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### **MEDICINE Basic Sciences**

# The neuroprotective effects of *Betula pendula* leaves extract in an AD-like rat model

Alexandra Sevastre-Berghian<sup>1</sup>, Irina Ielciu<sup>2</sup>, Timea Bab<sup>3,4</sup>, Neli Kinga Olah<sup>4,5</sup>, Vlad A. Toma<sup>6</sup>, Bogdan Sevastre<sup>7</sup>, Alina Hasas<sup>7</sup>, Gabriela A. Filip<sup>1</sup>, Simona Clichici<sup>1</sup>, Daniela Hanganu<sup>3</sup>, Andreea Bodoki<sup>8</sup>, Ioana Roman<sup>9</sup>, Ioana Bâldea<sup>1</sup>

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Corresponding Author: Alexandra Sevastre-Berghian e-mail: alexandra\_berghian@yahoo.com **Introduction.** Our study aimed to evaluate the effects of natural products mixtures in an AD-like animal model.

**Material and methods.** The chemical analysis of the natural products mixtures was performed by spectrophotometric and chromatographic methods (LC-MS). The targets of these natural compounds included different pathological mechanisms in AD, such as, oxidation products, inflammatory pathways and brain proteins expression.

**Results.** The chemical analyzes of the natural products mixtures revealed high amounts of chlorogenic, trans-p-coumaric acids, quercetol and quercitin, which have proven to have beneficial on the above mentioned mechanisms.

**Conclusion.** Our findings indicate that natural products mixtures with various pharmacological activities may play a relevant role in the AD drug discovery.

Acknowledgment. This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CNCS - UEFISCDI, project number PN-III-P1-1.1-TE-2021-0159, within PNCDI III (TE60/2022).

# Changes in lung ultrastructural and oxidant/antioxidant balance induced by gold nanoparticles – experimental *in vivo* study

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Corresponding Author: Gabriela Adriana Filip e-mail: gabriela.filip@umfcluj.ro **Introduction.** Nanotechnology and especially gold nanoparticles have been increasingly used therapeutically as drug delivery agents, but despite this, the details of the interaction of nanoparticles with biological systems are not precisely known. Green synthesis of gold nanoparticles, using compounds from natural extracts, can be a strategy to reduce their toxicity and increase the therapeutic effect. The study investigated, on experimental in vivo models, the effects induced by exposure to gold nanoparticles, in an attempt to understand their toxicity and potential role in therapeutic applications.

**Material and methods**. 24 adult male Wistar rats, divided into 4 groups (n=6) were treated orally daily with 0.5 mg/b.w. citrate-reduced gold nanoparticles (AuNP-citrate), or with 0.5 mg/b.w phytoreduced gold nanoparticles with Sambucus nigra extract (AuNP-SN), for 2 and 4 weeks. Oxidative stress, DNA damage, transcription factors and ultrastructural changes were evaluated in lung homogenates in parallel with the quantification of malondialdehyde (MDA) and reduced/oxidized glutathione (GSH/GSSG) levels, as well as catalase (CAT) and glutathione peroxidase (GPx) activity in the blood. Gold content in lung tissues was also measured. Both types of gold nanoparticles were characterized by ultraviolet-visible spectroscopy (UV-Vis), transmission electron microscopy (TEM) and zeta potential measurement.

**Results.** Both types of gold nanoparticles induced systemic and pulmonary oxidative stress, decreased antioxidant defenses and increased NF- $\kappa$ B activation, especially Sambucus nigra phytoreduced nanoparticles. AuNP-SN increased NF- $\kappa$ B activation, without toxic effect on DNA. TEM examination revealed ultrastructural changes in II pneumocytes and internalization of both gold nanoparticles in endothelial cells.

**Conclusion.** Administration of gold nanoparticles induced pulmonary and systemic cytotoxic effects, regardless of their synthesis method.

#### Physical training and antioxidant supplementation

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Corresponding Author: Daniela-Rodica Mitrea e-mail: rdmitrea@yahoo.co.uk **Introduction.** Physical effort triggers oxidative stress resulting in an alteration of the body's responses. Several studies have suggested that supplementing with antioxidants enhances physical performance. The aim of the study was to evaluate the efficacy of N-acetylcisteine (NAC) or rutin administration during physical training, in rats.

