variety of human diseases including cancer, inflammatory disorders and various degenerative ailments associated with aging. Antioxidants are chemical substances, which scavenge free radicals and ROS thereby minimizing the burden of oxidative stress generated in the body. Due to the presence of a reactive α,β unsaturated carbonyl group, chalcones and their derivatives possess a wide spectrum of antiproliferative, antifungal, antibacterial, antiviral, antileishmanial, and antimalarial pharmacological properties. Biological effects of chalcones have also been ascribed to their antioxidative activities as they exert indirect and direct redox activities. Chalcones undergo many chemical reactions as well as being used to synthesize heterocyclic compounds. Among the various derivatives of chalcones, pyrazolines has gained major attention due to their promising biological activities such as anticancer, antimicrobial, antidepressant, anti-inflammatory and antioxidant activity. The aim of our study was to investigate the antioxidant potential of some new thiazolyl-chalcones and their derivatives, thiazolyl-pyrazolines.

Material and methods. The antioxidant potential was evaluated in vitro, considering different possible mechanisms of action: hydrogen atom transfer, ability to donate electrons and metal ions chelation. Theoretical quantum and thermodynamical calculations were also performed.

Results. Some of the compounds (especially the series of thiazolyl-pyrazolines) exerted a good antioxidant effect (stronger than Trolox).

Conclusion. Based on these preliminary studies, some of the new compounds exhibited a promising antioxidant activity and can thus be considered for further investigations in experimental cell models.

PHARMACY Pharmaceutical Specialties

Detection of psychoactive substance use in drivers, correlated with saliva and urine tests during music festivals

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Corresponding Author: Maria-Georgia Ștefan e-mail: stefan.georgia@umfcluj.ro **Introduction.** Drug consumption in drivers is an increasing phenomenon that poses a significant threat to public safety. Attending music festivals (MF) is a known risk factor for psychoactive substance (PS) use. Two large-scale electronic MF take place in the Cluj-Napoca area annually. The aims of this study were to evaluate: 1) whether on-going MF increased the prevalence of drug consumption in drivers in the Cluj area; 2) which were the main PS that were used; 3) the correlation between the results of saliva and urine testing for PS.

Material and methods. The study retrospectively evaluated 601 cases of presumed drug use in drivers, for which samples were collected between 01.01-14.09.2022. Screening for PS use was performed on site, by saliva testing using immunoassays and laboratory confirmation of the obtained results was based on urine immunochemical analysis. The prevalence of confirmed cases and the types of PS identified during MF were compared to those obtained during the rest of the time period. The correlation between saliva and urine testing was evaluated depending on the type and/or number of PS that were identified.

Results. The mean number of cases/day of presumed drug use in drivers increased 4 fold during MF. The prevalence of positive results in both saliva and urine increased significantly during the festivals in comparison to the rest of the period. The correlation between the results of saliva and urine testing was strongest when only one PS was identified in saliva and decreased drastically when saliva tested positive for three or more PS. During MF, there was a higher overall rate of confirming the results obtained for saliva samples by urine immunochemical testing.

Conclusion. The prevalence of PS use in drivers increases markedly during MF. The most notable increases were in the cases of stimulant substances and THC. The results indicated a possible cross-reactivity during immunoanalysis for substances with structural similarities.

The influence of pH on the physical properties of natural compound-based nanocarriers

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Corresponding Author: Andreea Cornilă e-mail: cornila.andreea@yahoo.com **Introduction.** Natural polymers can be used as building blocks for drug nanocarriers intended for oral administration in children due to their high biocompatibility and vast usability, their reduced size allowing for their inclusion in low drug load dosage forms, such as minitablets. The aim of this study was to monitor the impact different polymers and pH conditions can have on the physical properties of nanocarriers.

Material and methods. Zein, along with loratadine, was dispersed in a 75% ethanol solution. The nanoparticles were obtained through antisolvent precipitation with an aqueous solution of either Poloxamer 188 or a mixture of sodium alginate and sodium

caseinate. After precipitation, the alcohol was evaporated and the remaining suspension was poured into chitosan dispersions with a pH of either 2.8 or 9.2. After centrifugation, the size and zeta potential of the nanoparticles were measured. A chromatographic method was developed to assess the encapsulation efficiency.

Results. Due to the slightly alkaline pH being inadequate for the gelation of chitosan, the Poloxamer-stabilized nanoparticles showed little to no charge compared to their acidic media counterparts. While the alginate/caseinate formulation showed a strong charge, the chitosan coating tempered it through its opposite charge. A significant increase in size has been recorded in both formulations when poured in the ungelled chitosan dispersion.

Conclusion. Due to the absence of a gel network designated to coat them in the basic chitosan dispersion, the nanocarriers showed a tendency to aggregate, their surface charge being largely affected by the final coating or lack thereof. The acidic media is preferred for the dispersion of chitosan, but it has been proven to be incompatible with sodium alginate. More experiments will be carried to identify the optimal formulation.

Acknowledgement. This research was supported by Iuliu Hațieganu University of Medicine and Pharmacy Grant no. 881/11/12.01.2022.

Evaluation of fermented whey as functional ingredient against aflatoxin B1 and ochratoxin A oral toxicity in vivo

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Corresponding Author: Denisia-Iulia Paşca e-mail: denisia_pasca@yahoo.com **Introduction.** Aflatoxin B1 (AFB1) and ochratoxin A (OTA) are the most toxic secondary metabolites produced by fungi, and are widely known for contaminating staple foods. To prevent the toxicity of these mycotoxins, the use of functional ingredients such as fermented whey (FW) has been proposed. FW contains several bioactive compounds that have beneficial properties such as antimicrobial and antiviral. Therefore, the aim of the present study was to assess in vivo the effect of FW on the gene expression induced by the chosen mycotoxins.

Material and methods. 7 groups of 5 Wistar male rats each were exposed for 28 days to contaminated feed prepared with AFB1 (7 mg/kg) and OTA (9 mg/kg) contaminated flour, individually and in combination, with or without FW, in parallel with the control group. For the transcriptional analysis, rats were sacrificed and RNA was extracted from tissue samples of small intestine. The following genes related to inflammation and apoptosis were considered for gene expression analysis in small intestine tissue by real time quantitative PCR: tumor suppressor protein (p53), Bcl-2 Associated protein X (Bax), B-cell lymphoma 2 (Bcl-2), nuclear factor kappa of activated B cells (NF- κ B) and interleukine 1 beta (IL-1B).

Results. In the small intestine, our data showed repression in the expression of p53, especially after exposure to AFB1. In FW treated groups, a similarity of gene expression between the control and the exposures to mycotoxins was observed. The genes p53 and Bax showed significant overexpression, especially in the group fed with the mixture of FW and AFB1 or OTA.

Conclusion. These data confirm the beneficial effect of FW at transcriptional level in the digestive system, preventing the toxicity of AFB1 and OTA.

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Clinical pharmacist involvement in the development of a protocol for the use of albumin in the hospital

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Corresponding Author: Ligia Ancuța Hui e-mail: ligiahui@yahoo.com **Introduction.** Human albumin (Alb) is a plasma substitute, used in case of septic or hypovolemic shock, nephrotic syndrome, refractory ascites, etc. It is a drug with a high cost and low availability on the market, which requires strict control of prescription and use.

Objective. The purpose of this study was to evaluate the impact of the implementation of a protocol regarding the use of Alb with the role of standardizing the way of its use, both regarding the prescription and the way of administration in order to increase the quality of the medical act and reduce costs.

Material and method. The protocol regarding the use of Alb was developed by the clinical pharmacist of the hospital. It applies to hospitalized patients, in order to evaluate and establish the therapeutic behavior. This protocol is a non-mandatory document that specifies the standards, principles and fundamental aspects of the management of a specific clinical case. The content of the protocol is subdivided into: Evaluation and diagnosis, Therapeutic conduct, respectively Follow-up and monitoring. Also, for an easier use of the protocol, there is included in its annexes a synthesized form, in a table form of the therapeutic conduct. The protocol was used by the hospital's management to approve the request reports for Alb, a medicine that is included in the list of products with high costs. Following the implementation of the protocol, a comparative study of Alb consumption before and after the implementation of the protocol was carried out.

Results. The consumption of Alb (number of units) was evaluated for the period September 2017 - February 2018, before the implementation, compared to the period September 2018 - February 2019, after the implementation of the protocol. A significant decrease of the consumption of Alb in the hospital was identified after the protocol implementation. In the analyzed periods, an increase consumption was identified before the implementation of the protocol and a significant decrease after its implementation.

Conclusions. The intervention of the clinical pharmacist contributes to a better control of the prescription and use of Alb in the hospital, with direct effects in reducing the costs associated with the use of this medicine.

Clinical pharmacist involvement in the development of a guideline for the management of Amanita phalloides poisoning in hospital

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2) "Dr. Constantin Papilian" Military Emergency Hospital, Cluj-Napoca, Romania **Introduction.** Poisoning with Amanita species, especially Amanita phalloides is considered a medical emergency, and for a favorable prognosis a rapid intervention with an effective drug treatment is necessary. Nevertheless, there are no widely accepted treatment criteria for Amanita phalloides poisoning and treatment guidelines are lacking in most hospitals. The paper describes the content and implementation stages of a guideline developed by the clinical pharmacist.

Material and methods. International recommendations on the treatment of



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Corresponding Author: Sandor Szabo e-mail: szabo sandor88@yahoo.com mushroom poisoning include drugs used off-label and in much higher doses than those usually administered for therapeutic purposes. The clinical pharmacist of the hospital, who is actively involved in the development of guidelines and therapeutic protocols, developed a local guidelines, based on the literature information and in collaboration with the physicians. The hospital's Medical Committee approved the guideline. Since several drugs included in the proposed treatment protocol are administered by IV infusion, the clinical pharmacist provided training for nurses.

Results. The proposed treatment protocol includes prevention of amatoxins absorption, elimination of absorbed amatoxins and potential antidotes therapy to protect the hepatocyte. During the first three days of treatment, activated charcoal, silymarin, N-acetylcysteine, penicillin G and a combination of aspartic acid and pyridoxine are administered. In the following days, the administration of silvmarin, N-acetylcysteine and aspartic acid with pyridoxine is continued. The doses of the drugs were established after consulting the literature, and the pharmaceutical forms are those available in Romania. Since in Romania there is no silymarin for parenteral administration, the pharmaceutical form was chosen for oral administration, with dose adaptation. One of the barriers encountered in developing the protocol was associated with the need to administer much higher doses compared to those commonly used in the hospital medical practice. The guideline also includes recommendations on drug dosage, administration schedule, route and method of administration, intended for nurses. Thus, the guideline was adapted to the needs of the hospital to be easier to accept and implement. The treatment protocol included in the guideline was successfully applied in the case of 6 patients poisoned with Amanita phalloides.

Conclusion. The hospital management, and health care professionals appreciated the major contribution of the clinical pharmacist, which proves their significant role to optimize the patient outcomes, and to increase the quality of care in the hospital.

Occurrence of antibiotics and antibiotic resistance profile of isolated bacteria in influent and effluent wastewaters

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 Electron Microscopy Centre, Faculty of Biology and Geology, Babeş-Bolyai University, Cluj-Napoca, Romania **Introduction.** The rise of antibiotics usage has led to an exposure of bacterial communities and ecosystems to a significant amount of antibiotic residues. Wastewater treatment plants (WWTP) represent one of the main sources of antibiotics release into various compartments of the environment. Even if antibiotic contaminated wastewaters are treated in WWTP, a complete removal of antibiotics is impossible in conventional plants. Antibiotic environmental contamination could contribute to increase resistant bacterial population or maintain the selective pressure on it.

The main aims of the study were to develop an analytical HPLC-MS method to quantify 7 antibiotics (amoxicillin, piperacillin, ciprofloxacin, norfloxacin, azithromycin, clarithromycin, doxycycline) from wastewater and to determine the antibiotic resistance profile of bacteria isolated from wastewater matrices.

Material and methods. A total of 18 influent and effluent wastewater samples were collected in autumn 2021, winter, spring and summer 2022 from 3 different

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Corresponding Author: Svetlana Iuliana Polianciuc e-mail: svetlanaiuliana@gmail.com WWTPs located in Romania. The extraction of antibiotics from WWTP was carried out using Oasis HLB Solid Phase Extraction cartridges. The analyses were carried out using a Shimadzu 2010 HPLC-MS system. By incubating the water samples with nutrient agar media, several bacteria were isolated and tested against the detected antibiotics.

Results. Residues of at least one antibiotic could be detected in all WWTP samples, both influent and effluent. The most commonly detected antibiotics were doxycycline, amoxicillin and piperacillin, with the highest concentration for amoxicillin. Several bacteria were isolated from the wastewaters and tested against these main antibiotics, some showing resistance to most of tested antibiotics.

Conclusion. Antibiotic residues were detected in the WWTP effluent, highlighting a potential impact on the aquatic ecosystem, including bacterial resistance which constitutes an emergence for the scientific community.

The evaluation of cardioprotective effects of Ajuga species aerial parts extracts

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Corresponding Author: Laurian Vlase e-mail: laurian.vlase@umfcluj.ro **Introduction.** Many Ajuga species are used in Romanian folk medicine for their diuretic, anti-inflammatory, wound-healing and hepatoprotective properties. Because their effects on the heart were not previously determined, the present work aimed to explore the cardioprotective potential of hydroalcoholic extracts of three Ajuga species aerial parts: A. genevensis, A. reptans and A. laxmannii.

Material and methods. The effect of pretreatment with Ajuga species extracts on the isoprenaline-induced infarct-like lesion in rats was determined by ECG monitoring and the assessment of serum levels of creatine kinase, aspartate transaminase and alanine transaminase. The total serum oxidative status (TOS), total antioxidant response, total thiols, nitric oxide, malondialdehyde and oxidative stress index (OSI) were also determined.

Results. Several polyphenolic compounds were identified by HPLC in Ajuga sp. extracts: catechin, syringic acid, gallic acid, protocatechuic acid, vanillic acid and rosmarinic acid. All extracts showed good in vivo antioxidant activity: A. genevensis and A. reptans extracts determined a significant decrease in the levels of OSI and TOS, while pre-treatment with A. reptans extract induced significant reduction of nitric oxide production.

Conclusion. These results show that Ajuga species extracts may exert cardioprotective effects against myocardial ischemia by reducing oxidative stress.

Psychological impact of the COVID-19 pandemic among healthcare professionals in Romania

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Corresponding Author: Aliteia-Maria Pacnejer e-mail: aliteia.pacnejer@umfcluj.ro **Introduction.** As of September 13, 2021, there were 224,511,226 confirmed cases of the SARS-CoV-2 virus and 4,627,540 deaths registered globally. Symptoms of stress and trauma are defining for the psychological impact of a pandemic on the population, especially among healthcare professionals.

The objective of this study was to evaluate the psychological impact of the COVID-19 pandemic among the healthcare professionals in Romania.

Material and methods. The questionnaire was distributed online during scientific events and on social media groups and took place between 25 May-25 September 2021. A total number of 208 healthcare professionals from Romania participated by completing the survey.

The survey includes 15 items, based on the Modified Event Impact Scale for COVID-19 (IES-COVID19). The total IES-COVID19 score is calculated by the sum of all 15 items. Scores greater than or equal to 24 indicate a psychological impact and a high degree of suffering regarding the current pandemic context and a possible installation of post-traumatic syndrome (PTSD).

Results. From the total number of 208 healthcare professionals, 40.8% were included in the 25-34 age group and 88.3% of them were female. Furthermore, 113 respondents obtained a total IES-COVID19 score between 0-23, 52 of the respondents obtained a score between 24-33 and 42 of them obtained a score greater than or equal to 33. Only one respondent obtained the maximum score of 75 points.

Conclusion. Quarantine measures are in most cases experienced as disruptive or traumatic. The SARS-CoV-2 virus caused a significant psychological impact on the entire population and especially among healthcare professionals, who faced a high risk of infection and an increased workload during the COVID-19 pandemic.

Antioxidant and cytotoxic activity of new polyphenolic derivatives of quinazolin-4(3H)-one: synthesis and in vitro activities evaluation

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 Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The development of hybrid molecules with significant human therapeutic properties is one of the main purposes of the pharmacological research. One of the most important pharmacophores is the quinazolin-4(3H)-one heterocycle moiety, due to its wide range of biological activities. By its derivatization with polyphenolic compounds, a complex activity has been observed.

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Corresponding Author: Gabriel Marc e-mail: marc.gabriel@umfcluj.ro **Material and methods.** Based on previous research that proved the good antiradical activity of ortho diphenolic derivatives of quinazolin-4(3H)-one, we developed two new series of compounds, with an additional phenolic group or with a different phenolic substituent. The methods used to evaluate the antiradical activity were reduction of oxidizing reagents and transition metals' ions chelation assays. Quantum descriptors were calculated. The biological activity was evaluated using normal human foreskin fibroblast cells (BJ) and two cancerous cell lines, lung adenocarcinoma cells (A549) and prostate carcinoma cells (LNCaP).

Results. The results obtained for the pyrogallol derivatives showed a high antioxidant activity compared to ascorbic acid and trolox. In vitro cytotoxic activity evaluation, compared to doxorubicin, showed a better safety profile on healthy cell line and a lower activity on tumor cell lines, for the compounds.

Conclusion. The pharmacological effects were deeply influenced by the addition of the third phenolic group in the synthesized molecules.

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Development of bioadhesive thin films with herbal extracts having wound healing properties using Design of Experiments

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Corresponding Author: Cătălina Bogdan e-mail: catalina.bogdan@umfcluj.ro **Introduction.** Impaired wound healing predisposes to severe complications, which lowers the patient's quality of life and raises costs in the healthcare system. The aim of this work was to obtain an optimal film formulation containing herbal extracts with wound-healing properties. The optimal films were considered to have adequate mechanical strength, swelling degree, flexibility, and adhesive properties that allow easy application, absorption of exudate, and non-traumatic removal from the wound.

Material and methods. Hydroalcoholic extracts of Lavandula angustifolia, Viola tricolor, Salvia officinalis, Agrimonia eupatoria, Glycyrrhiza glabra, Certraria islandica, Artemisia absinthium, Polyvinyl alcohol (PVA), apple pectin (Sigma-Aldrich, Germany), glycerol, hyaluronic acid LMW, Tragacanth gum (Elemental, Romania). A Plackett Burman experimental plan (Modde 12, Sweden) with 11 formulations. The input variables: PVA and glycerol ratio, type and polysaccharide ratio. Characterization of the films: adhesiveness and mechanical properties (CT3 Texture Analyzer, Brookfield USA) organoleptic analysis, uniformity of mass, swelling degree, thickness.

Results and discussion. Increasing the glycerol ratio resulted in higher thickness, mass, and mechanical strength of the films, and lower swelling degree and adhesiveness. The increased PVA ratio was responsible for the increase in swelling degree and mechanical strength. The Tragacanth gum used in higher ratios led to increased adhesiveness and decreased mechanical strength; conversely, increasing pectin ratios resulted in decreased adhesiveness and increased mechanical strength. Given the formulation factors' influences on the film properties, the optimal formula was prepared and characterized, with a good correlation between the theoretical and experimental values. The stability study highlighted the preservation of film properties during one-year storage at room temperature

Conclusion. The optimal film formulation with adequate mechanical strength, adhesiveness, and swelling degree was obtained, which may be promising for wound care.

DENTAL MEDICINE

Facial asymmetry and temporomandibular joint disorders in children and youths

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Corresponding Author: Daniel Corneliu Leucuța e-mail: dleucuta@umfcluj.ro **Objective.** The study aimed at compiling the most recent research on how mandible asymmetry in youngsters and temporomandibular joint disc displacement relate to one another.

Material and methods. The standard protocol criteria for systematic reviews and meta-analysis methodology statements were followed when conducting the systematic review. The research protocol was prospectively registered on the Open Science Framework network. Five databases were the subject of a systematic computerized search without restrictions.

Results. Eight records out of 1011 that were retrieved were assessed, and five of those were incorporated into the meta-analysis. In four studies, lateral cephalograms and five studies, postero-anterior cephalograms were utilized for radiological assessment. In the random-effects meta-analysis approach, youngsters with disc displacement had substantially shorter Menton to midline (in mm) distances than individuals without disc displacement [-1.75 (95% CI -2.43 to -1.07), p<0.001]. On the lateral cephalogram, there was an almost statistically significant increase in the distance from the Articulare to the Gonion (in mm) [1.98 (95% CI -0.11 to - 4.08), p=0.063] when disc displacement occurred in youngsters. In children with disc displacement, the distance from the Articulare to Menton (measured in mm) was substantially greater [3.74 (95% CI -0.32 to 8.63), p=0.069].

Conclusion. Children with disc displacement had considerably shorter distances from Menton to the midline on the postero-anterior cephalogram and longer distances from Articulare to Gonion on the lateral cephalogram than ones with normal disc position.

Acknowledgement. Part of this study has been previously published.

Current diagnosis and management of Garre's osteomyelitis of the mandible

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Corresponding Author: Ioan Barbur e-mail: drbarbur@gmail.com **Introduction.** Osteomyelitis is a chronic disease that can occur in special conditions. Itself can appear in special circumstances such as bisphosphonate treatment, osteoporosis, trauma and immunodeficiency. Garre's osteomyelitis of the jaw is a very rare disease in which bone lesions appear in young patients without any underlying conditions. There are many suppositions on its appearance and what determines the manifestation of the disease. Most common presentation include pain, modification of the bone contour, swelling, and puss. Another possible cause can be an overactivity of the periosteum with temporomandibular joint disease. Treatment includes often systemic antibiotics, corticotomies, and application of local antibiotics.

Material and methods. Prospective analysis of the dynamic of a patient suspected of Garre's osteomyelitis. From first clinical evaluation to radiological studies, to biopsy, systemic antibiotics, corticotomy, application of Gentamicin, we follow up on a case of a young female patient after two dental extractions (4.6, 4.7).

Results. The patient was referred by the dentist complaining of pain and swelling. The first diagnosis was of alveolitis after dental exactions. After the cone beam computed tomography studies (CBCT) we suspected osteomyelitis or Ewing sarcoma (due to the suggestive aspect). The bone biopsy was done, and the final diagnosis was of osteomyelitis of the mandible. Systemic antibiotics were administered. The symptomatology of the patients slowly decreased with a gradually favorable evolution. Gentamicin mini-pearls were applied to further help the patient.

Conclusion. The diagnosis of the Garre's osteomyelitis of the jaws is difficult. We have a lot of methods to support the clinical evaluation. We should exclude all other causes for the symptoms and do a full workup before we decide any further treatment. Biopsy is always needed to make the correct diagnosis and treatment. Although, we have a lot of measures to help patients who suffering from such disease, the prognosis is good, but very slow. Care should be taken not to overlook any details in the diagnosis and treatment.

Are temporomandibular disorders, alterations of the cervical spine, and malocclusion related? Review of the literature and a case study

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Corresponding Author: Andreea Kui e-mail: gulie.andreea@elearn.umfcluj.ro **Introduction.** The relationship between temporomandibular disorders (TMD), head posture, and skeletal patterns has been the subject of ongoing discussion. The functional relationship between class II malocclusion, TMJ dysfunction, and cervical spine position changes is still disputed. This study aimed at reviewing the literature on disk displacement (DD) in class II malocclusions or cervical vertebrae position changes in the context of a hypodivergent case report, associated with cervical pain, right anterolateral disk displacement with reduction, left anterolateral disk displacement with reduction.

Material and methods. Terms, such as "disc displacement", "disk displacement", "temporomandibular joint", "class II malocclusion" and "cervical vertebrae", were searched in the databases PubMed, Scopus, Embase, and Cochrane between March 2022 and April 2022, without time restrictions, and following PRISMA principles.

Results. For the case reported the absence of physiological lordosis, along with changes in the hyoid triangle and a reduced gap between the C2 and C3 vertebrae, might be the cause of the patient's symptomatology and increased pressure on the spinal nerves.

We review the literature that suggested that occlusal splints may enhance the vertical dimension of occlusion as a component of a comprehensive therapeutic approach, hence assisting in symptom relief.

Conclusion. Occlusal splint therapy has been shown to significantly improve TMJ function, whenever in TMDs. Malocclusion, postural modifications, and changes in craniofacial morphology have all been connected to temporomandibular disorders. The literature review brought results that were consistent with the case that was presented.

Modern means of dental tissue analysis. Finite Element Analysis (FEA)

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Corresponding Author: Radu-Andrei Moga e-mail: andrei.moga@umfcluj.ro In recent years *in vitro* analysis of dental tissues, due to the benefits of simplicity of analysis, accuracy of results, and the multitude of simulations that can be performed, has become widely used for scientific studies. However, although used in engineering with great accuracy (aerospace industry, construction and design of cars, construction and design of strength structures, strength of materials, etc.), in medicine and especially in dentistry it has provided results that frequently contradict clinical data. For this reason it began to be regarded with much reserve and an undeserved lack of confidence, with no studies attempting to explain these highly inconsistent results. For this reason our research group, which brings together representatives from both the University of Medicine and Pharmacy and the Technical University, has tried through a series of stepwise studies to find the causes of these inconsistencies and solutions to restore confidence in this extremely simple and accurate study method in other fields.

Acidic drinks and how they affect the properties of materials used in orthodontics

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Corresponding Author: Monica Laura Rusu e-mail: dascalu.monica@umfcluj.ro **Introduction.** The aim of the current study is to compare the behavior in acidic environment of two resin cements that are used in current orthodontic practice, BracePaste (American Orthodontics) and Transbond (3M).

Material and methods. The samples were immersed in different acidic environments, such as Coca Cola® and Red Bull®, as well as in artificial saliva for the control group. The absorption and solubility of the materials were investigated at different times of the 21-day immersion period. Electron microscopy (SEM) assessment of the samples were performed.

Results. Transbond presented a higher liquid absorption than BracePaste, especially of artificial saliva, followed by Coca Cola® and Red Bull®. The best absorption resistance was achieved by BracePaste in all immersion environments. Immersion in Coca Cola® showed values four times higher than the values recorded for artificial saliva. The solubility test shows that BracePaste is more soluble in artificial saliva and Transbond is more soluble in Red Bull® and Coca Cola®. SEM showed that BracePaste has a compact structure after immersion in all three environments, while Transbond showed a network of cracks that allowed the immersion liquid to penetrate deep into the material.

Conclusion. The study carried out on the two materials highlighted the fact that BracePaste material behaves better in acidic environments such as Coca Cola® and Red Bull®, compared to Transbond material which is more susceptible to the acid erosion caused by the two drinks.

SERS-based examination of saliva for head and neck squamous cell carcinoma detection

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Corresponding Author: Cosmin Ioan Faur e-mail: cosmin.faur@yahoo.com **Introduction.** Head and neck squamous cell carcinoma (HNC) prognosis depends on various factors, the stage of the disease at the time of diagnosis being one of the most important. Unfortunately, the majority of the patients see a doctor in advanced stages, hence the disease morbidity and mortality are high. Also, no screening methods for HNC detection are currently available. Nowadays, non-invasive techniques are studied to detect HNC in the early stages of the disease to improve the survival rate and the quality of life. We aimed to examine the exosomes from salivary samples using Surface Enhancement Raman Spectroscopy (SERS) and to investigate the capacity of SERS spectra to detect oral and oropharyngeal squamous cell carcinoma (OOC).

Material and methods. Patients suffering from OOC and healthy volunteer patients who were addressed to the Department of Oral and Maxillofacial Surgery were included in this study. The saliva was harvested before any surgical procedure. Ultracentrifugation technique was used for exosomes isolation, and NanoSight and SERS examination on solid plasmonic nanoparticles of silver substrate were performed for exosomes characterization. The resulted Raman spectra were statistically analysed using Principal Component Analysis and Linear Discrimination Analysis (PCA-LDA) and Area Under the Curve (AUC) to detect cancer samples.

Results. A total of 51 patients were included in this study. NanoSight examination proved that exosomes were present in the saliva samples after the samples' ultracentrifugation. Raman spectra illustrated different peek intensities in Thiocyanate, Proteins, and Nucleic acids between the saliva of cancer and control groups. A cancer detection of up to 99% was proved by chemometric analysis of SERS spectra.

Conclusion. SERS examination of saliva exosomes is a non-invasive detection method for oral and oropharyngeal cancer.

A rare cervical mass associated with preoperative Horner's syndrome

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Department of Oral and Cranio-Maxilofacial Surgery, Faculty of Dental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** This study presents the rarity of the sympathetic chain cervical schwannoma with preoperative Horner's syndrome and describes the imaging evaluations, surgical technique, histopathology and outcome.

Corresponding Author: Mircea Ciurea e-mail: mircea10ciurea@gmail.com **Case presentation.** A 51-year-old man was admitted to our department for a left neck mass associated with blepharoptosis, miosis and anhidrosis. The preoperative diagnosis of a sympathetic chain tumor relied on clinical and imaging studies. Horner's syndrome, which rarely appears preoperatively, was detected on preoperative clinical evaluation, contributing to a faster and more precise diagnosis. The internal carotid artery and internal jugular vein were altogether displaced antero-laterally on contrast-enhanced Computed Tomography (CT) and magnetic resonance imaging (MRI). The patient underwent surgical excision as the treatment of choice. Histopathological examination confirmed the diagnosis of sympathetic chain schwannoma. Postoperatively the patient had first bite syndrome, pain in the left shoulder, voice hoarseness and coughing, foreign body sensation, tongue biting and deviation that gradually disappeared during the following 18 months.

Conclusion. In the case of a cervical mass, schwannoma must be considered as a diagnosis, particularly when neurological signs are present. Preoperative diagnostic evaluation and rigorous planning of surgical intervention in cervical sympathetic chain schwannomas are essential. Our case supports the theory that a cervical schwannoma pushing forward both the internal jugular vein and the carotid artery suggests an origin from the sympathetic chain.

The radial forearm free flap used for reconstruction of soft tissue defects of the oral cavity and oropharynx following oncologic resection surgery - our experience

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Corresponding Author: Dragoş Alexandru Țermure e-mail: dragos.tarmure@gmail.com **Objectives.** Since its introduction in 1981, the well-known advantages make the radial forearm free flap (RFFF) suitable for the reconstruction of the oral cavity and oropharynx. Its popularity among reconstructive surgeons has rapidly grown and the RFFF emerged as the workhorse for free flap soft tissue reconstructions of medium and large size defect in all subsites of the oral cavity. In this presentation we evaluate our experience with the use of the RFFF for the reconstruction of oral cavity and oropharynx defects after tumor resection.

Material and methods. During a 5-year period, 46 patients were treated in our department for the reconstruction of oral defects after tumor ablation by means of RFFF. All patients were treated for malignant entities with primary reconstruction. We evaluated 20 variables and parameters for each patient. These included sociodemographic data, types of anastomoses which were used and the blood vessels used for the anastomosis, local, regional and general complications in the immediate follow-up period, pathological staging and the duration of OR time.

Results. Squamous cell carcinoma was present in all but one case and the majority of the patients were male. The cephalic vein was usually harvested as part of the venous drainage system of the flap and the facial artery was used as a recipient vessel in 100% cases. Oral wound dehiscence was seen in 7 patients, all of which with minor revision recovered uneventfully and the overall survival rate of the flap was 87%. All patients underwent a split-thickness skin graft harvested from the thigh for grafting the donor site, out of which, one case out of 43 resulted in total skin graft loss.

Conclusion. The RFFF is a reliable method for reconstructing a wide range of oral cavity and oropharyngeal defects with an acceptable low morbidity rate.

Benign pediatric jawbone lesions – a 10-year retrospective clinical and radiological study

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Corresponding Author: Emil Crăsnean e-mail: ecrasnean@yahoo.com **Introduction.** The aim of the study was to present a retrospective longitudinal cohort analysis of the pediatric jaw lesions treated at the Oral and Maxillofacial Surgery Clinic of Cluj-Napoca, Romania, during a 10-year period, and to describe their clinical and radiological characteristics, treatment outcome and incidence of recurrence.

Material and methods. All consecutive patients (<18 years) with histologically diagnosed odontogenic tumor (OT), nonodontogenic tumor (non-OT) or odontogenic cyst (OT cyst) between 2012 and 2021 were included in the study population. The following data were collected and analysed. age, dentition type, clinical symptoms, preoperative and postoperative radiological investigations, histopathological diagnosis, therapy and follow-up data at a minimum of 1 year after the diagnosis.

Results. Eighty-two cases fulfilled the criteria for study eligibility. Male-female distribution was 1.15:1, with a noted 64.4% mandibular predominance and also a 31.7% predominance of inflammatory radicular cysts. In our cohort, the majority of patients were asymptomatic (42.68%). The most common surgical procedure was enucleation (45.1%), followed by cystectomy (28%) and marsupialization (14.6%). The overall recurrence rate was 7.3%, while the most recurrent histopathological lesion was the odontogenic keratocyst.

Conclusion. This study enhances our knowledge of the prevalence of benign pediatric jawbone lesions and sheds new light on clinical and radiological characteristics, treatment outcome and recurrence rate. The results achieved show that epidemiology, clinical and imagistic details are useful tools to guide the diagnosis and could help improve the management of the treatment in children with jawbone lesions.

Saddle angle variation depending on the Sella Point positioning

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Corresponding Author: Cristina Ciobotaru e-mail: cristinadora9@gmail.com **Introduction.** The aim of this cephalometric study was to investigate the possible variations of the saddle angle (NSAr) as an indicator for sagittal mandibular position in relation to the placement of the Sella landmark (S - center of Sella Turcica) trough visual inspection compared to the assessment of its position according to measured parameters.

Material and methods. This study included 60 lateral cephalograms of patients who were attended at the Orthodontic Department, Faculty of Dental Medicine, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca. The age of the patients was over 12 years. The study was conducted by measuring the NSAr angle value after tracing the lateral cephalograms and localizing the point S trough visual inspection and subsequently, the same angle was measured after determining the center of Sella Turcica by a standard method introduced by Silverman and Kisling. This method traces the length

of the Sella Turcica from the Tuberculum Sellae to the tip of the Dorsum Sellae and the depth trough a line perpendicular to the length, passing trough the deepest point of Sella. The diameter is traced by drawing a line from the Tuberculum Sellae to the most distant point on the posterior inner wall of the fossa. The data collected was statistically analyzed using Kruskal-Wallis H test.

Results. Variations in the NSAr angle values with different tracing of the point S (visually localized and geometrically determined) were found, but they were not statistically significant. This result matches the findings from literature that state that the midpoint of Sella Turcica appears to be the least variable point among N, S and Ar.

Conclusions. This study appears to be a new one, compared to the methods previously used. The NSAr angle has an insignificant variability in relation with Sella point positioning, a result that documents the accuracy of the Sella Turcica midpoint visual localization.

Modern treatment of dental disorders

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Corresponding Author: Mirela Ioana Fluerașu e-mail: mfluerasu@yahoo.com Dental disorders are a challenge in dental practice. Bruxism is a major risk factor for tooth structure and dentures. In healthy subjects, bruxism is considered a behavior, with a potential risk on the dento-maxillary structures, being defined as a disorder only when consecutive lesions occur.

The etiology of bruxism is still not very well established. centric and eccentric forms, psychogenic and mechanical, diurnal and nocturnal forms of bruxism are described. This leads to a difficult and uncertain diagnosis of bruxism, but especially to a long-term treatment involving multiple therapeutic scenarios, but with less spectacular results. However, technological progress, digitalization and modern therapies have not bypassed this pathology either. Selective polishing for occlusal balance, programmed mandibular advancement trays, the use of fillers and botulinum toxin, the use of "smart" mobile applications for patient awareness and the evaluation of the intensity of the parafunction, find their role and indication in reducing the intensity and frequency of bruxism.

The specialized literature communicates variable results obtained from the use of the therapeutic techniques listed above. Therefore, the therapeutic decision and the prognosis in the case of patients with bruxism represent a real challenge for the attending physician, further research being necessary in order to establish a rigorous and effective therapeutic protocol.

The etiology of canine malpositions

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1) Department of Pedodontics, Faculty of Dental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Several factors influence the position of canines such as ontogenetic evolution, the morphology of canine, the characteristics of dental arches and occlusion relationships. The present work includes a retrospective observational study which aimed to analyze etiologic factors associated with canine malposition corroborated with a systematic review.

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Corresponding Author: Ioana Sătmar e-mail: ioanasatmar8@gmail.com **Material and methods.** Photomontages and X-rays of 169 patients, 107 females, 62 males were analyzed by following through 63 items regarding age, gender, absence / presence of the canine, unilateral changes, space on the arch, occlusion relationships, values of SNA, SNB angles, Angle class, skeletal class, profile types, and atypical changes. All the information were transferred in a data base and then statistically analyzed. The systematic review assessed 41 articles from top 5 different Orthodontic Journals on the topic of canine malposition. Each article was analyzed according with 6 characteristics regarding the type of the study, population, malposition, investigation, and the topic of each study.

Results and conclusion. A number of 611 canines were examined. 298 maxillary canines and 313 mandibular canines. We observed 19 impacted canines (8 maxillary and 11 mandibular), mesio-buccal rotation was much more frequent (194 canines) than distobuccal rotation (87 canines), 44 ectopic canines and just 7 entopic canines. Egression of canines is very rare. A number of 278 canines had not enough space on the arch, so this means an increased frequency for transverse hypo-development of the maxillary bone.

The results of systematic review showed that the Chinese population had an increased frequency for the ectopic canine which is often associated with lateral incisor inclusion. Cone beam computed tomography (CBCT) is more effective than conventional X-ray for canine malposition assessment. The mandibular canine transposition occurs more often in females and it can be caused by MSX1 gene mutation. Also, canine agenesis is very rare but has an increased frequency in the Asian females, on the maxillary arch.

Intelligent matrix systems for the multimodal treatment of periodontitis – an *in vitro* and *in vivo* evaluation

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 Department of Chemistry and Chemical Engineering of Hungarian Line of Study, Faculty of Chemistry and Chemical Engineering, Cluj-Napoca, Romania **Introduction.** The aim of the study was the evaluation of a novel biomaterial obtained through electrospinning, proposed for the adjuvant non-surgical periodontal treatment, based on polylactic acid (PLA) and nanohydroxyapatite (HAP), loaded with Doxycycline.

Material and methods. The antimicrobial effect of the materials (nine samples with different concentrations of antibiotics) was tested *in vitro*, through microbiological techniques, on two bacterial species. The material that presented the highest inhibition zones on the two periodontal pathogens was proposed for further studies.

Regarding the *in vivo* evaluation, periodontal lesions were induced in the lower incisors of rats, using the ligature technique, and treatments were applied. Saliva and plasma were harvested throughout the experiment for inflammatory markers evaluation. The tooth mobility and periodontal index scales were used for the intraoral assessment.

Results. In the *in vitro* study, the samples of materials that contained antibiotics led to larger inhibition zones, depending on their concentrations. In the *in vivo* study, reduced tooth mobility and periodontal index scores were observed in the rats treated

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Corresponding Author: Elena Dinte e-mail: edinte@gmail.com with the novel biomaterial. Statistically significant differences were obtained when comparing the salivary and plasmatic concentrations of proteolytic enzymes and metainflammation markers, between the control and test subjects.

Conclusion. The novel biomaterial had an inhibitory effect on two of the main periodontal pathogens. The application of novel matrix material enhanced the therapeutic intraoral results. Its use modulated the investigated salivary and plasmatic parameters, reducing the meta-inflammation markers in the tested fluids.

Acknowledgement. The present study was supported by project CNCS-UEFISCDI, PN-III-P2-2.1-PED-2019-3664 "Personalized intelligent matrices for tissue regeneration and meta-inflammation control" (PRIM_TISS), No. 348PED/03.08.2020.

Microcomputed tomography and microscopy investigation of full contour crowns fabricated by digital technology

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4) Department of Molecular and Cellular Biology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The use of digital technology has been gaining popularity lately, especially in the field of prosthodontics, in which the fitting accuracy of the prosthetic restorations has an impact on the long-term clinical performance. The study aimed to evaluate the global fit of the full contour crowns manufactured by digital technology using x-ray microcomputed tomography (micro-CT) and microscopy.

Material and methods. The crowns, of different thickness, were fabricated by computer-aided design/ computer-aided machining technique. group A (leucite glass ceramic), group B (hybrid ceramic), group C (graphene) and the dies were obtained using the 3D printing technique. After cementation, the samples from each group were scanned by micro-CT Skyscan 1172 (Bruker, Belgium). The internal gaps measurements were performed on all surfaces into the CT Analyser software. The marginal discrepancy was analyzed by SEM investigation.