**Material and methods.** Male albino Wistar rats (N=28; 180 - 200 g), were allocated randomly into 4 groups (N=7). The rats received the treatment (0.5 mL/ day), by oral gavage, one hour before the physical training, which was performed on a horizontal treadmill (5 days/week; 5 minutes/day), as follows: Group NS 0.9% -received normal saline 0.9%; Group CMC - carboxymethyl cellulose (CMC); Group NAC - 200 mg/day (2.85 mg/kg/day) of N-acetylcysteine (NAC); Group

Rutin - received rutin 50 mg/kg/day. On the last day of the experiment, immediately following physical exertion, blood and tissue samples (gastrocnemius muscle, lung parenchyma, aorta, and heart) were collected for oxidative stress and transmission electron microscopy investigations.

**Results.** The distance covered throughout the experiment did not show any significant modifications among the groups. However, the administration of NAC and rutin led to slight, non-significant increases, particularly in the latter stages of the study. The administration of rutin resulted in reduced lipid peroxidation and enhanced antioxidant protection in all samples, whereas NAC demonstrated limited positive effects on lipid peroxidation.

**Conclusion.** Rutin administration during physical training protected the investigated organs against oxidative stress.

### The impact of trimethylamine N-oxide on atrial fibrillation occurrence in patients with or without cardiovascular disease

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Corresponding Author: Cristian Marius Florea e-mail: fl.cristi@yahoo.com **Introduction.** Atrial fibrillation is the most prevalent arrhythmia in humans, but with a still largely unknown pathogenesis. Lifestyle changes such as weight reduction and diet modification have been shown to improve rhythm control strategies in maintaining sinus rhythm. TMAO, a gut microbiota-derived byproduct from red meat, has been linked to numerous cardiovascular and metabolic diseases such as atherosclerosis, heart failure, diabetes mellitus and dyslipidemia. The study aimed to evaluate the impact of serum TMAO levels on the occurrence of atrial fibrillation in patients with cardiovascular disease.

**Material and methods.** The fasting serum TMAO levels were measured in 153 patients with no cardiovascular disease and in patients hospitalized for cardiovascular disease with or without atrial fibrillation. Patient history and echocardiography data related to atrial fibrillation presence and progression was collected.

**Results.** Generally, patients with atrial fibrillation had more comorbidities without significant difference in TMAO levels compared to patients with cardiovascular diseases but without atrial fibrillation (p=0.57). Moreover, there was no difference between atrial fibrillation progression phenotypes (p=0.27). A positive significant correlation between TMAO levels and echocardiographic markers of diastolic function and filling pressures such as E/A ratio (r=0.27, p=0.01), LA volume (r=0.249, p=0.006), E/e' ratio (r=0.324, p<0.001) was found. Additionally, a weak negative correlation with LEVF (r= -0.330, p<0.001) was noted. In multivariate analysis, a significant association with atherosclerotic cardiovascular disease (p=0.04) and chronic kidney disease (p<0.001) but without significant TMAO association with atrial fibrillation (p=0.9) was found.

**Conclusion.** Aerum TMAO levels does not corelate atrial fibrillation presence and disease progression phenotypes in patients with cardiovascular disease.

Acknowledgements. This work was supported by the Iuliu Hatieganu University of Medicine and Pharmacy of Cluj-Napoca, Romania, through a grant: Doctoral Rsearch Project (PCD 2019), contract number 1529/22 from 18.01.2019.

### Antitumor effects induced by magnetic hyperthermia mediated by iron oxide nanoclusters linked with doxorubicin

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Corresponding Author: Ioana Bâldea e-mail: baldeaioana@gmail.com **Background and aim.** Magnetic hyperthermia (MH) requires tumor exposure to magnetic nanoparticles, followed by an external alternating magnetic field (AMF) which induces hyperthermia leading to selective apoptosis of tumor cells. We synthesized biocompatible iron oxide nanoclusters linked with doxorubicin, to increase efficiency and selectivity of chemo-magnetic hyperthermia and tested their antitumor efficacy in vitro against breast cancer cells MDA-MB-231 and MDA-MB-231AM (resistant to doxorubicin) and normal HUVEC cells.

**Material and methods.**  $Fe_3O_4$  magnetic nanoclusters (MNC), stabilized with 3,4-dihydroxybenzhydrazide were synthetized by solvothermal method and linked with doxorubicin in a ratio 20:1. Biological studies: cell toxicity - MTS assay, nanoparticles uptake - TEM, apoptosis and cell cycle - FACS.

**Results.** MNC were packed into clusters, with well-defined spherical shapes and size ~ 200 nm. MNC w/wt doxorubicin showed good biocompatibility up to 50  $\mu$ g/ml. MH mediated by MNC (50  $\mu$ g/ml) and AMF (30 Hz for 40 minutes) induced significant apoptosis, compared to control. Hyperthermia using MNC linked with doxorubicin, further increased apoptosis and induced cell cycle arrest of tumor cells. For immersed in FPCS solution, equal amounts (0.7 mg/ml) and subsequently placed at 37°C for 30 min. In order to remove excess of protein each sample was magnetic separated and rinsed three times with PBS. Afterwards they were dried in air and the obtained powders were analysed by FTIR.