Results. On the micro-CT images, the number and size of internal gaps was highest in group A crowns, while in group C crowns exhibited the smallest number and size of internal gaps. On the SEM images, the marginal gaps presented the smallest values in group A and the largest in group C. For group B samples, both internal and marginal gaps values were between the other two.

5) Department of Manufacturing Engineering, Faculty of Industrial Engineering, Robotics and Management Production, Technical University, Cluj-Napoca, Romania **Conclusion.** The micro-CT and SEM investigations provide the quantitative analysis of the internal and marginal gaps of crowns, showing that group A had the inadequate internal fit and the good marginal fit, group C the better internal fit, and inaccurate marginal fit, while group B was always situated in the two.

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CAD/CAM occlusal splints for temporomandibular joint disorders

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Corresponding Author: Oana Almăşan e-mail: ocrisst@gmail.com **Introduction.** This systematic review aimed to assess the therapeutic efficacy of computer-assisted or digitally constructed occlusal splints in comparison to conventional splint treatment for temporomandibular disorders or bruxism.

Material and methods. Four electronic databases, PubMed, Embase, Web of Science, and Scopus, were searched comprehensively. The following keywords were employed. "3D-printed", "additive manufacture", "computer-aided design/computer-aided manufacturing", "temporomandibular joint", "temporomandibular joint dysfunction", "bruxism", "disc displacement", "temporomandibular disorder", "splint', "oral splint", "occlusal splint", "occlusal device", "bite splint", "occlusal appliance". Two risk of bias evaluation instruments were used to assess the quality of the included studies.

Results. Following the application of the search strategy, a total of 557 publications were identified in the electronic databases. Seven eligible articles were finally included in the analysis. Six publications (85.7%) compared digitally manufactured occlusal splints to conventionally created splints, while one examined if the use of a facebow influences the performance of digital splints. Visual assessment scores or numerical rating scales of pain, optical axiography, tooth wear, and bruxism frequency were reported as outcomes.

Conclusion. Computer aided design occlusal splints provide equivalent outcomes to traditional splints. Some generated superior results, mainly due to the virtual articulator's greater precision and the splint materials' qualities.

Acknowledgement. Part of this work has been previously published.

The influence of gender on the relationship between oral hygiene habits and some demographic and systemic factors in patients with cardiovascular diseases

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 Department of Periodontology, Faculty of Dental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Poor oral hygiene is a risk factor for periodontitis development and progression. Frequent associations between periodontitis and cardiovascular diseases have been reported. The objective of this study was to observe the influence of some demographic and systemic factors on the quality of the oral hygiene in patients with 2) Department of Cardiology Rehabilitation, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

Corresponding Author: Bogdan Caloian e-mail: bogdan912@yahoo.com cardiovascular diseases.

Material and methods. Patients with cardiovascular diseases completed a questionnaire related to oral hygiene habits, consisting of 8 questions, analyzing the quality of their oral hygiene, the hygiene methods and devices, as well as the number of annual check-ups at the dentist. Each answer was scored with 1 or 0, if oral hygiene habits were adequate or inadequate, respectively. An efficiency behavioral scale (0-8 points) was established.

Results. A number of 37 men and 47 women were included in the study. A percentage of 76.6% of the investigated women had a poor oral hygiene habits score (0-2 points), and 23.4% a moderate score. None of the patients fell into the good score class (6-8 points). Of the total number of male patients, 52.16% had a poor oral hygiene habits score, 35.13% a moderate and 2.71% (1 patient) a good score, obtaining 7 points. Both women and men from the urban environment obtained a better hygiene score than those from the rural environment (women. 2.11±1.36 vs 1.76±1.23, p=0.18; men. 2.44±1.69 vs 2.25±1.39, p=0.46). In women under 65 years, the average score was 1.88±1.04, and in those over 65 it was 2±1.46 (p=0.38). Men under the age of 65 had an average score of 2.42±1.81 while those over 65 had an average score of 2.37±1.36 (p=0.46). The score differences were not statistically significant.

Conclusion. According to our study results, oral hygiene behaviors were deficient in patients with cardiovascular diseases, regardless of gender, age or background.

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Chronic apical periodontitis between local and general effects

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4) Department of Histology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The end of the road for a pulpal inflammation is represented by the gangrene that can determine chronic apical periodontitis (CAP) thus, representing a potential source for inflammatory factors with impact on general health. The main objective of the study was to evaluate the implication of the periapical lesions on the general health and inflammatory status.

Material and method. A number of 200 patients were enrolled in the SALIVAGES project which was a cross-sectional study, conducted between September 2018 and January 2020. The periapical inflammation was determined by two independent evaluators based on orthopantomography, in a total number of 73 patients. The investigations used for patient evaluation were represented by blood count, total lipids, serum inflammatory factors and carbohydrate metabolism markers. Also, anthropometric measurements and associated diseases were recorded on the time of clinical exam. The markers of the nitro-oxidative stress were assessed in the plasma, urine and saliva. The following markers were evaluated. the nitric oxide, total oxidative status, total antioxidant capacity, the oxidative stress index, malondialdehyde and total thiols.

Results. Parameters of the oxidant/antioxidant balance were presented in total number of the subjects and divided by Group 1 and Group 2. Fructosyllysine (FruLys)

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Corresponding Author: Antonia Boca e-mail: toniboca07@gmail.com and Total antioxidant capacity (TAC) collected from plasma, Tiols (Tioli) collected from saliva and from urine after tooth brushing were significant higher in group where more than 50% of the units were affected by CAP. Pyralin (Pyr) collected from plasma and from saliva, Oxidative stress index (Osi) collected from saliva after tooth brushing were significantly statistically smaller in group where more than 50% of the units were affected by CAP. Arginine (Arg) collected from the saliva had slightly lower values in the group of patients with more than 50% of the dental units were affected by CAP.

Conclusion. Our study suggests that periapical disease contributes to the general pool of oxidative stress markers.

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Use of whitening toothpaste in the general population

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Corresponding Author: Irina Lupșe e-mail: irinalupse@yahoo.com **Introduction.** The use of dentifrice in conjunction with a dental brush ensures a potentiated cleaning and has a polishing effect on the tooth surface. In addition, the toothpaste can serve as a carrier for different active substances and the small particles of activated charcoal play an abrasive role on the extrinsic enamel discolorations. This questionnaire-based study evaluated the perspective and the knowledge of the patients on the use of charcoal based toothpastes.

Material and methods. A number of 81 subjects consented to participate in the questionnaire study. The included subjects were healthy and without any periodontal disease as well as free of any whitening procedures in the last twelve months. Specific items were assessed by questioning (toothpaste recommendations from the dentist; parameters taken into account when choosing toothpaste; usage of a whitening toothpaste).

Results. The majority were women (86.4%), with a mean age of 29.1 ± 3.292 years. Most of participants stated that they only sometimes use whitening toothpaste (56.8%). Often their dentist did not recommend the use of whitening toothpaste (84%) or the use of activated charcoal toothpaste (92.6%). The main consideration taken into account when using toothpaste is the presence of fluoride (90.1%).

Conclusion. Our study reveals that the main parameter taken into account when selecting toothpaste is the presence of fluoride. According to our results, there is a lack of patient information regarding the use of whitening toothpastes.

Evaluation of teeth eruption patterns

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Corresponding Author: Olimpia Bunta e-mail: olimpia.bunta@yahoo.com **Introduction.** Tooth eruption can be defined as a continuous biological process which implies that the developing teeth emerge through the jaw bones and gingival mucosa in order to reach the oral cavity and their final functional position in the occlusal plane. The aim of this study is to determine the time and sequence, gender differences and symmetry patterns of the permanent teeth eruption in the Korkhaus area, which are important factors in the development of dento-maxillary anomalies and orthodontic treatment planning.

Material and methods. This study was carried out on a group of 110 Romanian children aged 6-11 years. Their panoramic X-rays were evaluated in order to determine the status of eruption of the permanent teeth targeted by this study.

Results. The study revealed that the classical patterns of eruptions in the upper arch are maintained in most of the examined patients, less than one quarter having modifications in the eruption sequence. For the lower arch, the conventional eruption order is no longer valid in most of the patients, a new pattern being evidenced. In terms of symmetry, girls more than boys presented left right discrepancies.

Conclusion. Classical eruption patterns are still valid for the upper arch, but not so relevant for the lower arch, as new patterns of eruption tend to emerge.

Surgical management of a muco-gingival deficiency around an implant of an upper lateral incisor – a case report

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Corresponding Author: Ștefan-Adrian Petruțiu e-mail: dr_ady17@yahoo.com A good management of the soft tissue at the time of implant placement may not be enough to obtain a fully esthetic result. Mucogingival surgeries after implant placement and loading can improve the outcome.

The aim of the presentation is to report the steps needed to be followed in order to perform a predictable management of the soft tissues around an implant for a better esthetic outcome.

After discussing the expectations with the patient and the prosthodontist, we started with the modification of the provisional restoration that was in place at the moment.

After the gingival maturation with the new provisional a connective tissue graft associated with a coronal advanced flap was performed. At the end of the maturation period of the graft, the gingival sculpting was done with the aid of composite added to the previous provisional restoration.

The esthetical aspect of the case improved at the end of the treatment. Therefor a muco-gingival approach can be used in order to achieve better esthetic result in cases with muco-gingival deficiencies around implants.

Effects of occlusal splint therapy combined with craniotemporomandibular kinesiotherapy in patients with temporomandibular disorder

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6) Department of Maxillofacial Surgery and Implantology, Faculty of Dental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Occlusal splints are used in the non-invasive treatment of patients diagnosed with temporomandibular disorders (TMD). Another non-invasive treatment option for TMD patients is kinesiotherapy, which may be utilized alone or in conjunction with occlusal splint therapy. Cone beam computed tomography (CBCT) has been shown to be an accurate and reliable examination for volumetric and linear measurements on TMJ (temporomandibular joint) structures. Given the controversy regarding the effectiveness of occlusal splints and the extent of kinesiotherapy's contribution to TMD resolution, the aim of this study was to assess the changes in the intraarticular spaces before and after occlusal splints therapy combined with cranio-temporomandibular kinesiotherapy in patients with TMD.

Material and methods. Twenty-four patients diagnosed with TMD according to Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) were included in this study. They underwent occlusal splint therapy combined with cranio-temporomandibular kinesiotherapy. CBCT images were taken before and after treatment. On CBCT images were measured anterior, superior, posterior and medial joint spaces. Additionally, the thickness of glenoid fossa, medio-lateral width and condylar height were measured. Paired t-test, Wilcoxon's signed rank, Stuart-Maxwell and chi square tests were applied.

Results. Condylar ratio was significantly higher after treatment (p=0.05). The changes in dimension of anterior, superior, posterior and medial joint spaces were not statistically significant.

Conclusion. The sagittal position of the condyle did not change statistically significantly to a more central position after occlusal splint therapy combined with cranio-temporomandibular kinesiotherapy in patients with TMD.

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Does the orthodontic treatment have any effect on oral parafunctions / bruxism?

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Department of Dental Propedeutics and Esthetics, Faculty of Dental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** This literature review aims to update the information regarding the effect of the orthodontic treatment on parafunctional masticatory forces / bruxism. All types of orthodontic treatments (fixed orthodontic treatment, removable and clear aligner therapy) were included in the research.

Corresponding Author: Amelia Anita Boitor e-mail: amelia.boitor@gmail.com **Material and methods.** Medline (PubMed), Cochrane Library and Scopus database were searched for relevant articles with no restrictions placed on the language or date of publication according to the pre-determined PICO question. The following search strategy and keywords were employed: ((bruxism) OR (parafunctional masticatory forces)) AND ((orthodontic treatment) OR (orthodontic therapy)).

Results. A total of 367 studies were computed. All the relevant articles were imported onto the Covidence platform. The inclusion criteria consisted of both *in vitro* and clinical studies regarding orthodontic treatments and their effect on awake or sleep bruxism. Using the PRISMA method, 110 duplicates were found and removed to obtain 257 studies to be screened by title and abstract. A total of 6 studies were eligible to be reviewed.

Conclusion. Based on the existing studies, rapid maxillary expansion performed in children improves undesirable parafunctional sleep masticatory forces.

Previous studies show a correlation between fixed orthodontic treatment and the improvement of oral parafunctions. However, more recently, this hypothesis is questioned. Nowadays research is oriented towards clear aligner therapy. No influence was found on the bruxism index while wearing clear aligners.

Efficency in root canal shaping with two different heat-treated Ni-Ti rotary instruments

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Corresponding Author: Sanda Ileana Cîmpean e-mail: sandacimpean@yahoo.com **Introduction.** The objective of this study was to evaluate the effectiveness of two rotary Ni-Ti systems in the instrumentation of curved root canals, by highlighting the changes in the original root canal trajectory and preparation time.

Material and methods. A number of 20 transparent resin blocks with simulated curved root canals were randomly assigned in two groups. G1 - Neolix group (n=10) and G2 - 2Shape group (n=10). The prisms were instrumented according to the following protocols. G1- C1 (25/12) and A1 (20/06 or 25/06); G2- TS1 (25/04), TS2 (25/06). Photographies were used to analyze postoperative changes before and after instrumentation. Preoperative and postoperative images were analyzed and evaluated using 2 programs. GIMP 2.10.22 software (GNU Image Manipulation Program) and Image J 1.46r software (Image Processing and Analysis in Java).

Results. The results showed that Neolix group tended to remove a greater amount of resin from the middle third of the simulated root-canal but had a better centering ability than 2Shape system in the coronal half of root-canal, while 2Shape system achieved better centering in the apical half of this one. No statistical significant difference (p < 0.05) was observed between the amount of root-canal transportation between the two groups regardless of the root-canal third. However, there were significant statistical differences in the degrees changes of root-canal curvature with both systems. On the other hand, no significant differences were revealed between the 2Shape system and the Neolix system, in terms of root-canal preparation time.

Conclusion. Both heat-treated rotary systems are equally effective, safe and easy to use. 2Shape system achieved better centering of the instruments in the apical half of the canal and modified to a lesser degree the curvature of this one. Preparation time required for both systems was similar.

Occlusal characteristics in patients with bruxism - an observational study

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Corresponding Author: Simona Maria Iacob e-mail: simona72cj@yahoo.com **Introduction.** Bruxism is defined as a repetitive jaw-muscle activity characterized by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible. The current study aimed to evaluate the occlusal characteristics in patients with and without bruxism.

Material and methods. The current research is an analytical, observational, transversal, case-control study. The study was carried out in two stages. In the first phase an original bruxism questionnaire was distributed to the 180 subjects included in the study. Based on the answers two groups were formed: subjects with self-reported bruxism (n=60) and the second group without bruxism (n=120). In the second phase an intraoral examination was performed, including static and dynamic occlusion. Dental signs of bruxism were also identified and registered (dental wear, gingival retraction or dental mobility).

Results. Occlusal dysfunction was more frequently diagnosed in patients with bruxism (83.3% vs 16.7%). In this study, a statistically significant correlation was detected between bruxism and non-functional anterior guidance (p=0.02), and non-functional lateral movement (p=0.05). During the occlusal examination, 60% of patients presented a non-functional anterior guidance (90% of subjects with bruxism had a non-functional anterior guidance compared to 45% of subjects without bruxism). Active premature contacts were more common in lateral (37%) and propulsive movement (54%) in both patients with bruxism and those without bruxism. Related to bruxism type, a higher frequency was observed for sleep bruxism (48%), comparing to awake (18%), or mixed (34%).

Conclusion. Bruxism is more frequent in patients presenting occlusal imbalance. Dental signs in patients with bruxism are represented by pathological wear, dental fissures or fractures, mobility and gingival retraction.

Good faith and legal liability related to dental treatments during the COVID-19 outbreak

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Corresponding Author: Anca-Ștefania Mesaroș e-mail: mesaros.anca@umfcluj.ro Oral health has been one of the first health sectors where the COVID-19 safety measures were implemented to prevent infections. But the pandemic demonstrated no patterns in infection transmission, and no one can currently claim to have control on it. During daily treatments, dentists fear that they will be held liable if one of patients is infected with Coronavirus.

The aim of this presentation is to provide some insights related to the assessment of dental doctors understanding toward possible legal claims raised by non-emergency dental care performed during the COVID-19 pandemic. The central research question is: could be dental care personnel liable for dental malpractice, if patients get infected in the dental office/clinics?

After the analysis of participants' answers, we can conclude that, unfortunately, they can still be sued, and they will not be surprised to see COVID-19 raised in litigation. Dentists could potentially find themselves facing liability claims from patients who allege they contracted COVID-19 while receiving treatment at a dentist's office due to the practice's negligence.



DOCTORAL SCHOOL

Doxorubicin-induced acute cardiac toxicity is associated with increased oxidative stress and autophagy in a murine model

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Material and methods. Thirty adult male Wistar albino rats were randomly divided into two groups: DOX group - animals received a single intraperitoneal injection of 10 mg/kg Doxorubicin and a control group which received a single intraperitoneal injection of 5 mg/kg saline solution. Electrocardiography (ECG) followed by echocardiography were performed at 3-, 7- and 10-days. At these time points, rats were euthanized under anesthesia. Blood, heart, liver, spleen, and kidneys were harvested from each rat for consecutive analyses.

Results. Autophagy and oxidative homeostasis were disrupted as soon as seven days after DOX treatment, alterations that occurred even before the significant increase of NT-proBNP, a clinical marker for cardiac suffering. Alterations in both electrocardiography and echocardiography of treated rats were found as early as three days.

Conclusions. These findings suggest that DOX-induced myocardial toxicity started early after treatment initiation, possibly marking the initial phase of the unfolding process of cardiac damage. Further studies are required to completely decipher the mechanisms of DOX-induced cardiotoxicity.

Ear surgery training using sheep head

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Corresponding Author: Mihai-Ionuț Tănase e-mail: dr.mihaitanase@gmail.com In surgical specialties, training is a very important tool for correct and complete development. Taking into consideration the more and more difficult access to human models, doctors all around the world tried to find alternative solutions for this problem. Thus, animal experimental models have been developed so that inexperienced surgeons may improve their skills and techniques. In ENT one of the most used animal models is the sheep because of its anatomical similarities. It has been studied for its usability in a wide range of otorhinolaryngology interventions. In otologic surgery, techniques like tympanoplasty, ear tube insertion, stapedectomy, hearing implant insertion, and mastoidectomy can



be practiced. In this study, we are going to identify and examine the usefulness of the sheep head in otologic surgery by comparing it directly with human anatomy. From an anatomical point of view, the sheep's temporal region and the components of the ear are very similar to the human one. This experimental animal model is suitable for practicing maneuvers at the tympanic membrane and ossicular chain level. One of the particularities discussed in this presentation is that in most cases the ovine facial nerve is dehiscent in its middle ear trajectory, which can be one of the biggest challenges for an ear surgeon. One of the biggest advantages is the ease of obtaining the model because of its low cost and high availability. The purpose of this study is to show a comprehensive description of the similarities and differences between human and ovine otologic anatomy, in order to facilitate the understanding and aid the surgical training approach.

The impact of *Gypsophyla paniculata* ethanol extract on oxidative stress markers, triglyceride-glucose index and metabolic control in a rat model of Streptozotocin-induced diabetes mellitus

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Corresponding Author: Lia-Oxana Usatiuc e-mail: lia.usatiuc@yahoo.com **Introduction.** Diabetes mellitus (DM), a global public health problem, is considered one of the major causes of morbidity and mortality worldwide. Adjunctive therapies focused on the use of plant bioactive compounds are intensively studied for their effect in the management of DM and its complications. The present study aims to investigate the effect of *G. paniculata* ethanol extract on TyG index, nitro-oxidative stress parameters, glucose levels and lipid profiles in Streptozotocin induced DM in rats.

Material and methods. Sixty Wistar-Bratislava white male rats, weighing between 250 and 300 grams were randomly divided into six groups as follows: negative control were injected with citrate buffer, Streptozotocin (SZT) group that received 55 mg/100 g body weight (b.w.) SZT by intraperitoneal administration, SZT+Metformin (SZT+M) (100 mg Metformin/100g b.w.) and three groups that received SZT+*G. paniculata* tincture extract (GPT) (100 mg/1mL w/v) administrated in three dilutions (GPT 100%, GPT: solvent 1:1 = 50%, GPT: solvent 1:3 = 25%). For ten days the animals received by gavage water in control and SZT groups, respectively the three dilutions of the extract in the GPT groups. After ten days, all the animals were sacrificed by cervical dislocation and serum was separated and stored. The serum levels of parameters of oxidative stress, total cholesterol and triglycerides were evaluated. Additionally, we monitored the fasting glucose levels for each day during the experiment and we calculated the triglyceride-glucose (TyG) index using the formula TyG = ln [Fasting triglyceride (mg/dl) × fasting glucose (mg/dl)]/2.

Results. TyG index was significantly decreased by G. paniculata 100% (9.64 \pm 0.27 SD, p<0.001) and 50% concentration (9.65 \pm 0.3, p<0.001) compared to SZT group, with similar results to those obtained in the Metformin group (9.88 \pm 0.067 SD). There were no statistically significant differences between the two concentrations regarding TyG index. There was a positive correlation between TyG index and oxidative stress markers: TOS (r=0.35, p=0.003), OSI (r=0.35, p=0.003), AOPP (r=0.46, p=0.005), NO (r=0.76, p<0.001). All of the tree GPT extract concentrations
(100%, 50% and 25%) significantly lowered the serum levels of malondialdehyde (MDA), total oxidative status (TOS), oxidative stress index (OSI) and nitric oxide (NO) compared to SZT group. Advanced oxidation protein products (AOPP) reduction was observed only for 100% and 50% GPT concentrations. Regarding the antioxidant system parameters, both total antioxidant capacity (TAC) and thiols were significantly increased by GPT extracts in a dose-dependent manner. Glucose levels, total cholesterol, triglycerides were significantly decreased by 100% and 50% GPT concentrations.

Conclusion. Increased TyG index levels characterize DM and are correlated with nitro-oxidative stress markers. *G. paniculata* ethanol extract exerts hypoglycemic, lipid lowering and antioxidant effects, which may influence the disease progression and the association of the disease.

Effects of conventional curcumin and curcumin nanoparticles in addition to diclofenac sodium in acute inflammation

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6) Department of Pathophysiology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Acute inflammation (AI) is an immediate, adaptive response with limited specificity caused by injury, infection or other insults. We aimed to evaluate the anti-inflammatory and analgesic effects of conventional curcumin (cC) and curcumin nanoparticles (nC) associated with diclofenac sodium (D) in a carrageenan-induced AI.

Material and methods. Seven groups of 8 Wistar-Bratislava rats were included. The first group was the control and the second group was the AI group, both groups were treated with saline. In all other groups, AI was induced and the rats were treated with D 5 mg/kg b.w. in the third group, cC a single dose of 200 mg/kg b.w. in groups 4 and 5, respectively nC, a single dose of 200 mg/kg b.w. in groups 6 and 7. Rats from groups 5 and 7 also received D (a single dose of 5 mg/kg b.w.) in addition to cC or nC. Paw pressure test was performed at 1, 3, 5, 7, and 24 hrs after AI induction. Plasma levels of tumor necrosis factor α (TNF- α), interleukin-6(IL-6) and IL-1 β were evaluated.

Results. Both cC and nC exhibit a nociceptive effect, but not statistically significant compared to the AI group. An addition of D to cC and nC led to a significantly better nociceptive response when compared with the AI group at 3, 5, 7, and 24 hrs. The cC and nC slightly reduced the levels of TNF- α , IL-6, IL-1 β compared to the AI group, but the reduction of pro-inflammatory cytokines was statistically significant when D was added to cC and nC (p<0.05). The plasma levels of the evaluated cytokines in the cC and D group were similar to those of the control group (p \geq 0.9999) and nC and D better reduced plasma levels of TNF- α and IL-6 than cC and D.

Conclusion. Administration of cC and in a dose of 200 mg/kg b.w. has limited analgesic and anti-inflammatory effects in acute paw inflammation induced by carrageenan. The association of cC or nC to D potentiates the anti-inflammatory effects of D, with the best results obtained for nC.

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Histopathological lesions of COVID-19 autopsies: the first wave of deaths

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Corresponding Author: Ioana-Andreea Gheban-Roșca e-mail: andreeaioana.rosca@yahoo.com **Introduction.** SARS-CoV-2 is a new strain of coronavirus reported at the end of December 2019, leading to a global pandemic of the COVID-19 disease within months. The present study aimed to investigate histopathological lesions in patients who have died from severe COVID-19 disease and to show the importance of autopsies during pandemics caused by future novel pathogens.

Material and methods. All regional COVID-19-related deaths autopsied between April 2020 and December 2020 at the Institute of forensic medicine in Cluj-Napoca were included in the study. Tissue samples were harvested from the lungs, heart, liver, kidney, spleen, and brain and prepared as microscopic slides stained in hematoxylin and eosin.

Results. Fifty-one autopsies were evaluated, 13 females and 38 males. The most frequently observed comorbidities were hypertension, myocardial infarction, chronic obstructive pulmonary disease, diabetes mellitus type II, chronic renal failure, and obesity. Diffuse alveolar injury, interstitial pneumonia, vascular microthrombi, interstitial fibrosis, bacterial pneumonia, intra-alveolar hemorrhage, and vascular congestion were the most common lung microscopic findings. The heart presented myocarditis, diffuse cardiosclerosis, or infarction. Hepatobiliary manifestations consisted of congestion, steatosis, and hepatitis. The renal lesions were acute tubular necrosis and chronic pyelonephritis. The spleen presented various lymphocytic depletion, and several cases of encephalitis were reported.

Conclusion. As expected, valuable information on characteristics that are harder to identify in antemortem was identified, information that could improve the clinical approach and treatment strategies. Postmortem examination remains the gold standard for a better understanding of diseases.

Acknowledgment. The authors would like to express their gratitude to those who offered their bodies to science, which allows anatomical studies to be conducted.

An experimental model of acute venous thrombosis in rats: establishment of the Carrageenan dose

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2) Laboratory Animal Facility -Centre for Experimental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Thrombosis is the pathophysiological process characterized by forming an abnormal solid mass called a thrombus. It consists of circulating elements of the blood flow. Carrageenan is a high molecular weight sulfated polysaccharide used for experimental animal models such as inflammation and thrombosis. The current research aimed to identify the best carrageenan dose for the experimental model of thrombosis in rats.

Material and method. The experimental model of thrombosis was performed on Wistar Bratislava white male rats weighing 300-400 g. Specimens with a tail longer 3) Cell Biology, Histology and Embryology, Department 1, Faculty of Veterinary Medicine Cluj-Napoca, USAMV Cluj-Napoca, Romania

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Corresponding Author: Valeriu-Mihai But e-mail: butvaleriu@yahoo.com than 13 cm were selected. K-Carrageenan was injected in the dorsal vein of the tail. Two groups of five specimens each were evaluated: group 1 received intravenously (i.v.) a single dose of 1 mg/kg body weight (b.w.) as previously described, while group 2 received i.v. also a single dose of 4 mg/kg b.w. The length of the rat tail thrombosis was measured using a graduated ruler 24 hours after the injection.

Results. No macroscopic changes in the tails were observed in any rats receiving 1 mg/kg b.w. K-Carrageenan. All rats that received 4 mg/kg b.w. K-Carrageenan showed thrombosis in the tails with a median length of the thrombosed region of 9.22 cm.

Conclusion. Higher K-Carrageenan dose proved efficient in thrombosis induction, so this experimental rat tail thrombosis model will be further used to test the nutraceutical effectiveness.

The antioxidant effect of *Artemisia Dracuonculus* extract on experimental inflammation induced by turpentine oil in rats

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Corresponding Author: Mădălina Țicolea e-mail: madalinaticolea@gmail.com **Introduction.** The *Artemisia* genus of the *Asteraceae* family includes over 500 species worldwide, with several antimalarial, antihepatotoxic, antibacterial, antifungal, and antioxidant effects. The aim of the study was to evaluate the antioxidant activity of Artemisia Dracuonculus in an acute experimental rat inflammation.

Material and methods. In this study we used 10 groups (n=9) of Wistar rats with body weights 200-250 g. *A. Dracuonculus* extract was prepared by repercolation method. Inflammation was induced with turpentine oil (6 mL/kg bw) administered i.m, and then, for 10 days the following were administered orally by gavage: tap water (1 mL/rat) to the rats from control and inflammation groups, extract (1 mL/rat) in 3 dillutions (100%, 50% and 25%) to the *A. Dracuonculus* treatment groups, diclofenac (10 mg/kg bw) in the anti-inflammatory control, and trolox (50 mg/kg bw) in the antioxidant control group. At completion the experiment blood was withdrawn by retroorbital puncture and total oxidative status (TOS), oxidative stress index (OSI), nitric oxide (NO), advanced oxidation protein products (AOPP), malondialdehyde (MDA), thiols (SH), transaminases (ALT, AST), creatinine and ureea were determined.

Results. *A. Dracuonculus* extract reduced TOS, OSI, MDA and AOPP compared to the inflammation group, and the dilution 50% was the most efficient. *A. Dracuonculus* activity on TOS, OSI and NO was better than the activity of diclofenac, and comparable to that of trolox. *A. Dracuonculus* had no important effect on TAC, but increased SH. These effects were better than those of diclofenac and trolox.

Conclusion. In experimental acute inflammation induced by turpentine oil, *A. Dracuonculus* extract reduced oxidative stress by decreasing oxidants plus increasing thiols, *A. Dracuonculus* 50% beeing the most efficient. *A. Dracuonculus* antioxidant activity was better than diclofenac and trolox.

Hand-held ultrasound device for echocardiography: too good to be true?

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Corresponding Author: Mariam Haji-Hassan e-mail: mariam.hadassah33@gmail.com **Introduction.** We evaluated the ability of a hand-held ultrasound device to reach a correct diagnosis and to perform accurate measurements of cardio-vascular structures by comparing a hand-held Kosmos (Echonous device) with the scans done with a high-end device as the gold standard.

Material and methods. Patients who were referred from June to August 2022 to one Cardiology ward, regardless of the presenting diagnoses, BMIs (Body Mass Index), or other factors, were eligible for the study. Patients underwent two heart ultrasound examinations and were scanned by the same two operators. The first examination was performed with a hand-held ultrasound device by a resident, while the second was performed with a high-end device by an experienced physician.

Results. Forty-three patients were consecutively included in the study, and 42 were evaluated. Linear measurements showed good inter-rater agreement between conventional and hand-held ultrasounds, with only two values that exceeded the upper bound of agreement. For valvular disease, the lowest agreement was observed on mitral valve regurgitation, which was missed in half of the mild and moderate mitral regurgitation patients.

Conclusion. The Kosmos ultrasound device allows concordant measurements but underestimates valvular diseases. However, image quality is still inferior to that offered by larger high-end ultrasound devices, as well as color-Doppler and spectral Doppler modalities. Further developments affirmatively would make echocardiographic examinations more rapid and less operator-dependent.

Triple primary malignancies: tumor associations, survival and clinicopathological analysis. A single-institution experience

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Corresponding Author: Iulia Almăşan e-mail: almasan.iulia@gmail.com **Introduction.** Multiple primary malignancies (MPMs) are defined as two or more malignant tumors that are histologically distinct and arise in the same individual. Despite their rare occurrence rate, the detection of MPMs is on the rise mainly due to increased longevity and advancements in cancer treatment and diagnostic procedures. This research aimed to determine the prevalence, triple tumor associations, overall survival, and the association between survival time and independent factors in patients with triple primary malignancies.

Material and methods. This single-center retrospective study included 117 patients with triple primary malignancies admitted to a Romanian tertiary cancer center between 1996 and 2021.

Results. The observed prevalence was 0.082%, and more than half (50.4%) had two synchronous and one metachronous occurring malignancies. The majority of

patients (73%) were over fifty at the first tumor diagnosis, and regardless of gender, the lowest median age occurred in the metachronous group. In female patients, the initial tumor occurred earlier, with over 31% being under the age of fifty. The most common tumor associations were found between breast-urogenital-digestive, breast-urogenital-urogenital, breast-urogenital-skin, and urogenital-urogenital-lung. The male gender and being over the age of fifty at the first tumor diagnosis are associated with a higher risk of mortality. Compared to the metachronous group, patients with three synchronous tumors demonstrate a risk of mortality 6.5 times higher, while patients with one metachronous and two synchronous tumors demonstrate a risk of mortality three times higher.

Conclusions. Although our findings reinforce the fact that triple primary malignancies are a rare occurrence, with an observed prevalence of 0.082%, the likelihood of a subsequent malignancy should always be considered throughout the short and long-term surveillance of cancer patients to ensure prompt tumor diagnosis and treatment.

Burnout syndrome in palliative care nurses

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Corresponding Author: Marius Colceriu e-mail: marius.dorincolceriu@yahoo.com **Introduction.** Palliative care nurses are exposed to different stressors in their daily practice favoring the burnout syndrome.

Material and method. A prospective, multicenter study was conducted between March-April 2020 in nurses working in palliative care settings. The Maslach Burnout Inventory (MBI) was the main objective of the research. The 42 subjects included in the study were primary assessed according to the level of burnout. A secondary analysis within 3 groups was performed using the length of time working in the palliative care units (0-2 years), (3-5 years) and >6 years.

Results. The mean age of the subjects was 39.29 ± 12.40 years. 30 subjects showed a low level of burnout (71.43%), 12 subjects showed a medium level of burnout (28.57%), and no subjects showed a high level. 22 nurses were aged between 23-40 years and 20 nurses between 41-68 years. No correlation was observed between the age and the burnout level (p=0.61). According to the length of time, 16 nurses were working in palliative care units for 0-2 years, 15 subjects for 3-5 years and 11 nurses for over 6 years. There was no significant correlation between the duration of work in a palliative care ward and the burnout level (p=0.41).

Conclusion. A low to medium level of burnout is present in nurses working in palliative care settings. Future research on a larger number of nurses from different hospital wards is needed, to get a more realistic picture of this syndrome in the country.

Long COVID – the ongoing mystery burden

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1) Department of Pneumology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Since the end of the year 2019, the novel coronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) emerged causing coronavirus disease 2019 or COVID-19, which became a world pandemic. Now, three years after the start of the outbreak, we have to face the consequences and recognize



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Corresponding Author: Ruxandra Puiu e-mail: ruxi.puiu@yahoo.com that the COVID-19 disease poses long term effects on a patient's health. It is now very well acknowleged that some patients who have suffered from COVID-19 can have health related problems after. Long COVID is now a very wide spread term and CDC recognizes it as ongoing, new or recurrent complex health problems that can only be related to the personal history of COVID-19 disease after at least four weeks post infection. Our objective was to describe the post COVID-19 syndrome of patients who have requested specific evaluation. Our purpose was to shed light onto the health related consequences of COVID-19 disease at 1-3 months after the infection.

Material and methods. We analyzed a cohort of patients who have requested a post COVID-19 follow-up and have been evaluated at Pneumophtihsiology "Leon Daniello" Hospital in Cluj Napoca, Romania. The patients taken into the study were all patients officially diagnosed with COVID-19 infection either by RT PCR SARS-COV-2 testing or with rapid antigen testing. The data were collected during one year between June 2021 and June 2022. Data regarding the initial infection was collected in a retrospective manner using discharge forms. We took into account for each patient its sex, smoking status, comorbidities, symptoms, severity of the illness, whether the patient was hospitalized, days of hospitalization, intensive care unit admission, need for supplemental oxygen and treatment at discharge. Patients included in the study came at follow up after at least one to three months after the initial infection. We designed a prospective, observational study to describe the most prevalent characteristics of patients who seeked post COVID-19 disease evaluation.

Results. We evaluated 210 patients. We report that the median age of patients at post COVID-19 evaluation follow up was 60.39 years. More patients were men (54.3% men vs 45.7% women) and the majority had a non smoker status (45.1% non-smoker, 29.9% used to smoke and 9% smoker). Regarding the severity of the illness, 17.9% of patients have had mild disease, 19.6% had moderate and 58.7% had severe disease. The most prevalent comorbidities throughout our cohort were hypertension, obesity, Diabetes Mellitus type II and hypothyroidism. In our cohort, 75.5% of patients required hospitalization for their initial infection, while 9.8% of them were admitted in the intensive care unit. 50.5% of the hospitalized patients needed supplemental oxygen. At the time of discharge, 85% of patients were prescribed additional treatment. At 1-3 months after the infection during the follow-up visit, 95.1% of patients report symptoms. The most prevalent ones being dyspnea, fatigability and exercise intolerance. After the evaluation, 64.6% of patients required additional treatment while 7% needed supplemental oxygen.

Conclusions. COVID-19 is a multisystemic disease that affects different and various organs in ways that are not yet understood. Patients who have been diagnosed with COVID-19 disease carry the burden of numerous symptoms that can most of the time only be attributed to the history of infection. We report that most patients that seeked post COVID-19 follow up at 1-3 months were mostly middle-aged men and had severe disease. They were mostly non smokers with metabolic disease and most likely have been hospitalized. The majority of the patients reported symptoms and because of this required additional treatment, while only a few still needed supplemental oxygen. More research is needed regarding the pathophysiological mechanisms involved, specific diagnotic tetests, and management methods.

Time to tackle surgical site infections in Romania

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Corresponding Author: Alexandru Coman e-mail: coman.alexandru@elearn.umfcluj.ro **Introduction.** Healthcare associated infections (HAI) are underreported in Romania with an overall incidence of less than 0.5%. Official data on this topic show a distorted image, with C. Diff infections being the most frequent HAI. This proves the lack of reliable data needed for developing infection prevention strategies at the national and local level. Our aim was to describe the practices regarding surgical site infections (SSI) in both public and private hospitals in Romania in order to develop educational programs.

Material and methods. This is a descriptive study. We conducted an online survey in 62 hospitals in Romania (approximately 12% of total numbers of hospitals). Data were collected from infection prevention specialists, operating theatre coordinators, and head nurses. We followed the One Together recommended structure of the survey with questions related to preoperative, operative and postoperative phases of SSI prevention strategy. Invitations to complete the online survey were sent by email. Data were collected anonymously, the information could not be traced back to the contributors.

Results. Our results show the SSI practices in Romanian Hospitals: preoperative screening - 54% of cases, decolonization - not available for all colonized patients, body hair trimming - 20%, antibiotic prophylaxis - 40% following guidelines, poor infrastructure and equipment - >30% are just a few examples or our results.

Conclusion. SSI practices in Romanian Hospital is sub-optimal. We will use these data to develop interventions and guidelines adapting the "One Together" approach.

Comparative efficacy of remdesivir versus remdesivir plus tocilizumab in patients with severe COVID-19 pneumonia

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Corresponding Author: Damiana Maria Vulturar e-mail: damiana_vulturar@yahooo.com **Introduction.** No specific golden standard treatment has been proven to be effective in the treatment of patients with severe COVID-19 pneumonia.

Objectives. The aim of this paper was to evaluate the efficacity and the potential benefit of remdesivir (R) versus remdesivir plus tocilizumab (RT) in severe COVID-19 pneumonia, by including the change in oxygen support, ICU admission, secondary bacterial infection, mortality rate, and the evolution of inflammatory biomarkers at seven days after treatment.

Material and methods. We conducted a retrospective cohort study including 182 patients with severe COVID-19 pneumonia hospitalized between March and October 2021 in the Pneumology Hospital from Cluj-Napoca, Romania. Among patients treated with standard of care 100 patients received remdesivir (R group) and 82 patients received the combination of remdesivir plus tocilizumab (RT group). The patients received R or RT depending on the type of oxygen requirement and on the inflammation markers.

Results. Patients treated with R evaluated at seven days from baseline had a substantial improvement in Borg score (p=0.02), a better increase in lymphocytes count (p=0.03) and a decrease in oxygen requirement (p=0.049) compared to RT group. RT led to a significant decrease in the C-reactive protein and ferritin levels after seven days

of treatment (p=0.012 respectively p=0.004). However, patients treated with RT had a statistically significant higher rate of superinfection (p=0.04). There was not any statistical difference between the groups in the ICU admission or mortality rate (p=0.378, p=0.838).

Conclusion. The combination of remdesivir plus tocilizumab led to a significantly improvement in the inflammatory markers and a decrease in the oxygen requirement. Although the superinfection rate was higher in RT group than in R group, no significant difference was found in the ICU admission and mortality rate between the groups.

The role of 3D speckle-tracking echocardiography in the diagnosis and evaluation of patients with obstructive sleep apnea syndrome

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Corresponding Author: Damiana-Maria Vulturar e-mail: damiana_vulturar@yahoo.com **Introduction.** Obstructive sleep apnea (OSA) represents a serious health problem. There is a well known relationship between OSA and cardiovascular diseases. Obstructive sleep apnea may affect the function and structure of the heart, mostly of the right ventricle (RV). Therefore, echocardiography could be an important tool for diagnosing OSA and its severity. The novel echocardiographic methods, like three-dimensional speckle tracking echocardiography (3D STE) is more precise compared with 2D STE. Thus, the purpose of our study was to evaluate whether 3D STE measurements are associate with the positive diagnosis and severity of OSA.