Acknowledgement. This work was supported by a grant of the Ministry of Research, Innovation and Digitization, Romania, CNCS - UEFISCDI, project number PN-III-P1-1.1-TE-2021-0498, within PNCDI III.

### Anti-inflammatory activity of Grape pomace extract in ratinduced chronic inflammation

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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.** One of the most important by-products in the winemaking industry is represented by grape pomace (GP), generated in important quantities during the winemaking process, representing approximately 30% of total waste. The disposal of GP causes important ecological issues like pollution and therefore numerous solutions for its valorization are proposed, including the use of GP as a valuable source of bioactive compounds with health and pharmaceutical applications. Accordingly, numerous studies have shown that GP, mostly because of the phenolic

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 Research Station for Viticulture and Enology Blaj (SCDVV Blaj), Blaj, Romania

Corresponding Author: Raluca Maria Pop e-mail: raluca\_parlog@yahoo.com compounds composition and high concentration possesses various pharmacological activities among which, the antioxidant and anti-inflammatory effects with multiple implications in the prevention and progression of various chronic diseases.

**Material and methods.** The antioxidant and anti-inflammatory activity of GP was studied using a rat model of induced chronic inflammation with complete Freund's adjuvant (CFA). Grape pomace extract was characterized for its total polyphenols content with the Folin Ciocalteu method and its antioxidant activity with the 2,2-diphenyl-1-picrylhydrazyl (DPPH) method. For this study, sixty Wistar-Bratislava rats were used and divided into 6 groups. The CFA inflammation was induced in all rats and differently treated with saline solution (group 1), sodium diclofenac (7.5 mg/kg - group 2), white GP extract (0.5 mL/kg body weight (b.w.) - group 3), red GP extract (0.5 mL/kg b.w. - group 4), diclofenac and white GP extract (0.5 mL/kg b.w. white GP extract and 7.5 mg/kg diclofenac - group 5) and diclofenac and red GP extract (0.5 mL/kg b.w. red GP extract and 7.5 mg/kg diclofenac -group 6). Edema assessment and thermal hyperalgesia evaluation were performed at the following time points - days 0, 1, 3, 7, 14, and 20. Plasma levels of tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), interleukin-6 (IL-6), and IL-1 $\beta$  were measured.

**Results.** The ethanolic GP extract had 32 g polyphenols/100g white GP and 82 mg polyphenols/100g red GP, respectively. The antioxidant activity was 34 mMT/100g white GP and 53 mMT/100g red GP. All administrated treatments reduced significantly over time the paw edema as compared to the control group. The values of proinflammatory cytokines varied differently according to the administrated substances but overall, they all had significantly reduced levels when compared with the control group by the end of the experiment.

**Conclusion.** The administration of GP alone presented the anti-inflammatory effect as expected, but long-time administration is necessary to obtain this effect. The red grape pomace had a better anti-inflammatory effect as compared to white grape pomace. The administration of diclofenac with red grape pomace had the best anti-inflammatory result.

## The use of ALT free flap in the reconstruction of sternectomy defect after oncologic resection: case report

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 Thoracic Surgery, Clinical Hospital of Pneumophthisiology "Leon Danielo" Cluj-Napoca, Romania **Introduction.** Reconstructive surgery is required for defects of the anterior chest wall following wound dehiscence after cardiac procedures or infections of the mediastinum in order to achieve wound closure. Less frequently it is performed after oncologic resections. Tumors of the sternum are rare, primary tumors include sarcomas, desmoid and skin tumors. Metastatic tumors are more infrequent and among reported primary sites have been breast and thyroid. Reconstruction options include pectoralis major, latissimus dorsi, restus abdominus, omentum, and ALT flaps.

**Material and method.** We are reporting on the case of a female patient with previous history of breast cancer who underwent mastectomy and subsequent radiation and chemotherapy. CT imaging confirms a metastatic tumor at the level of the sternum. During surgery part of the manubrium and the superior two thirds of the body of the sternum have been resected along with the corresponding costal cartilages and the

Corresponding Author: Ioana Țichil e-mail: tichil.ioana@gmail.com overlying skin and subcutaneous tissue. Stability of the chest wall was achieved by polypropylene mesh and cross sutures. Soft tissue reconstruction was performed using a chimeric fasciocuteneous and muscle ALT flap.