Material and methods. We enrolled 69 patients with OSA and 37 healthy volunteers. 2DE and 3DE were performed in all patients. 3D RVGLS was measured by 3D STE.

Results. 3D strain parameters were reduced in patients with OSA, compared with control group. All parameters were able to discriminate between severe and mild-moderate cases of OSA.

Conclusion. 3D STE may be a valid method for diagnosing OSA. 3D right ventricle global longitudinal strain showed to be a reliable parameter in recognizing sever cases of OSA.

Differential cytokine production profiles in stimulated mononuclear cells of patients with systemic sclerosis and controls

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2) Rheumatology, Emergency County Hospital Cluj-Napoca, Romania **Introduction.** Altered innate and adaptive immune responses represent the link between microvascular injury and fibrosis in systemic sclerosis (SSc) pathophysiology. Peripheral monocytes and lymphocytes are responsible for the secretion of cytokines with proven pro-inflammatory and pro-fibrotic activities. Chronic immune activation in SSc is supported by distinct serum and peripheral blood mononuclear cell (PBMC) cytokine profiles in relation to disease duration, autoantibody subtype, as well as severity of clinical manifestations. The objectives of our study were to: (1) evaluate

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Corresponding Author: Iulia Szabo e-mail: iulia szabo90@yahoo.com the PBMC cytokine production in SSc patients versus healthy controls (HC) after in vitro stimulation with lipopolysaccharide (LPS) and heat-killed Candida albicans and (2) distinguish different SSc clinical phenotypes based on their cytokine signature.

Material and methods. Eighteen SSc patients (8 limited cutaneous, 9 diffuse cutaneous, 1 sine scleroderma) and 17 age and gender matched HC were enrolled between February 2020 and October 2021. PBMCs were isolated and further subjected to stimulation with LPS and Candida albicans. Cytokine production was measured after 24 hours using ELISA kits for interleukin (IL)-1 β , IL-1 receptor antagonist and IL-6. IL-17 and interferon gamma (IFN- γ) concentrations were determined at 7 days from samples stimulated with Candida albicans-in the presence of 10% human pooled serum.

Results. Significantly elevated IL-1 β and IL-6 concentrations were detected in SSc patients compared to HC after stimulation with either LPS or Candida albicans. IL-17 cytokine production was also enhanced in SSc patients compared to HC after stimulation with Candida albicans for 7 days, but no difference was identified with respect to IFN- γ . No significant statistical difference was demonstrated between cytokine levels and extent of cutaneous involvement. Furthermore, no association was observed between autoantibody subtypes and cytokine production. Patients with diffuse cutaneous SSc and those positive for anti-Scl-70 antibodies revealed elevated C-reactive protein (CRP) levels.

Conclusions. SSc patients exhibit a pro-inflammatory phenotype irrespective of the extent of cutaneous involvement or autoantibody profile. This appears to be mediated through increased production of innate immune cytokines, which correlated to elevated Th-17 responses on later time-points. Elevated CRP levels might define a subgroup of SSc patients with specific disease characteristics. Validation of these findings and mechanistic assessment needs to be warranted in larger cohorts of patients.

Characterization of lymph nodes by computer analysis of ultrasound images and artificial intelligence algorithms

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Corresponding Author: Georgiana Delia Ciuca e-mail: deliaciuca@gmail.com Early detection, benign/malignant differential diagnosis and follow-up of the superficial lymph nodes are important factors in the diagnosis and prognosis of local or systemic disease. Ultrasound is currently the most widely used imaging method, being non-invasive, easily repeatable, without adverse effects and relatively inexpensive. Ultrasound criteria for lymph node malignancy are quite clear. However, there is great variability in image interpretation depending on the examiner's perception and experience and the performance of the machine model used. In recent years there has been increasing interest in the use of artificial intelligence (using neural networks) in medical diagnosis, relying on non-invasive methods (such as ultrasound), thus leading to as little human intervention as possible. Artificial intelligence can be defined as the ability of a system to interpret relevant data, learn from it and then use it to make decisions. This research aims to develop neural network-based algorithms to analyze images acquired by ultrasound techniques for use in the differential diagnosis of (malignant/benign) superficial nodule pathologies. In this project we aim to simplify the medical act and reduce the need for invasive diagnostic methods that risk reducing patient compliance.

Early detection of mild cognitive impairment in patients with inflammatory bowel disease - research protocol

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Corresponding Author: Oliviu Florențiu Sârb e-mail: sarboliviu@yahoo.com **Introduction.** Mild cognitive impairment is global public health problem and a leading cause of social isolation and a burden for the health system and for the families of the affected patients. Inflammatory bowel diseases (IBD), represented by Crohn disease (CD) and ulcerative colitis (UC), are pathologies caused by the alteration of the intestinal barrier, a component of the gut-brain axis. Gut-brain axis might be implicated in the development of neurodegenerative diseases. The aim of this study is to check the epidemiology of mild cognitive impairment and dementia among patients diagnosed with IBD's compared to healthy population. A second objective is to find a biomarker which might serve as a prognosis factor of cognitive decline installment.

Material and methods. One hundred patients diagnosed with Crohn disease or ulcerative colitis, according to the diagnosis criterion, will be recruited in this study. Furthermore, one hundred healthy controls will be also selected so we can do matching on sex, age, education, presence of atrial fibrillation and other cardiovascular diseases. A third group consisting of 25 patients diagnosed with dementia will be selected. Patients will be questioned about concomitant diseases, medication, and the stage of the disease. After that a MMSE, MOCA testing, forward and backward digit span tests will be performed. A blood sample will be taken from patients, split into five groups: 15 healthy controls, 15 patients with CD, 15 patients with UC, 15 patients with dementia and 15 patients with irritable bowel syndrome (IBS). Patients will furthermore be examined at 6 months, 1 year and 2 years with the same neuropsychological tests.

Expected results. The results of this study are expected to allow us to see if a proper screening of an early cognitive decline is required among the patients suffering of inflammatory bowel diseases. The results obtained from the blood samples might reveal an early marker of cognitive decline in the preclinical state.

Use of the Clock Drawing Test in the follow-up of patients with symptomatic bradyarrhythmias after pacemaker implantation

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2) Cardiology Department, Clinical Rehabilitation Hospital, Cluj-Napoca, Romania **Introduction.** Bradyarrhythmias frequent occur in the elderly, leading to the necessity of pacemaker implantation. The patient with symptomatic bradyarrhythmia frequently describes syncope, dizziness, visual disturbances, and decreased exercise tolerance, symptoms that are caused by a decreased cardiac output secondary to a decreased heart rate. There are sporadic studies in literature that also indicate the association between bradyarrhythmias and cognitive dysfunction, namely the improvement of cognitive performance after pacemaker implantation. The aim of this study was to evaluate cognitive function in patients with symptomatic bradyarrhythmias at the time of admission and at 3 months after pacemaker implantation.

Material and methods. As psychometric scale, we used was the Clock Test, a simple to use and widely applied cognitive test. The interpretation of the obtained results

Corresponding Author: Alexandru Marțiș e-mail: alexandru_martis2387@yahoo.com was carried out by applying the scoring system described by Sunderland et al. (semiquantitative evaluation), with a score from 1 to 10 points depending on the integrity of the representation.

Results. Twenty-four subjects were evaluated, average age 70 years, 54% male. An average Clock Test score of 6 points was observed in the studied group at the cognitive assessment before the implantation of the pacemaker. At the 3-month assessment, there was a statistically significant improvement of the cognitive performance, with a 3.4 points increase in the score (average score 9.4 points, p < 0.001).

Conclusion. In conclusion, there is a significant improvement in cognitive function after pacemaker implantation in patients with symptomatic bradyarrhythmias, most likely due to the increase in cardiac output and implicitly in cerebral perfusion.

Giant renal cell carcinoma - a case report

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Corresponding Author: Florin Ioan Elec e-mail: ioan.elec@gmail.com **Introduction.** The standard of care for large renal cell carcinoma tumors is complete surgical resection of the tumor by means of radical nephrectomy. The purpose of this case report is to present the importance of precise preoperative and intraoperative diagnostic in order to achieve an adequate surgical resection.

Case Presentation. We present the case of a 54 year old male patient, heavy smoker, with a 1 year history of a growing left flank abdominal mass, left side lumbar pain, intermittent hematuria and severe weight loss (16 kg in 1 year). Laboratory tests showed mild anemia (HGB -11.9 g/dl). Abdominal ultrasound showed a large tumoral mass located in the left flank, which affected the left kidney, a floating thrombus in the Inferior Vena Cava and a large adenopathic conglomerate in the retroperitoneal space. The CT scan showed a large left retroperitoneal mass of renal origin, originating from the inferior renal pole, which measured approximately 15/16/19 cm. We made the decision to proceed with surgery as a curative and diagnostic method. We chose a transperitoneal modified Gibson incision (extended to the left flank), which revealed a 20/15 cm large tumor, with multiple neoformation vessels - surgical dissection proved difficult due to the lack of cleavage from the transverse colon and multiple peritumoral adherences. We located a large thrombus in the left renal vein extending to its emergence in IVC. After carefully dissecting and isolating the IVC, we performed cavotomy, extraction of the thrombus and cavoraphy, followed by radical nephrectomy and lateroaortic lymphadenectomy. Due to the profound invasion of the paravertebral and psoas muscles, we could not achieve complete excision of the tumor without the risk of damaging the lumbar spinal nerves. The patients' postoperative course was favorable and he was discharged 7 days post-surgery. Histopathological examination showed pT4NxMx clear renal cell carcinoma Fuhrman 2 grading, invasion of the renal vein and positive oncological resection margins. We referred the patient to the oncology department for targeted therapy. 1 year follow up showed stable disease by RECIST criteria, with good tolerance of the targeted therapy. The patient currently maintains a good performance status and quality of life, immunotherapy with Nivolumab remaining as a projected therapy in case of Cabozantinib failure.

Discussion. Due to the indolent nature of the disease during its course and the lack of early symptoms, patients are diagnosed in late stages which require either curative radical or palliative surgery.

Conclusion. Modern surgical planning is made using high performance imaging techniques such as CT, MRI and ultrasonography. Even with all of this large amount of data at the surgeons' disposal, intraoperative "surprises" may arise on occasion and make us reconsider our initial therapeutic plans.

Insufficiency fractures mimicking axial spondyloarthritis in a patient with severe osteoporosis secondary to a smoldering myeloma

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Corresponding Author: Daisy Ana Maria Vaida Voevod e-mail: daisy.vaida.voevod@gmail.com **Introduction.** We present the case of a young female with insufficiency fractures due to severe osteoporosis secondary to a smoldering myeloma.

Results. A 38-year-old female, with a 2 year history of lumbar and pelvis pain, with bone marrow edema on the right sacrum side of the sacroiliac joint on MRI, interpreted as sacroiliitis and minimal inflammatory syndrome, was diagnosed with axial spondylarthritis HLA-B27 negative. Symptoms aggravated despite NSAIDs and sulfasalazine treatment. Dorso-lumbar and pelvis MRI showed hypointense lines surrounded by bone edema on the femoral head, interpreted as insufficiency fractures. Bloodwork showed high creatinine, proteinuria 2830 mg/24h, monoclonal band on urinary immunoelectrophoresis, Kappa light chains 149 mg/l (NV<22.4 mg/l), secondary Fanconi syndrome, severe osteoporosis on DXA, 10-20 plasmocytes on bone marrow aspiration. We interpreted the case as smouldering myeloma.

Conclusion. Clinical and on imaging, axial spondylarthritis is a major imitator for numerous pathologies which affect the axial skeleton.

Autoimmune encephalitis as a differential diagnosis of firstepisode psychosis: when should we test for neuronal antibodies?

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Corresponding Author: Denis Pavăl e-mail: paval.denis@yahoo.com **Introduction.** While autoimmune encephalitis (AE) remains an essential differential diagnosis of first-episode psychosis (FEP), there is currently no consensus regarding the testing for neuronal antibodies in FEP patients. Studies have so far focused on the antibodies against the N-methyl-D-aspartate receptor (NMDAR), since up to 85% of the patients with anti-NMDAR encephalitis present with psychiatric features indistinguishable from FEP. Most of these patients eventually develop neurological symptoms and display abnormal findings on ancillary tests (EEG, MRI, or cerebrospinal fluid (CSF) analysis), which facilitate the diagnosis. Nevertheless, up to 4% of patients anti-NMDAR encephalitis display an isolated or predominant psychiatric clinical course, which led to numerous studies searching for neuronal antibodies in Gezade, there are ongoing debates regarding the testing for neuronal antibodies in FEP patients. This study aims to summarize the current perspectives regarding the testing for neuronal antibodies in FEP.

Material and methods. We conducted a non-systematic review of the current literature.

Results. While a definitive AE diagnosis requires the presence of neuronal antibodies in the CSF, these studies remain scarce in FEP patients. Some authors recommend routine screening for AE in all FEP patients, yet three recent studies report on 279 FEP patients in which CSF analysis revealed no antibodies. Conversely, other investigators endorse selective screening for neuronal antibodies in patients having warning signs for AE. Some authors identify "yellow" and "red flags" for AE in psychiatric patients, such as decreased level of consciousness, movement disorders, and autonomic dysfunction, among others. However, these warning signs appear later in the course of the disease, which leads to a delay in diagnosis and treatment. This has prompted some authors to search for a specific psychiatric phenotype in order to identify patients with AE in an early phase. Other authors argue that the psychiatric features of anti-NMDAR encephalitis meet the criteria for cycloid psychosis: acute psychotic episodes with a sudden onset and a fluctuant clinical pattern mostly characterized by confusion, delusions, hallucinations, motility disturbances (including catatonia) and oscillations of mood. Thus, identifying this risk phenotype early in the disease course would ensure rapid diagnosis and initiation of therapy before the onset of neurological warning signs.

Conclusion. Despite numerous studies, there is currently no consensus regarding the testing for neuronal antibodies in FEP patients. While some authors recommend routine screening, others argue for selective testing in patients with either warning signs for AE or risk psychiatric phenotypes such as cycloid psychosis. Thus, the pursuit of shaping clear criteria regarding the testing for neuronal antibodies in FEP patients continues and warrants further studies.

Small cell lung cancer in a patient with idiopathic pulmonary fibrosis

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Corresponding Author: Sergiu-Remus Lucaciu e-mail: lucaciuserju@gmail.com **Introduction.** Small-cell lung cancer (SCLC) is considered to be the most aggressive type of lung cancer with less than 10% survival rate overall on a span of 5 years. Idiopathic pulmonary fibrosis (IPF) is a fibrotic lung disease that causes dyspnea worsening and a progressive loss of the lung function. One out of 10 patients affected by this disease will develop lung cancer as well.

Case Report. A 72-years-old patient, ex-smoker, with no exposure admitted to the pulmonology cabinet is presenting dyspnea, a marked decrease in exercise tolerance and a predominantly dry cough.

Objective. Without digital hipocratism, bilateral basal crepitant rales, SaO2-88%. The thoracic CT scan visualizes the angulated cleft, small lower lobes, traction bronchiectasis, reticular pattern, predominantly subpleural location and at the level of the lower lobes, honeycomb changes. The spirometry (2017) highlights mild restrictive ventilatory dysfunction. From the immunological tests the rheumatoid factor was slightly increased to 39.3 IU/mL. The diagnosis of IPF was established and antifibrotic treatment was initiated. In evolution, the reduction of DLCO and the appearance of a subpleural LSD nodule was observed. Guided puncture biopsy was performed: bronchopulmonary carcinoma with small cells. The patient followed chemotherapy courses, without interrupting the treatment with Pirfenidone.

Discussion. The diagnosis of idiopathic pulmonary fibrosis within the multidisciplinary discussion requires the exclusion of other causes of fibrosing

interstitial pneumopathy, the presence of the UIP pattern to HRCT, and the correlation of the histopathological results where the biopsy was performed and the HRCT. Extensive epidemiological proof supports a corelation between idiopathic pulmonary fibrosis and lung cancer. For patients with IPF, an individualized therapeutic strategy should be provided to prevent the risk of IIP exacerbation. SCLC patients with IPF currently have limited therapeutic options.

Conclusion. Patients with idiopathic pulmonary fibrosis are at increased risk of bronchopulmonary cancer (requires close imaging follow-up). The association of bronchopulmonary cancer with IPF leads to decreased survival in these patients. A multidisciplinary team is necessary for the therapeutic management of patients with idiopathic pulmonary fibrosis and bronchopulmonary cancer.

Rectal mucinous adenocarcinoma: an overview

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Corresponding Author: Mihaela Berar e-mail: mihaella.berar@gmail.com **Introduction.** Colorectal cancer is one of the most frequent malignancies worldwide and rectal cancer consists of 28% of the cases. Adenocarcinoma is the most common histological type, followed by mucinous adenocarcinoma, with 5-20% of all rectal cancers. The hallmark of this subtype is lesions with >50% of pools of extracellular mucin. Although the outcome of the rectal mucinous adenocarcinoma is less favorable, the treatment course does not differ from the other subtypes. The aim of this review was to assess the existing information regarding rectal mucinous adenocarcinoma (RMA) in order to pursue new research routes.

Material and methods. We performed a systematic search of PubMed, Google Scholar and the Web of Science databases, evaluating studies regarding clinicopathological and genetic features as well as survival outcomes on RMA.

Results. We selected 23 studies, 10 regarding the diagnostic implications and 13 discussing the treatment and prognosis of this histological subtype. There were six studies addressing the imaging aspects of the rectal mucinous adenocarcinoma, detailing the MRI features that were proven to help with the underdiagnosing of this subtype. The molecular specifics of the RMA were detailed in four studies, describing the genetic mutations such as KRAS, PIK3CA, BRAF and microsatellite instability. Twelve studies addressed the prognosis and treatment course of the RMA, all of them describing the poor results regarding the treatment response rate, disease free survival and overall survival compared to typical rectal adenocarcinoma and one study evaluated the inflammation index prognosis. One study analyzed the complete response to adjuvant radiochemotherapy and one focused on the surgical aspects.

Conclusion. In this review, we encapsulated the molecular and clinicopathological characteristics of RMA, as well as diagnostic and treatment approaches in order to establish a baseline of references for further research.

Biofilm-forming bacteria in chronic obstructive pulmonary disease

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Corresponding Author: Pavel Șchiopu e-mail: pavelschiopu@gmail.com **Introduction.** Certain bacteria can attach to the respiratory mucosa and form complex, multi-layered colonies named biofilms. This multicellular structure protects the bacteria from antimicrobials and the immune system. The chronically inflamed airways of chronic obstructive pulmonary disease (COPD) patients are humid, lack of mucocilliary clearance and have disrupted local immunity, all of which promote biofilm formation. In this paper, we reviewed the scientific literature for evidence that biofilm-forming bacteria are present in the respiratory tract of COPD patients.

Material and methods. We searched four databases according to PRISMA guidelines, namely PubMed, PubMed Central, EMBASE and Web of Science Core Collection in October 2022. We included studies that detected biofilm-forming bacteria in respiratory harvested samples (sputum, endobronchial aspirate, bronchoalveolar lavage, protected specimen brush) from COPD patients, either using microscopy or culture. We excluded non-English language studies, unpublished material, reviews, editorials, letters and studies that sampled endobronchial valves.

Results. We screened 520 records of which 16 were eligible for review. 15 of these studies showed that bacteria isolated from COPD patients form biofilms when cultured. The majority of the studies used acellular culture media in polystyrene 96-well plates. The bacterial species for which biofilm formation was demonstrated were *Haemophilus influenzae*, *Pseudomonas aeruginosa* and *Streptococcus pneumoniae*. One study employed fluorescence microscopy to directly detect the Pseudomonas aeruginosa biofilm in sputum sampled from a COPD patient.

Conclusion. Bacteria isolated from COPD patients form biofilms when cultured. However, direct microscopical evidence of biofilms in the respiratory tract of COPD patients is insufficient and must be addressed by further research.