**Results.** Flap viability was monitored hourly in the first 72 h using handheld doppler devices. There were no complications. Drains were removed at 10 days, at two weeks postop sutures were removed as stable wound healing was achieved with minimal morbidity to the donor site.

**Conclusion.** The ALT flap is a reliable option for reconstructing large composite defects of the anterior chest wall. It provides adequate skin coverage and sufficient bulk to efficiently close dead spaces and prevent further complications.

### New insights into the multivariate analysis of SER spectra collected on blood samples for prostate cancer detection: towards a better understanding of the role played by different biomolecules on cancer screening - a preliminary study

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Corresponding Author: Vlad-Cristian Munteanu e-mail: vladcristian.munteanu@gmail.com **Introduction.** Prostate cancer (PCa) poses a significant global health issue, being the second most diagnosed cancer and the sixth leading cause of cancer death, with 1.3 million cases and 359,000 deaths worldwide in 2018. To address this issue, this study investigates the capability of Raman spectroscopy and its advanced form, surface-enhanced Raman spectroscopy (SERS), combined with multivariate analysis (MVA), in providing an innovative and precise diagnostic tool for PCa. A particular emphasis is placed on assessing the efficacy of these techniques when applied to serum and plasma samples from both healthy individuals and prostate cancer patients.

**Material and methods.** Blood and prostate tissue samples were collected from 103 prostate cancer-diagnosed patients at the Institute of Oncology "Prof. Dr. Ion Chiricuță" in Cluj-Napoca, Romania. We ensured that none of the participants had undergone prior prostate cancer treatment or were diagnosed with other known diseases. The prostate cancer patient cohort had an average age of 61, while the healthy donors, referred for routine urological check-ups, were all aged over 50 years.

**Results.** SERS analysis on both plasma and serum samples revealed distinctive vibrational peaks with prominent intensity differences between healthy individuals and PCa patients. The multivariate analysis, spanning the entire spectral range (350–2200 cm–1), underscored the superior performance of serum samples in differentiating between PCa patients and healthy donors. Serum samples offered an improved accuracy (97.7% vs. 87.8%), precision (100% vs. 86.7%), sensitivity (96.6% vs. 96.3%), and specificity (100% vs. 71.4%) as compared to plasma samples, highlighting their potential in enhancing the PCa diagnostic process.

# Optimizing orthopedic surgical planning through reverse engineering and rapid prototyping

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Corresponding Author: Iustin-Gavril Zaieț e-mail: z.iustin@yahoo.com **Introduction.** The arena of orthopedic surgery is undergoing a transformative phase due to the integration of advanced technologies. Notably, Reverse Engineering (RE) and Rapid Prototyping (RP) are emerging as vital tools for refining preoperative strategies.

**Material and methods**. Utilizing RE, orthopedic surgeons have the capability to convert complex anatomical structures from medical images into comprehensive digital models. This methodology provides a deeper understanding of individual patient pathologies and distinct anatomical details. Concurrently, RP is employed to bring these digital designs to life by creating tangible 3D models. These models allow surgeons to gain tactile insights, enabling them to simulate various surgical routes.

**Results.** The combined application of RE and RP is ushering in a novel era for orthopedic surgery. By promoting a thorough and immersive preoperative planning process, these technologies aim to enhance the accuracy of surgical procedures and improve patient outcomes.

**Conclusions.** This e-poster delves into the complexities, benefits, and prospective paths of integrating RE and RP in orthopedic preoperative planning.

# Changes in medical students' academic and physical education performances before and after the COVID-19 lockdown

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Corresponding Author: Andrada Elena Urda-Cîmpean e-mail: aurda@umfcluj.ro **Introduction.** The lockdown implemented in 2020 to stop the spread of COVID-19 caused disruptions to daily activities, especially educational ones, in numerous countries across the world. Through this study, we aimed to determine if the students' academic achievement and athletic performance at a Romanian medical faculty changed from before to after the COVID-19 lockdown.

**Material and methods.** We selected two academic years before (2017–2019) and after (2020–2023) the COVID-19 lockdown. For both periods we included students' grades in the same two subjects, known for testing logical problem-solving and memory. The same three athletic assessments—burpees, push-ups and abdominal crunches—were used to collect data on the students' sports performance for each period. Descriptive statistics, chi-square and non-parametric tests were used to analyze the data using IBM's v.25 SPSS software.