Mycotoxins exposure assessment in female population through human urine biomonitoring by HPLC-QTOF-MS

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2) Epidemiology and Environmental Health Joint Research Unit, FISABIO– Universitat Jaume I–Universitat de Valencia, Valencia, Spain

3) Spanish Consortium for Research on Epidemiology and Public Health (CIBERESP), Madrid, Spain **Introduction.** Human exposure to mycotoxins is a global concern since fungi can contaminate food from crops to ready-to-eat meals. Besides well-known regulated aflatoxins and ochratoxin, special attention should be paid to non-regulated mycotoxins, whose presence in food products has been detected and potential harmful effects have been shown in recent studies. To assess human exposure, urine analysis is an alternative to food correlation studies, as this matrix allows to know more accurately the recent intake of mycotoxins. Therefore, the aim of this work was to apply a previously validated method to determine the concentration of ten selected mycotoxins, Enniatin A, Enniatin B1, Beauvericine, Aflatoxin B1, Aflatoxin B2, Aflatoxin G1, Aflatoxin G2 and Ochratoxin A, as well as simultaneously perform a screening of other untargeted mycotoxins and their metabolites.

Material and methods. Urine samples from 540 women participating in the INMA



Corresponding Author: Nuria Dasí-Navarro e-mail: nuria.dasi@uv.es (Environment and Childhood) Spanish project were analysed. Extraction method was based on a Quick, Easy, Cheap, Effective, Rugged and Save (QuEChERS) followed by High Performance Liquid Chromatography coupled to Quadrupole Time of Flight Mass Spectrometry (HPLC-QTOF-MS). Urine creatinine concentration was used to normalize results. Untargeted mycotoxins and metabolites were identified using METLIN database.

Results. Studied mycotoxins and metabolites were detected in the 81% of samples. Respecting targeted mycotoxins, 7 out of 10 of them were quantified in 151 samples. Mostly quantified mycotoxins were: Enniatin B [% of detection (concentration range)] = 26% (0.5 – 33.8 ng/ml) and Enniatin B1 = 7% (0.4 – 11.4 ng/ml). Regarding untargeted screening of the samples, higher incidence was observed for Deepoxy-deoxynivalenol (45%), Ochratoxin B (18%) and Ochratoxin α (17%).

Conclusion. The obtained results show the importance of the control carried out on the legislated mycotoxins in food products, and the importance to introduce emergent mycotoxins in the state regulations.

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EC-SERS detection of thiabendazole in apple juice using goldbased screen-printed electrodes

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Corresponding Author: Rebeca Moldovan e-mail: rebeca.magda@umfcluj.ro **Introduction.** Electrochemistry (EC) and SERS (Surface Enhanced Raman Spectroscopy) have been entangled since the time when the first SERS spectra were recorded from an EC roughened silver electrode. Since then, great progress has been made in using this technique for various analytical purposes. In this work we report the first EC-SERS detection of thiabendazole (TBZ), a fungicide that can be found as a contaminant in various foods.

Material and methods. Measurements were performed using a portable Raman spectrometer and a potentiostat. An EC roughening procedure was optimized for commercially available gold screen-printed electrodes (AuSPEs). TBZ was detected from PBS and unprocessed apple juice. The pH-dependence of the SERS response in the range 2 - 8 was also investigated. The EC-SERS substrate was integrated and tested in a miniaturized flow cell.

Results. A double-step chronoamperometric procedure in 0.1M KCl generates nanostructures on the AuSPEs. An applied potential (-0.8 V vs. Ag/AgCl) increases the SERS signal of TBZ allowing its detection down to 0.06 ppm, with a relatively wide linear range (0.5 - 10 μ M) and good intermediate precision (RSD% < 10). The recovery of TBZ from unprocessed juice was more than 82%. Furthermore, by using a microfluidic setup, it was found that TBZ has a good affinity for the activated gold surface and it can be preconcentrated on the substrate.

Conclusion. An EC-assisted SERS method was developed for simple, fast (2 minutes), and selective detection of residual TBZ in unprocessed apple juice, using EC roughened AuSPEs. The proposed method allows for a LOD in juice relevant for

its trace detection in food samples. Furthermore, the EC-SERS sensors were assembled into miniaturized flow cells and preliminary evaluation of their performance under flow conditions was demonstrated.

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Potential use of spent coffee grounds as a food ingredient in bakery products

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Corresponding Author: Luigi Castaldo e-mail: luigi.castaldo2@unina.it **Introduction.** Spent Coffee Ground (SCG) represents one of the major wastes derived from the coffee industry. To date, several scientific studies are focused on an alternative strategy to reuse SCG. Indeed, further bioactive molecules, known for their beneficial properties on human health, are still present inside. Based on the above, the purpose of this study was to improve the bioactive potential of baked food by adding a waste matrix possessing a considerable residue of bioactive compounds.

Material and methods. Briefly, the effect of the addition of 5 g SCG in cookie preparation was studied. Antioxidant activity and polyphenolic compound were evaluated on the polyphenolic fraction and during in vitro gastrointestinal digestion to assess the spent coffee grounds-enriched cookies (SCGc) polyphenol bioaccessibility. To quantify the potentially health-promoting bioactive compounds still present in SCG and SCGc an ultra-high-performance liquid chromatography coupled with Orbitrap high-resolution mass spectrometry (UHPLC Q-Orbitrap HRMS) analysis was performed.

Results. Results reported the presence of up to thirteen different polyphenolic compounds in the assayed samples, belonging to the chlorogenic acid family. Total CQA represented from 84.8 to 85.8% of total CGA detected in SCG and SCGc samples, respectively. The most significant CGA found in the SCG and SCGc samples (116.4 mg/100 g and 8.2 mg/100 g respectively) was represented by 5-caffeoylquinic acid. As regards the antioxidant activity, SCGc samples exhibited significantly higher values than the control samples. The highest bioaccessibility of SCGc polyphenols was observed after the colonic stage, suggesting their potential advantages for human health.

Conclusion. Therefore, the incorporation of SCG material in baked foods could represent an effective opportunity for the coffee industry to valorize coffee waste and minimize the environmental impact, providing enriched food products with enhanced biological activity, which may exert potential health benefits.

Fermented whey modulated AFB1 and OTA-induced hepatotoxicity and nephrotoxicity *in vivo*

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 Laboratory of Food Chemistry and Toxicology, Faculty of Pharmacy, University of Valencia, Burjassot, Spain **Introduction.** Aflatoxin B1 (AFB1) and ochratoxin A (OTA) are well-known to promote hepatotoxicity and nephrotoxicity *in vivo*, which may be counteracted by natural compounds like fermented whey (FW). Carbamoyl phosphate synthetase 1 (CPS1) and

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Corresponding Author: Massimo Frangiamone e-mail: Massimo2.frangiamone@uv.es kidney injury molecule 1 (KIM-1) are typical biomarkers used to detect liver and kidney damage, respectively.

Material and methods. Thus, RT-qPCR and droplet digital PCR analysis were performed to assess the potential beneficial effect of FW against AFB1 and OTA-induced hepatotoxicity and nephrotoxicity in male and female rats by analyzing the altered gene expression of hepatic CPS1 and renal KIM-1 after 28 days of oral exposure. All feed types were prepared at the laboratory and the concentrations were the following: 1) control feed; 2) AFB1 (5 \pm 0.6 mg/kg); 3) OTA (10.2 \pm 1.1 mg/kg); 4) AFB1 and OTA (8.8 \pm 1.5 and 10.9 mg/kg respectively); 5) FW (1%) feed; 6) FW (1%) and AFB1 (6.1 \pm 1.4 mg/kg); 7) FW (1%) and OTA (6.1 \pm 0.3 mg/kg); 8) FW (1%) with AFB1 and OTA (8.4 \pm 0.3 mg/kg and 8.4 \pm 0.4 mg/kg respectively).

Results. In males' liver, the most damaging treatment was AFB1 by reducing CPS1 expression, which was reversed by FW-administration. This bioactive compound also improved gene expression changes induced by OTA and mycotoxins mixture. In females, the damage triggered by mycotoxins as well as the protective effect of FW were less pronounced. In males and females kidney, mycotoxins exposure induced toxic effects by upregulating KIM-1, being OTA the most detrimental. In this organ, FW-supplementation mitigated mycotoxin-induced gene expression changes but sex-related responses were not clearly observed.

Conclusion. These data confirm that AFB1 and OTA-promoted hepatotoxicity and nephrotoxicity in vivo, which could be mitigated by dietary compounds like FW.

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Molecularly imprinted polymer-based drug delivery system for the sustained release of ruxolitinib intended for post-resection treatment of glioblastoma

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4) Department of Pathology, IMOGEN Research Centre, Cluj-Napoca, Romania **Introduction.** We planned to overcome the current limitations of glioblastoma (GBM) chemotherapy by developing a local molecularly imprinted polymer (MIP)based drug delivery system for the sustained release of RUX within the tumor postresection cavity, targeting residual infiltrative cancerous cells with minimum toxic effects. Three different acrylic-based MIPs were developed and further characterized, with one of them successfully reaching *in vivo* stage.

Material and methods. MIPs were synthesized by precipitation polymerization using acrylamide, trifluoromethacrylic acid, and methacrylic acid as monomers. Drug release profiles were evaluated by real-time and accelerated release studies with phosphate buffer solution as release medium. Polymers were evaluated *in vitro* by CCK8 and cell viability assay, and *in vivo* after an orthotropic model in Wistar rats was developed.

Results. Trifluoromethacrylic acid-based polymer (MIP2) turned out to be superior in terms of loading capacity (38.01 µg RUX/mg MIP), drug release, and efficacy on GBM cells. Accelerated drug release studies show that after 96 hours, MIP2 released 41.99% of the loaded drug, with its kinetics fitted to the Korsmeyer-Peppas model. CCK8 cell viability assay proved that all the polymers provide high

Corresponding Author: Alexandra Iulia Bărăian e-mail: alexandra.iuli.baraian@elearn. umfcluj.ro efficacy and low toxicity. Within *in vivo* evaluation, the survival time of animals significantly increased from 20 to 50 days for animals treated with MIP2.

Conclusion. Three different acrylic MIPs were developed and characterized within this study, with the purpose of obtaining a Drug Delivery System for the local administration of RUX in GBM. MIP2 proved its efficacy by increasing survival time of animals with 30 days.

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Magnetic beads SELEX technology: aptamer selection for hepatocellular carcinoma serum biomarker

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Corresponding Author: Magdolna Casian e-mail: magdolna.casian@elearn.umfcluj.ro **Introduction.** Hepatocellular carcinoma (HCC) has a high mortality rate and the limitations in diagnosis often lead to low survival rate. Aptamers are short single-stranded DNA or RNA sequences capable of interacting with a wide range of target molecules with high affinity and specificity. This poster presents our main strategy for the selection of an aptamer through magnetic beads SELEX technology for Golgi protein 73 (GP-73), a valuable serum HCC biomarker that will be further explored for its potential early-stage diagnosis of HCC.

Material and methods. The target protein percentage covalently bounded onto magnetic beads (MBs) functionalized with tosyl groups, after 16 h of incubation at 37°C and pH=7.4 was analyzed and optimized using Bradford assay. For negative SELEX, bovine serum albumin (BSA) was chosen as a target protein, as for positive SELEX, GP-73.

Results. The functionalization of MBs with BSA showed a binding yield of 93.89%. The amount of protein successfully immobilized onto the MBs was calculated as a difference between the amount of protein found in the supernatant and the amount used for immobilization (50 μ g). Further experiments envision the functionalization of GP-73 onto MBs and the optimization of the selection steps.

Conclusions. Selection of a GP–73 specific aptamer via SELEX technology and its incorporation into an electrochemical aptasensor for early HCC diagnosis would further allow the implementation of early-stage treatment strategies and would potentially reduce mortality and healthcare costs.

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Investigation of the voltammetric profile of methamphetamine for its fast on-site detection in seized samples

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Corresponding Author: Ana-Maria Drăgan e-mail: ana.dragan@umfcluj.ro **Introduction.** Methamphetamine (MA) is a synthetic psychoactive drug, internationally classified as a controlled substance and frequently abused for its psychostimulant properties, being reported as the most widely consumed synthetic stimulant drug in the world. Attempting to aid law enforcement agencies in disrupting the illicit drugs trafficking, the present study aimed to explore the potential of electrochemical detection of MA in confiscated samples.

Material and methods. For analysis, square wave voltammetry and disposable graphite screen-printed electrodes plugged into a portable potentiostat connected to a smartphone or laptop were employed. Firstly, the optimal buffer was selected, after which the analytical characterization of the method was performed. Thereafter, the selectivity towards MA in mixtures with other illicit drugs as well as common adulterants/cutting agents was evaluated. Finally, confiscated samples were analyzed, and the analytical performance was compared to that of other portable devices used in forensic analysis.

Results. For the optimized method, a limit of detection (LOD) of 16.6 μ M was obtained. Moreover, a change in the voltammetric behavior of MA was observed, two different zones in the window of potential being identified for MA detection. These identification zones were successfully employed for MA detection in the tested mixtures and samples. Furthermore, the analytical performance of the method was similar or superior to that of the other portable devices interrogated.

Conclusion. The electrochemical method exhibited a LOD suitable for forensic analysis and good analytical performance, displaying its potential for on-site testing in the field of forensic analysis.

Acknowledgement. This study was supported by a PhD Research Project PCD 883/3/January 12, 2022, offered by "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj–Napoca, Romania.

Development of an extract enriched in polyphenols from *Rosa canina* L. pseudo-fruits using an optimized extraction method

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Department of Pharmaceutical Botany, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** *Rosa canina* (Rosaceae) pseudo-fruits are known for their phytochemical composition and therapeutical potential. The present study aimed to optimize the process of extraction using ultrasound-assisted and enzymatic-assisted extraction, in order to obtain extracts enriched in polyphenols.

Corresponding Author: Andrei Mocan e-mail: mocan.andrei@umfcluj.ro **Material and methods.** The software Modde 13.0 (Sartorius) was used to develop an experimental design (DoE), in order to determine the influence of extraction parameters (time, amplitude and plant:solvent ratio) on the total phenolic content (by Folin-Ciocâlteu assay).

Results. The optimal extraction parameters determined were 50 minutes, 50% amplitude and 1:20 ratio. Combining UAE (UAE = ultrasound-assisted extraction) and EAE (EAE = enzymatic-assisted extraction) obtained extracts with higher TPC (32.64 mg GAE/dw) in comparison to using only UAE (29.37 mg GAE/dw).

Conclusion. Combining the optimal extraction parameters by UAE and EAE obtained a higher total phenolic content.

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Comparative study of the extraction of bioactive compounds from Moldavian cornelian cherry fruits (*Cornus mas* L.)

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Corresponding Author: Andrei Mocan e-mail: mocan.andrei@umfcluj.ro **Introduction.** *Cornus mas* L., a member of Cornaceae family, is widely distributed in Europe and around the world, being used in folk medicine for the treatment of a wide range of diseases, such as digestive ailments, liver and renal diseases, and diabetes. The aim of this study was to evaluate the influence of 4 extraction methods (decoction, maceration, ultrasound-assisted extraction (UAE), and enzymatic-assisted extraction (EAE)) on phytochemical profile of resulted extracts and their antioxidant and enzyme inhibition capacities.

Material and methods. Extractions were performed using standard protocols found in scientific literature. Evaluation of phytochemical profile was assessed using Folin-Ciocîlteu and AlCl₃ protocols. Total antioxidant capacity of the extracts was assessed using DPPH, FRAP and TEAC protocols, and enzyme inhibition capacity of the extracts was tested against α -amylase, α -glucosidase, lipase, and achetylcholinesterase enzymes.

Results. *Cornus mas* extracts were characterized by different quantities of total polyphenolic and flavonoidic compounds, depending on the implemented method of extraction. UAE obtained extract was the most potent extract in terms of total antioxidant capacity and enzyme inhibition potential (except for anti-lipase potential).

Conclusion. Extraction method is an important factor in recovery of bioactive compounds from cornelian cherries. For a better extraction yield and a potent total antioxidant capacity and enzyme inhibitory potential, UAE is the most suitable extraction method for this food matrix.

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Aptamer-functionalized magnetic nanocarriers for the targeted delivery of sorafenib

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Corresponding Author: Alexandra Pusta e-mail: alexandra.pusta@umfcluj.ro **Introduction.** Sorafenib (SOR) is the drug of choice for the treatment of hepatocellular carcinoma and has certain drawbacks that could be overcame by encapsulating it in cancer cell specific carriers. Specificity can be ensured by functionalization with bio-mimetic elements, such as aptamers. In order to quantify SOR loaded and released form the carriers, electrochemical methods can be developed. The objectives of this study were to develop magnetic nanocarriers modified with aptamers and loaded with SOR and to develop an electrochemical method for SOR quantification.

Material and methods. Two types of magnetic nano-carriers were used: azelaic acid functionalized magnetic nanoparticles (MNP) and poly-tartaric acid functionalized magnetic nanoclusters (MNC). For aptamer functionalization, the amino-terminated TLS11a aptamer was used to ensure selectivity towards HepG2 cells. Aptamer functionalization was obtained after NHS/EDC activation of the carboxylated magnetic carriers. The next step consisted in loading SOR into the modified magnetic carriers and performing SOR release studies. For electrochemical quantification of SOR, its electrochemical behavior was analyzed using cyclic voltammetry on a variety of electrodes by using different conditions.

Results. Aptamer functionalization was confirmed using UV-Vis spectrophotometry and electrochemical impedance spectroscopy in the case of MNP. Both SOR loading and release were confirmed by UV-Vis spectrophotometry. Higher encapsulation efficiencies and loading capacities were obtained in the case of MNP compared to MNC. In the case of SOR electrochemical detection, the optimal surface and pH were chosen for detection.

Conclusion. MNP and MNC were successfully functionalized with aptamer TLS11a, loaded with SOR and the SOR was released in vitro. An electrochemical method for SOR detection was also developed.

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Electrochemical detection of amphetamine in street samples using an innovative nanomips-based sensor

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1) Department of Analytical Chemistry and Instrumental Analysis, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The prevalence of recreational substance abuse amongst young adults has markedly increased over the past two decades and it remains one of the major problems facing our society today worldwide. Amphetamine (AMP) is one of the most common substances abused and one of the most potent sympathomimetic amines with respect to stimulatory effects on the central nervous system.

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Corresponding Author: Florina Maria Truță e-mail: florina.truta@umfcluj.ro The direct electrochemical detection of AMP is a challenge because the molecule is non-electroactive at the potential window of conventional graphite SPEs. In this regard, a molecularly imprinted polymer (MIP) for AMP detection was synthesized.

Material and methods. The MIPs nanoparticles (nanoMIPs) were synthesized in the presence of a template molecule. After polymerization and removal of the template, MIPs were embossed with complementary cavities and functionalities.

Results. The technology presented herein could potentially help to rapidly determine AMP from confiscated street samples. The voltammetric sensor for AMP detection uses electroactive nanoMIPs, produced by introducing ferrocene monomer into the polymeric structures, which serves as an efficient transducer of electrochemical response. For the immobilization of nanoMIPsonto the surface of graphite SPEs different approaches were tried, and the best results in terms of stability, sensitivity, and specificity were obtained after the direct deposition of a suspension that contains chitosan, nanoMIPs, and graphene oxide (GPHOx).

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Optical characterization of two heated universal resin composites

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Corresponding Author: Corina Mirela Prodan e-mail: corinamirelaprodan@gmail.com **Introduction.** To evaluate the color characteristics of two different universal resin composites after one cycle of heating.

Material and methods. A total of 56 disks (n=14) (diameter 10 mm, thickness 1 mm) were manufactured from 2 universal composites (Omnichroma-Tokuyama and Optishade universal MD – KavoKerr). 14 specimens from each group were fabricated from unheated composite and the rest were obtained after heating them (45°C, 1h, Ease-it, Ronvig). The specimens were gradually formed (Porcelain sampler, SmileLine), polymerized on both sides through a Mylar band (Woodpecker Led.H Orto) and immersed (24 h) in distilled water. The color parameters L* (lightness), a*, b* (color coordinates in scale a* and b*) were measured with a non-contact spectrophotometer (SpectroShade (MHT) before and after heating, on white, black, and grey backgrounds. Differences ΔL^* , Δa^* , Δb^* , color difference $\Delta E00$, translucency differences ΔTP , and differences in Whiteness index Δ Wid were determined between control and heated specimens.

Results. Δ E00 varied between 0.79 – 1.76, while Δ L* ranged between 0.06 – 0.98, Δ a* between -0.27 – -0.03 and Δ b* between -2.18 – 0.06. Δ TP had values between -2.03 – -0.18 and Δ Wid between 0.04 – 3.54.

Conclusions. The universal resin composite Omnichroma (Tokuyama) had values that exceeded the perceptibility thresholds showing that 1 cycle of heating induced color variations.

Acknowledgment. This study was supported by the Research Project PCD 1032/55.

Artificial intelligence models for clinical usage in dentistry with a focus on dentomaxillofacial CBCT: a systematic review

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Corresponding Author: Sorana Mureşanu e-mail: sorana.muresanu@gmail.com **Introduction.** This study aimed at performing a systematic review of the literature on the application of artificial intelligence (AI) in dental and maxillofacial cone beam computed tomography (CBCT) and providing comprehensive descriptions of current technical innovations, to assist future researchers and dental professionals.

Material and methods. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA) Statement was followed. The study's protocol was prospectively registered. The following databases were searched, based on MeSH and Emtree terms: PubMed/MEDLINE, Embase and Web of Science.

Results. The search strategy enrolled 1473 articles. Fifty-nine publications were included, which assessed the use of AI on CBCT images in dentistry. According to the PROBAST guidelines for study design, seven papers reported only external validation and 11 reported both model building and validation on an external dataset. Forty studies focused exclusively on model development. The AI models employed mainly used deep learning models (42 studies), while other 17 papers used conventional approaches, such as statistical-shape and active shape models, and traditional machine learning methods, such as thresholding-based methods, support vector machines, k-nearest neighbors, decision trees, and random forests. Supervised or semi-supervised learning was utilized in the majority (96.62%) of studies, and unsupervised learning was used in two (3.38%). Fifty-two publications included studies had a high risk of bias (ROB), two papers had a low ROB, and four papers had an unclear rating.

Conclusion. Applications based on AI have the potential to improve oral healthcare quality and expedite dental procedures. More research and validation need to be conducted before these models are viable for clinical practice, particularly to tackle the challenges of limited data availability and insufficient standards in development and reporting.

Predatory journals: open access scientific bogeyman

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To date, the face-lift of the disreputable journals can mislead both experienced and novice researchers. We present the case of the International Journal of Innovative Research in Medical Science (IJIRMS). Affirmatively it is an open-access publication, with a publication fee ranging from US \$180 (letters and mini-review articles) to US \$260 (review articles). Affirmatively, the journal is indexed in PubMed, but on the same page the following information could be found: "The application for indexation in Emerging Sources Citation Index (ESCI), Science Citation Index Expanded (SCI-E) of the Web of Science (Clarivate Analytics), PubMed Central and TR Index has been performed." The search for the journal in PubMed returns no results. Submission is done via the journal website after registration, and affirmatively the manuscript is scanned for plagiarism with iThenticate. Once submitted, the attempt to retract the manuscript sent by e-mail led to the requirement for payment of the article publication fee while the title, authors, and abstract are published on the journal web-page. After the retraction note was sent by e-mail by the corresponding author to IJIRMS, the manuscript was submitted to another journal; the editor asked the corresponding author to explain the similarity between the two manuscripts since the manuscript shared the same title and abstract (100% identity with the one published by IJIRMS). So, what to do next?: 1) pay the retraction fees; 2) pay the publication fee (identical to the retraction fee); 3) explain to the editor of the reputable journal the situation. The lesson to be learned: once you click on the submission button and the journal is predatory, you are a victim, and in most cases, your research data is wasted and could not be recovered to be published in a reputable journal. So, open your eyes, closely verify the journal's legitimacy, and ask a more experienced researcher if you have any doubts.

RESEARCH CENTERS

Tissue, plasma and plasma exosome microRNAs as possible biomarkers for lung cancer

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Corresponding Author: Lajos Ráduly e-mail: lajos.raduly@umfcluj.ro **Introduction.** Non-small cell lung cancer (NSCLC) represents more than 80% of lung cancers, with high incidence and mortality worldwide mostly in the male population. Thus, it is imperative to improve the existing diagnosis and develop minimal invasive approaches for lung cancer patients to benefit from therapy to the highest extent. Recent studies have shown that circulating and tumor tissue miRNA profiles give important information regarding lung cancer development and progression; therefore, we identified some microRNA as potential biomarkers for NSCLC.

Material and methods. MiRNA profile analysis was performed in public datasets LUSC (male patients) from TCGA. For validation, a total of 40 patients with a diagnosis of LUSC were enrolled in the study. For the control group, we enrolled healthy subjects for blood sample donation (plasma controls). From each patient blood, plasma and lung tumor and normal adjacent tissues were collected according to the hospital protocol (the informed consent and study were approved by the ethical committee). The evaluation of miRNAs has been done in tissue, plasma and plasma exosomes of NSCLC patients. Exosomes were obtained using ultra-centrifugation protocol. For miR-21-5p and miR-181a-5p analyses were conducted by using Comprehensive Meta-Analysis software, version 2.2.050 (Biostat Inc., Englewood, NJ, USA). Hazard ratio was used as an indicator of effect sizes. Each study was coded for moderators referring to the type of cancer (i.e., colorectal, pulmonary, etc).

Results and discussion. From the TGCA dataset analysis we identified 2 overexpressed and 1 underexpressed miRNA. We validated by qRT-PCR from plasma and tissue samples miR-21-5p, miR-181a-5p and miR-155-5p with altered expression. The same validation for miRNA profiling was performed in NSCLC patients' exosomes obtained from plasma samples. The miRNAs were further analyzed in what concerns their putative target genes, as well as the canonical pathways in which they are involved. As expected, the most frequently altered biological processes were associated with cancer, cell growth and migration, apoptosis, and inflammation. Our data show the same dysregulation of miRNAs in tissue, plasma and plasma'exosomes.

Conclusion. By integrating and interpreting the results obtained in our study with the ones presented in the literature, we concluded that microRNAs like miR-21-5p, miR-181a-5p and miR-155-5p could represent potential biomarker roles for early diagnosis and characterization of lung cancer using minimal invasive approaches.

Dysregulated miRNAs in Sabutoclax treated triple negative breast cancer cell lines

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Corresponding Author: Laura Ancuța Pop e-mail: laura.pop@umfcluj.ro **Introduction.** Breast cancer is still the most diagnosed cancers in women, with over 2 million new cases each year, and a high recurrence and mortality rate, over 684996 deaths yearly, according to Global Cancer Observatory 2021. Triple negative breast cancer (TNBC) is the subtype of breast cancer that lacks estrogen, progesterone and Her2/New receptor and is a very aggressive type of cancer that is diagnosed mostly in younger women and still has no targeted treatment. Sabutoclax is a pan-BCL2 inhibitor that has shown good result in prostate cancer cell lines (PC-3, M2182, DU-145) and prostate cancer mouse models (C57BL/6, Balb/c Nu/Nu).

Material and methods. Three different TNBC cell lines (MDA-MB-231, HS578T and BT549) and one normal cell line (MCF-12A) were treated with Sabutoclax and different timelines and concentration and the IC50 was selected for each cell line. Cells treated with IC50 concentration of Sabutoclax were analyzed using apoptosis assays, colony formation and expression of genes involved in BCL-2 pathway, using real time PCR technology. We selected miRNAs to be validated for Sabutoclax treatment after analyzing networks between the BCL-2 pathway genes and targeted miRNAs.

Results. We observed that Sabutoclax treatment inhibits cancer cell proliferation, colony formation and dysregulates the expression of miR-21, miR-10a, miR-29b and miR-125a. Also, these four miRNAs are correlated to TP53, MCL-1, CASP3 and STAT3, genes involved in apoptosis pathway and observed to be dysregulated in triple negative breast cancer.

Conclusion. Our study showed dysfunctionalities in the selected miRNAs and an improvement after Sabutoclax treatment, being considered for further in vivo studies and possible implementation in clinical studies.

New biomarkers in oral cancer - clinical applications

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 Department of Oral Health, Faculty of Dental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Oral squamous cell carcinoma (OSCC) is considered the sixth most common cancer worldwide. Literature data emphasized the important role miRNAs and long noncoding RNAs as a biomarker for diagnosis and prognosis in oral squamous cell carcinoma. We aimed to investigate the expression levels of a panel of four miRNAs and long noncoding RNA in oral cancer in order to identify new biomarkers.

Material and methods. The study included a cohort of 33 patients who were diagnosed with oral squamous cell carcinoma (fresh frozen tumors and their paired adjacent normal tissue). The expression of miR-21-5p, miR-93-5p, miR-200c-3p and miR-205-5p, H19, MALAT1 and BCL-2 was done using real-time PCR technology. The obtained results were analyzed using GraphPad Prims. Immunohisto chemistry was used

Corresponding Author: Cristina Ciocan e-mail: cristina.ciocan@umfcluj.ro for the validation of the RT-PCR results at protein level for BCL-2.

Results. We observed that miR-21-5p and miR-93-5p were upregulated, while miR-200c-3p and miR-205-5p were down-regulated. The expression level of H19, MALAT and BCL-2 was also downregulated. The present study indicated the important role of miR-21-5p, miR-93-5p, miR-200c-3p, miR-205-5p, and H19 in OSCC. Differential expression of these transcripts at sub-sites, may serve as a diagnostic marker with further elaboration on a larger sample size.

Conclusion. The identification of alteration of miR-21-5p, miR-93-5p, miR-200c-3p, miR-205-5p, H19 and MALAT1 could be a useful target for clinically application in OSCC. Additional validation as molecular biomarkers for early diagnosis, prognostic monitoring and appropriate therapy in larger patient cohort should be considered. The heterogeneity of the OSCC due to different localization is influenced by numerous tissular factors, environmental and habit aspects such as smoking. Differential expression of these transcripts at sub-sites, may serve as a diagnostic marker with further elaboration on a larger sample size.

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LncRNA-MALAT1 contributes to the doxorubicine resistance in triple negative breast cancer cells

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Corresponding Author: Cornelia Braicu e-mail: braicucornelia@yahoo.com **Introduction.** Long non-coding RNAs (lncRNAs) are entangled in many cellular processes by a transcriptional regulation mechanism of their direct target genes, acting as oncogenes or tumor suppressors. Metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) was altered in various types of tumors, including triple negative breast cancer, a particular subtype having the worse prognostic. In our generated doxorubicine-resistant triple negative breast cancer cells it was proved to be overexpressed. This study was set to investigate the regulatory role of MALAT1 on the chemosensitivity TNBC cell lines to doxorubicin.

Material and methods. Functional studies and transcriptomic evaluation were done for the assessment of the implication of this transcript in the regulation of drug resistance mechanisms using MDA-MB-231 and Hs578T and its related doxorubicin resistant cell lines using MALAT1-specific siRNA transient transfection.

Results. MALAT1 was highly expressed in the TNBC cancer tissues, moreover, being correlated with overall survival rate. Additional, MALAT1 expression was significant increase in doxorubicin resistant cells. The treatment of siRNA for MALAT1 decreased key drug resistance genes in doxorubicin resistant cell and increase cell sensitivity to doxorubicin, by regulation of miR-181 family members. The molecular mechanisms for lncRNA regulation of doxorubicin resistance is complex, revealing as key element of miRNA-lncRNA network generated with miRNET is represented by MALAT1, interconnected with miR-181 family members.

Conclusion. MALAT1 decreased the sensitivity of resistant TNBC cell lines to doxorubicine by regulating miR-181 family members.

Role of TP53-MALAT-TAZ and their regulatory miRNAs in prostate cancer

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Corresponding Author: Liviuța Budișan e-mail: liviuta.petrisor@umfcluj.ro **Introduction.** Prostate cancer (PCa) is the second most common cause of cancer deaths among men, particularly in the western countries. TP53 is a critical gene regulator in prostate cancer. In this study, we investigated the roundabout of TP53-MALAT1-TAZ and their regulatory miRNAs (miR-15a-5p, miR-25-3p, miR-34a-5p, and miR-141-3p) in prostate adenocarcinoma (PRAD).

Material and methods. Using online data we evaluated the expression level, correlation with overall survival and clinical parameters, the mutational signature for these genes was done using cBioPortal, then were evaluated mRNA-miRNA interactions using miRNet. The most hub transcripts of the network were validated by qRT-PCR.

Results. The TCGA analysis revealed that the mRNA expression levels of TAZ and TP53 have been found overexpressed. MALAT1, interconnected with these two genes was identified as overexpressed in PRAD. TAZ and MALAT1 are interconnected with TP53, the hub miRNAs from the network (miR-15a-5p, miR-25-3p miR-34a-5p, miR-200a-3p, miR-375, miR-9-5p, and miR-141-5p) were overexpressed in PCa tumor tissue versus normal tissue. On the same patient cohort was confirmed same expression level for TP53, TAZ, and MALAT1 as those obtained from TCGA dataset.

Conclusion. Through these results, we demonstrated the outstanding function of TP53, TAZ, and MALAT1 and its related miRNAs in tumor control, underlying the role of future therapeutic and biomarker strategies with important implications in prostate cancer management.

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Emerging roles of mRNA/miRNA/lncRNA networks in non-small cell lung cancer

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Corresponding Author: Cecilia Bica e-mail: cecilia.bica@umfcluj.ro **Introduction.** Lung cancer represents the second most diagnosed cancer worldwide (11.4% of the total cases), and the most diagnosed cancer in men (14.3%) and represents the leading cause of cancer death in both men and women (18%). The involvement of noncoding RNAs in various processes such as cellular proliferation and apoptosis, miRNAs and lncRNAs performing similar roles, the idea of an interaction between these molecules arised. One notable hypothesis is the competing endogenous RNA (ceRNA) in which lncRNAs may act as molecular sponges for miRNAs. The study focused on identifying a lncRNA-miRNA-mRNA network with connection to biological processes altered in lung cancer pathogenesis. Using this approach, we aimed to identify potential

targetable molecules that would improve lung cancer patients' response to therapy and thus, their survival rate.

Material and methods. In silico analysis for identification of significant differentially expressed miRNAs, lncRNAs and mRNAs and subsequent survival analysis of LUAD and LUSC TCGA datasets using UALCAN database. Correlation analysis of mRNA/miRNA/lncRNA pairs in lung cancer was performed using the starBase database. Validation of mRNA/miRNA/lncRNA expression using two independent cohorts of lung adenocarcinoma and lung squamous cell carcinoma patients in a quantitative RT-PCR experiment.

Results. The study allowed the identification of top dysregulated mRNA/miRNA/ lncRNA transcripts in LUAD and LUSC TCGA datasets. Survival analysis performed the TCGA datasets based on the expression of the selected dysregulated transcripts allowed the identification of potential mRNA/miRNA/lncRNA pairs that could serve as prognostic biomarkers. Moreover, the expression pattern of the mRNA/miRNA/lncRNA in the TCGA datasets was confirmed in the qRT-PCR experiments performed on tumor tissue and the corresponding adjacent normal tissue.

Conclusion. The present study revealed differences in terms of molecular imbalance in the two subtypes of NSCLC.

Connecting morphology, molecular pathology, and cancer genomics to discover better early-stage lung cancer biomarkers

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Corresponding Author: Paul Chiroi e-mail: chiroi.paul@umfcluj.ro **Introduction.** Lung cancer (LC) is the largest cause of cancer-related death worldwide, accounting for over 1.8 million deaths each year. Despite all technological advancements made so far, 57% of patients are diagnosed in late stages. Hence, the central focus of our study was understanding the alterations in lung morphology, tumor microenvironment (TME) and genomic landscape of LC, to unlock a new avenue for discovering novel, early-stage biomarkers.

Material and methods. A cohort of 51 patients with early-stage LC were diagnosed between January 2013-December 2016. Histological diagnosis and staging were done according to standard protocols. Immunohistochemistry staining was used for E-cadherin, p53, CD4, and CD8. Tumor zones with more than 15% tumor cells were marked for further isolation and molecular analysis. Total RNA was extracted from FFPE tissues using Qiagen RNeasy FFPE Kit. We used miRNET to identify miRNAs that could be used as biomarkers for early-stage diagnosis. The synthesis of cDNA was performed using 100ng of total RNA. The qRT-PCR data analysis was done using $\Delta\Delta$ Ct method. Based on IHC markers and early-stage LC clinical biomarkers we generated a network of interactions between miRNAs and their target genes.

Results. Histology results divided our patient cohort in 43.1% lung adenocarcinomas, 41.1% lung squamous cell carcinomas and 15.8% neuroendocrine lung tumors. The pathological stages included 47.1% stage IA, 37.2% IB and 15.7% of IIA cases. E-cadherin IHC was intensely positive in 19 cases and moderately positive in 32 cases. P53 IHC was positive in 23 cases and negative in 28 cases. TME analysis showed a moderate to high peritumoral inflammatory infiltrate in 80% of the



cases. Differential expression analysis of the selected miRNAs revealed a statistically significant down-regulation of hsa-miR-29b-3p and hsa-miR-181a-5p in tumor tissue, while hsa-miR-205-5p and hsa-miR-25-3p were upregulated in LC tumor tissue when compared with adjacent controls.

Conclusion. Our study is an in-depth characterization of TME in a subset of early-stage LC that includes both NSCLC and SCLC. These tumors are immunologic active with an 80% moderate to high inflammatory TME, as most inflammatory infiltrate is localized in the stromal compartment where TLS were present in 74,5% of the cases. The main component of the TME were CD4 cells. Based on the bioinformatic analysis we managed to validate 4 miRNAs (hsa-miR-29b-3p, hsa-miR-181a-5p, hsa-miR-205-5p, hsa-miR-25-3p) that were dysregulated in the tumoral tissue compared with the adjacent normal zones, and that could be further investigated as potential biomarkers for early-stage LC. Approaching such a heterogeneous disease as LC from multiple angles including morphology, molecular pathology, bioinformatics, and cancer genomics allows us to assemble different pieces of the same puzzle in the quest for novel, early-stage biomarker identification.

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"Clinical and economic impact of personalized targeted anti-microRNA therapies in reconverting lung cancer chemoresistance", CANTEMIR, no. POC-P_37_796/2016.

Peripheral blood stem cell mobilization using human chorionic gonadotropin

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4) Department of Pathology, "Ion Chiricuta" Oncology Institute, Cluj-Napoca, Romania **Introduction.** For many hematological and solid malignancies, stem cell transplantation (SCT) offers a potentially curative treatment. Given the rising number of patients requiring STC who do not have HLA-matched donors, graft rejection and graft versus host disease (GVHd) remain significant treatment-related complications that compromise post-transplant survival, even in patients undergoing intensive immunosuppressive therapy. Bone marrow stem cell mobilization is an essential step in peripheral blood STC (PBSCT). However, insufficient mobilization is one of the limitations of the current approach using the granulocyte-colony stimulating factor (G-CSF). Our previous results *in vitro* and *in vivo* have shown that marrow-derived stem cells respond to human chorionic gonadotropin (HCG) stimulation leading to improved hematopoiesis.

Material and methods. We used a murine model to assess the efficacy of HCG in PBSCT. Bone marrow mononuclear cells were harvested from healthy donor mice after additional mobilization using HCG, followed by haploidentical PBSCT. Engraftment efficacy and GVHd were evaluated in the recipient mice after transplantation.

Results. The addition of HCG to the current standard approach using G-CSF influenced the engraftment of donor stem cells and the outcomes of the treatment, impacting GVHd duration and severity.



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Corresponding Author: Andrei Cismaru e-mail: cosmin.cismaru@umfcluj.ro **Conclusion.** HCG has the ability to improve the mobilization and engraftment of marrow derived stem cells, influencing the outcomes of PBSCT. This can be mainly attributed to the response of hematopoietic and mesenchymal stem cells to HCG with influences on GVHd.

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Alteration of the primary structure of microRNAs belonging to the miR-181 family and miR-21, potential anti-tumor therapies with artificial microRNAs

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MicroRNAs are a class of non-coding RNAs that are involved in the regulation of numerous processes and cellular homeostasis. Dysregulation in microRNA expression can be associated with a cellular pathological phenotype and increasing evidence demonstrated that these microRNAs contribute to the development and progression of numerous malignancies by targeting and degrading RNAs encoded by oncogenes or suppressor genes of tumors. Therefore, a microRNA can target multiple cellular transcripts, similarly a cellular transcript can be targeted by multiple microRNAs. Some studies suggested that the specificity for cellular transcripts can be influenced by the secondary structure of microRNAs, so starting from this hypothesis, in the present study, through bioinformatics analysis methods, we highlighted that the alteration of the primary structure in the seed region of mature microRNAs belonging to the miR-181 (a, b, c and d) family and miR-21, result in secondary structures with specificity for other cellular transcripts compared to native wild-type variants, indicating a pantumoral therapeutic potential. This strategy of obtaining artificial microRNAs by mutagenesis may constitute a basis for the implementation of targeted anti-tumor therapies.

Overview of MAPK inhibitor's effects on NSCLC cell lines

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Corresponding Author: Andreea-Mihaela Nuţu e-mail: andreeanutu.an@gmail.com **Introduction.** LC is the leading cause of cancer-related mortality worldwide. NSCLC remains the most common type of LC, and increasing evidence supports that the abnormal expression of MAPKs represents important players in cancer cell proliferation, differentiation, and apoptosis. MAPK signaling pathway may be a potential source of biomarkers for predicting the progression and prognosis of patients with NSCLC. Therefore, assessing the efficacy of MAPK inhibitors as a novel treatment approach for LC has become a central focus in cancer research.

Material and methods. TCGA data were downloaded and prepared using Feature extraction and Gene Spring software to investigate expression profiles for lung cancer. Further, the level of expression of MAPK genes was checked using RT-qPCR on four lung cell lines. As a next step, we investigated four tumour and normal epithelial cell lines treated at several doses and time points with 4 MAPK inhibitors, selected based on their capacity to modulate p38/MAPK activity. Initially, we identified through IC50 and scratch assay the best dose at the best time. We performed using the Celigo equipment analysis in vitro of functional assays as follows: apoptosis, cell cycle, and invasion.

Results. A TCGA data analysis was performed to check the level of expression of p38/MAPK and STAT3. Different expression levels were detected using control of a normal epithelial cell line. Data on treatment with the 4 MAPK inhibitors were obtained using Celigo-Nexcelcom Cytometer and Fast Plate Scanning for Image Acquisition and Analysis. Our data showed different responses for cell cycle, apoptosis, and invasion assays.

Discussion and conclusion. Our data suggest that the MAPK pathway is a powerful target in lung cancer treatment, primarily using specific inhibitors that can improve tumor cell death and control drug resistance. Further investigations using translational tools are needed to propose a reliable therapeutic model to improve lung cancer-targeting drugs.

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Cellular reprogramming – an innovative approach to study breast cancer

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 Research Center for Functional Genomics, Biomedicine, and Translational Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Breast cancer is one of the most common types of cancer in women and a leading cause of mortality and morbidity. It is well known that tumor microenvironment (TME) plays considerable role in cancer development by sustaining its growth and dissemination. Besides this, a growing number of studies support a novel contribution of TME cells in speeding up the cancer malignancy by undergoing
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Corresponding Author: Cornelia Braicu e-mail: braicucornelia@yahoo.com differentiation and cellular reprogramming. Taking this into account, we aimed to provide a comprehensive understanding of potential molecular changes occurring in normal epithelial cells and adipocytes, key players of the breast cancer TME.

Material and methods. To investigate the potential implications of selected cells in regenerative medicine, primary human mammary epithelial cells and stem cells were isolated post-surgery. Immunocytochemistry staining was performed using several representative markers in order to highlight mesenchymal origin of the cells. The microarray technique was used to identify the main transcriptomic altered patterns in normal epithelial cells and adipocytes at third cellular passage versus first cellular passage.

Results. Using bioinformatics tools, alteration of immune system genes and cell cycle regulation were emphasized in both cell types.

Conclusion. Finally, this study provides valuable data for developing new potential applications in regenerative medicine.

Lung adenocarcinoma chemotherapy induced cardiotoxicity as a major side effect

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Corresponding Author: Oana Zănoagă e-mail: oana.zanoaga@umfcluj.ro **Introduction.** Clinical application of chemotherapy in lung cancer is limited due to the different side effects, including cardiotoxicity, the mechanisms of which are still not entirely understood. The aim of the current study was to determine the in vitro cardiotoxicity effect of carboplatin and vinorelbine using a co-culture model.

Material and methods. Ventricular normal human cardiac fibroblasts (NHCF-V) and two lung adenocarcinoma cell lines (Calu-6 and H1792) were used for the present study. All the functional tests have been performed for a dose of 100 μ M carboplatin and 1 μ M vinorelbine. The biological effects of carboplatin and vinorelbine as single and combined therapy were evaluated at cellular and molecular level at 48h after treatment for mono- and co-culture experiments. We selected miR-205-5p, miR-21-5p and miR-30a-5p among the miRNA modulated by anticancer treatments and with effect on cardiotoxicity.

Results. Vinorelbine and carboplatin treatment induced apoptosis and autophagy in lung cancer and NHCF-V cells at a higher degree compared to the respective control groups. The role of several miRNAs (miR-21-5p, miR-30c-5p and miR-205-5p) in a co-culture system of cardiomyocytes with lung cancer cell lines was investigated by qRT-PCR, data revealing the alteration of miRNAs pattern due to the vinorelbine and carboplatin therapy on lung cancer cells, but also on cardiomyocytes.

Conclusion. Our data suggested that therapeutic agents used in lung cancer treatment induced cardiotoxicity. Furthermore, miR-21-5p, miR-30c-5p and miR-205-5p can be used as potential new biomarkers of chemotherapy-induced cardiotoxicity in lung cancer patients.

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Insights in targeting Megakaryocytic leukemia using anti-CD41 CAR T cells – a preliminary study

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Corresponding Author: Adrian Bogdan Țigu e-mail: adrianbogdantigu@gmail.com **Introduction.** According to the FAB classification, AMkL was classified as M7 subtype and represents no more than 5% of all AMLs. This disease is a frequent AML diagnosed in children, with a high frequency in children with Down Syndrome, while in adult, M7-AMkL accounts 1% of the total diagnosed cases. Our desire is to generate a path for many studies regarding the M7-AMkL and to investigate if the anti-CD41 CAR T cells can inhibit the growth of M7-AMkL cells.

Material and methods. Plasmid information. The Construct of CAR vector. The full length of chimeric antigen receptor was synthesized and subcloned into lentivirus vector by Creative Biolabs.

Cells and Flow cytometry evaluation. DAMI Luc2 and Jurkat cells were purchased from ATCC and the Jurkat cells were further processed, with the CAR construct inserted in the cells. The samples were analyzed by Flow cytometry and the CD41 and GFP+/- populations were determined.

Cell membrane integrity. The LDH activity was evaluated with the LDH Cytotoxicity Assay Kit.

Results. Five different co-culture ratios were established. The GFP+ CD41-APC- events (CARs) were compared to GFP- CD41-APC+ events (DAMI Luc2). We observed a limited inhibitory effect on DAMI Luc2, the highest inhibitory effect was observed at 24h of co-culture, in the groups with 50%, 20% and 10% CAR T cells. In the groups with more CAR T cells, we observed no inhibition in DAMI Luc2 cells. The groups that have less CAR T cells initially seeded present the highest LDH activity compared to the group containing DAMI Luc2 alone.

Conclusion. Our anti-CD41 CAR T cells had limited effect against the M7-AMkL target cells, thus further investigations are needed to enhance the CAR-T cells effect and inhibit M7-AMkL on a long-term study.

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Novel pre-clinical patient-derived liquid xenograft mouse model for monoclonal gammopathy of undetermined significance

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Corresponding Author: Gabriel Ghiaur e-mail: ghiaurgabriel@elearn.umfcluj.ro **Introduction.** Monoclonal gammopathy of undetermined significance (MGUS) is characterised by the presence in the blood of an abnormal protein usually called M protein. The pathology is specific to older man and is not generally associated with an increased health risk. However, in some cases, MGUS can shift to more serious conditions, including multiple myeloma and lymphoma. The cause of this transition is poorly understood and there is no approved therapy for MGUS. Therefore, novel animal models that can resemble the characteristics of MGUS pathology are essential.

Material and methods. Eight weeks old NSG-S severe immunocompromised mice were included in the study. On Day 2 mice were injected intraperitoneally with 100 ul of liposomal clodronate and busulfan (30 mg BU/kg) at the same site. The dose of busulfan was adapted in house after a previous dosing experiment on NSG-S mice. 24 hours after busulfan injection, donor MGUS patients' bone marrow cells were infused into recipient animals' tail veins. Mice were monitored to recognise a possible graft versus host disease or other pathological signs. Flow cytometry was used to assess disease installation at day 28.

Results. The results confirmed the proliferation of human cells within the recipient mice. Due of limited sample availability, the pilot trial included only two mice. One mouse started losing weight rapidly and died at day 29 possibly due to GVHD caused by rapid proliferation of human T cells confirmed via flow cytometry, whereas the other one survived the experiment (week 6).

Conclusion. From our knowledge this is one of the first experimental attempts for creating a preclinical model of MGUS. To avoid T cell induced GVHD, the mice cohort will be expanded and the human samples CD3 depleted before mice transplantation.

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Development of a LC-IM-MS method for the chiral analysis of proteinogenic amino acids

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1) MedFUTURE-Research Center for Advanced Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Lately D-amino acids have been recognized to play key roles as potential biomarkers in certain pathologies. Even though relevant platforms for chiral metabolomics have been developed, analysis of D-amino acids in complex biological matrices is still troublesome. The aim of this study was to develop a sensitive and highly accurate UHPLC-IM-MS quantification method for the enantiomers of all proteinogenic amino acids, applicable on biofluids.



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Corresponding Author: Radu-Cristian Moldovan e-mail: moldovan.radu@umfcluj.ro **Material and methods.** An indirect chiral separation method was developed, taking into consideration the most important variables that could influence the separation (three qualitative variables and three quantitative ones). Their influence was assessed, then the final separation conditions were optimized by a design of experiments approach. Travelling wave ion mobility spectrometry was used to measure the collisional cross sections (CCS) of the diastereomers.

Results. A comprehensive screening of the variables revealed that using (S)-NIFE as chiral derivatizing agent and performing the separations on a phenyl stationary phase offered the most promising results in terms of chiral resolution. Further optimization of separation conditions led to baseline chiral separation (Rs>2) of the derivatives of all 19 proteinogenic amino acids. Moreover, small but significant differences in the CCS values of the diastereomers were recorded. The method was found to be applicable to plasma samples, after minimal sample preparation.

Conclusion. The developed LC-IM-MS method offers baseline chiral separation of all proteinogenic amino acids in a single run of less than 20 minutes, combining high-throughput and high accuracy provided by ion-mobility spectrometry.

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The secretome signature of NCT503 treated TNBC cell lines

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Corresponding Author: Cristina-Adela Iuga e-mail: iugac@umfcluj.ro **Introduction.** Cancer secretome is essential when validating cancer hallmarks e.g. energy metabolism changes, therapy resistance, uncontrolled proliferation, reduced apoptosis and epithelial to mesenchymal transition. Here, we employed serum-free cell culturing of three TNBC cell lines for the characterization of the secretome changes upon NCT503 treatment.

Material and methods. A label-free shotgun proteomics approach was used to investigate alterations in the secretome profiles of three TNBC-representative cell lines after treatment with a PHGDH inhibitor. Cells were treated with NCT503 at IC20, washed and left for 12 h in serum-free medium (starvation step). The starvation medium (10 mL) was used for MS-based secretome analysis. First, the secretome was concentrated to 100 μ L using 10kDa microconfilters, further extracted by methanol-chloroform precipitation, solubilized in Rapigest® and digested (using trypsin). Resulting peptides were analyzed by Acquity M-Class nanoLC coupled with Synapt G2-Si HDMS. Raw UDMSE data was processed by Progenesis®QIp while enrichment analysis and data representations were made with ShinyGO.76.2 and EnrichR.

Results. Upon treatment, 25, 35 and 332 proteins were found significant changed compared to respective control in MDAMB231, MDAMB468 and HS578t. Although, NCT503 induced heterogeneous responses in the secretome of the TNBC cell lines (<5% shared proteins), enrichment analysis confirmed identification of proteins present in the extracellular region, in vesicles and membrane bounded.

Conclusion. NCT-503 treatment affects pathways related to extracellular matrix organization, downregulates cholesterol biosynthesis in mesenchymal cells and nucleotide catabolism in MDAs, it seems to impair signal transduction pathways, transport of small molecules and vesicle-mediated.

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Flow cytometry of CD5-positive hairy cell leukemia

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Material and methods. Diagnosis: The immunophenotype of both nodal and extranodal HCL, bone marrow biopsy immunohistochemistry for CD20, tartrate-resistant acid phosphatase (TRAP), annexin 1A and CD72 and genetic assessment of the BRAF V600E mutation. Immunophenotyping: the bone marrow aspiration sample is processed by flow cytometry for expression of CD38, CD20, CD11c, CD25, CD19, CD103 and CD5, CD10 as well. Flow cytometry evaluation. The processed sample expresses CD20, CD19, as well as CD11c, CD25 and CD103, and positive staining for CD5 and CD10.

Results. Positive staining for CD20 (very bright), CD22 (very bright), CD11c (very bright), CD25 (very bright), CD103 (bright) as well as atypical expression for CD5 and CD10, being considered one of the few cases reported of positive CD5 HCL.

Conclusion. CD5 marker is associated with T-cell and B-cell receptors. A bright CD5 is a mark of B cell activation. CD5 expression is a rare situation of CD5+ being heterogeneously expressed in HCL patients; CD5+ HCL might be considered by some a significant subgroup of lymphoid malignancies.

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Serum proteome profiles in Crohn's disease patients with different phenotypes towards biomarker identification

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1) Department of Medical III, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Crohn's disease (CD) is a chronic inflammation of the gastrointestinal tract leading to progressive, often irreversible bowel damage, such as strictures, fistulae and/or functional impairment. The complexity and heterogenous presentation highlight the need for individualized therapeutic approach. We aimed to analyze the CD serum proteome by mass spectrometry, to identify novel candidate biomarkers.



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Corresponding Author: Maria Iacobescu e-mail: ilies.maria@umfcluj.ro **Material and methods.** We prospectively included 30 CD patients, who had confirmed strictures or penetrating disease at the inclusion (n=15), and with persistent inflammation but no strictures or fistulae (n=15) and 15 healthy controls (HC). Serum samples were collected and subjected to label-free nano-LC coupled with Q-TOF mass spectrometry analysis.

Results. The serum proteome was characterized and a total of 21 proteins, including haptoglobin, plexin, serum amyloid 1 distinguished between CD and HC groups. A 28 protein panel was identified between the B1 versus B2/B3 phenotypes. 24 proteins were significantly abundant in the B1 phenotype group compared to the B2/B3 group, including: Interleukin-18, Cilia- and flagella-associated protein 36, Plexin-A2, Plasma serine protease inhibitor. In the B2/B3 group, there was a significant elevation of 4 proteins in comparison to the inflammatory group. WD repeat-containing protein 31, Leucine-rich alpha-2-glycoprotein, Serum amyloid A-1 protein, Plexin-A1.

Conclusion. Proteomic analysis by MS can differentiate among inflammatory and complex CD. Some of the proteins were found to be implicated in acute inflammatory response, Th1 and natural killer cell immune responses, innate and adaptative immune response, coagulation, cellular proliferation, adhesion, and migration. Unique biomarker panels based on protein sets were identified and could provide significant insight into CD progression.

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Serum proteome profiling of intrahepatic cholangiocarcinoma towards diagnostic biomarker identification

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 Prof. Dr. O. Fodor Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca, Romania **Introduction.** Intrahepatic cholangiocarcinoma (iCCA), is the second most common subtype of liver cancer, fourth leading cause of cancer related deaths, with incidence rates rising very fast. There is an urgent need for the development of an accurate diagnostic tool, one encouraging option being a proteomic-based biomarker signature. Thus, the aim of this study was to explore the serum proteome of iCCA patients in comparison to hepatocellular carcinoma (HCC), primary sclerosing cholangitis (PSC), liver cirrhosis (LC) and healthy controls (HC) by mass spectrometry.

Material and methods. Blood samples were collected from 60 patients (15 iCCA, 15 HCC, 15 PSC, and 15 LC) and 15 HC. Serum samples were subjected to label-free mass spectrometry proteomics analysis.

Results. Based on the MSE spectra and protein intensities of the individually analyzed samples, the serum proteome was characterized. Approximately 300 non-redundant proteins were identified in each sample with good coefficient of variation (CV<15%). Several proteins sets that could aid iCCA diagnosis, but also differentiation of iCCA from HCC, PSC and LC were identified and comprise potential biomarker signatures. A set of proteins was selected for further validation using complementary

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Corresponding Author: Maria Iacobescu e-mail: ilies.maria@umfcluj.ro methods, such as ELISA, in an independent cohort.

Conclusion. This is the first study to employ UDMSE detection towards serum proteome characterization of iCCA in comparison to HCC, PSC, LC and HC. Unique biomarker signatures based on proteins sets were identified and could be further used towards iCCA diagnosis. Furthermore, a set of proteins was selected for further validation in an independent patient sample cohort. We consider iCCA clinical management directed towards a biomarker signature validation and clinical implementation a crucial opportunity.

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Investigating the interactions between plasmonic gold nanoparticles and cellular media by means of hyperspectral microscopy

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Corresponding Author: Rareş Ionuţ Ştiufiuc e-mail: rares.stiufiuc@umfcluj.ro **Introduction.** Gold nanoparticles have been extensively used for a wide range of biomedical applications due to their unique physicochemical properties. Over the time, various methods of synthesis and functionalization have been developed. In this regard, polyethylene glycol (PEG) coatings are the most used biopolymers, increasing stability and biocompatibility of nanostructures. This study proposes a facile synthesis method of PEGylated gold nanoparticles (PEGAuNPs) and describes their interactions with biological samples.

Material and methods. AuNPs were synthesized using PEG1000 as a stabilizing and reducing agent. The nanoparticles were purified and concentrated through Tangential Flow Filtration procedure and followed by a rigorous characterization. After that, the cytotoxicity of PEGAuNPs was evaluated on two cell lines: a normal cell line (LX2) and a hepatocarcinoma cell line (SK-HEP-1) using MTT assay. PEGAuNPs – cells interactions were analysed using dark field (DF) and hyperspectral imaging.

Results. UV-Vis spectrophotometry measurements indicated a maximum absorbance at 525 nm. TEM revealed a mean diameter of 20 nm, 3-4 nm representing the thickness of PEG coating. The zeta potential of nanoparticles was -20.4 mV. By performing MTT assays, there was no significant decrease in cell viability, meaning that PEG functionalized AuNPs possess a reduced cytotoxic effect. DF microscopy allowed the assessment of nanoparticles cellular internalization, highlighting their distribution around the nucleus. Hyperspectral microscopy indicated that PEGAuNPs spectral behavior depends on their localization site in the cell.

Conclusion. The occurrence of such phenomenon plays a significant role in biomedical applications, allowing the development of novel imaging techniques.

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Role of CYP26 in the bone marrow stroma and HSC function

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Corresponding Author: Gabriel Ghiaur e-mail: ghiaurgabriel@elearn.umfcluj.ro **Introduction.** Cyp26a1 and Cyp26b1 are enzymes involved in the clearance of retinoic acid, an important signaling molecule. These proteins play an essential role in the regulation of retinoid homeostasis *in vivo*. Postnatal KO of these genes in mice leads to a reduced lifespan, weight gain, dermatitis, splenomegaly, reduced bone marrow (BM) cellularity and an abnormal bone phenotype. We hypothesized that the dysregulation of hematopoietic stem cell homeostasis after the loss of these two genes is the key event leading to the specific phenotype.

Material and methods. The KO of genes was induced in mice by tamoxifen injections using standard Cre-Lox technology. The genotype was assessed by gel electrophoresis from DNA extracted from mouse tail. Blood counts were evaluated. Flow cytometry was used to investigate mature cells and LSKs/Progenitor cells from peripheral blood (PB), BM and spleen. The measurement of the proliferation and differentiation of stromal cells was done using CFU-F assay from spleen and PB. Femurs were characterized using μ CT. Hematopoietic and non-hematopoietic BM cells were sorted using FACS and scRNAseq was performed to evaluate the expression level of genes involved in the establishment of the phenotype.

Results. Cyp26 KO was induced and confirmed by genotyping. BM hematopoiesis of CYP26 KO mice was impaired, left shifted and myeloid biased. The KO model had a lower cellularity and increased frequency of HSC in BM, increased circulating HSCs, spleen and PB CFU-F, bone/BM remodeling defects and reduced bone fat content. Moreover, scRNAseq highlighted the differential expression of certain genes involved in cell migration, differentiation and cell-to-cell interaction.

Conclusion. CYP26 activity is required to maintain bone marrow microenvironment homeostasis. CYP26 KO results in profound bone remodeling and immigration of the MSCs and hematopoiesis out from the bone marrow into extramedullary organs.

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