**Results.** During the pre- and post-COVID-19 lockdown periods, the percentage of female students enrolled at the Faculty of Medicine was significantly higher (61.5% and 70.6%) than the one of enrolled male students (34.9% and 29.4%, Chi-square test: p<0.05). In terms of academic achievement, written examination results and

final grades were significantly lower during the post-lockdown period than they were during the pre-lockdown (Mann-Whitney U test: p<0.001). Between the pre- and post-lockdown periods, there was a significant decline in the number of grades considered very good academic results (final grades  $\geq 9$ ; Chi-square test: p<0.001), but there were no significant differences in female and male students' very good academic results (Mann-Whitney U test: p>0.05). In terms of physical performance, we found that the number of repetitions decreased significantly from the pre-lockdown to the post-lockdown period only in the abdominal exercise test (Mann-Whitney U test: p<0.001).

**Conclusion.** Following the lockdown period, academic performance declined more than physical performance did.

#### **Relevance of vitamin D axis in lung cancer**

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Corresponding Author: Ciprian Silaghi e-mail: silaghiciprian@yahoo.com **Introduction.** Lung cancer has an unfavorable prognosis with a rate of low overall survival. This is due, in part, to the difficulty of diagnosing in the early stages as well as resistance to the therapeutic methods used. In recent years, there have been various therapies that use specific molecular targets that are effective in prolonging survival in cases of advanced disease. It is, therefore, necessary to find more specific biomarkers that can identify early changes in carcinogenesis and allow for the earliest possible treatment. Vitamin D has been shown to play an important role in other metabolic pathways, such as immunity and carcinogenesis. The genes that encode it are intensely polymorphic and vary greatly from one human population to another. Their involvement in various types of cancer has been extensively studied in the past, but related information indicates that involvement in lung cancer is reduced.

**Objective.** Based on the existing literature which reported the gene expression of vitamin D dependent proteins in lung cancer, one purpose was to discuss the impact of vitamin D dependent proteins gene expression and their modulation during chemotherapy in lung cancer patients.

Material and methods. Literature research.

**Conclusion.** The study of VDR polymorphism is an invaluable lung cancer prognostic tool. Taking these even further, analyzing different haplotype genetic variants improves the accuracy and specificity of these instruments. It is important to mention that even if these parameters are studied, their actual clinical applicability is, unfortunately, rarely considered. They are used mainly for academic research purposes. Furthermore, it is worth mentioning that this strategy is not limited to the prediction of lung cancer evolution. Still, it can extend its use to predict other types of cancer. However, the great number of factors contributing to the phenotypical dynamics could project the factual clinical relevance of SNPs to marginal relevance.

### Morphometric study comparing post mortem evaluation of fetal heart by pm-MRI at 7T vs. conventional autopsy

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Corresponding Author: Camelia Albu e-mail: a.camelia82@yahoo.com **Introduction.** Except for data on foetal heart weight, there are no morphometric studies providing morphometric data on normal cardiac sizes depending on gestational age.

This poster will present in a comprehensive manner the results of our study, in which we aimed to determine whether post-mortem MRI at 7T can perform threedimensional measurements of the fetal heart and to obtain results comparable to postmortem macroscopic measurements made at autopsy, in fetuses with a body weight of less than 500 g.

**Material and methods.** For this study, 12 second trimester fetuses with gestational age of between 13 and 19 weeks of amenorrhea were considered. All fetuses resulted from the therapeutic termination of pregnancy (TOP) due to plurimalformative syndromes or the presence of chromosomal abnormalities. All cases were properly fixed in 10% formaldehyde solution, and were subsequently examined using a 7T MRI machine. After post-mortem imaging examination, all cases were subjected to conventional autopsy. Three-axis cardiac measurements were carried out by both methods of examination, using the same cues.

**Results.** The results of our study show a strong correlation between post-mortem MRI measurements at 7T and autopsy measurements, with p<0.001. The correlation coefficient (r) for all three axes measured was greater than or equal to 0.90. Bland Altman's graphs showed good overall agreement between the measurements made by both methods.

**Conclusion.** Using 7T post-mortem MRI for three-dimensional morphometric evaluation of the fetal heart in second-trimester fetuses with a body weight of less than 500 g, results comparable to macroscopic measurements performed during conventional autopsy are obtained.

#### Melanoma of the lung – a case report and review of the literature

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2) Department of Histology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction and aim.** Lung melanoma is commonly seen as a metastatic tumor rather than a primary tumor. Malignant melanoma with rhabdoid features, with pulmonary localization, is a rare entity, with few cases reported in the literature. Rhabdoid melanoma is an uncommon and aggressive variant of malignant melanoma, characterized by the presence of large cells resembling rhabdomyoblasts, with eosinophilic hyaline intracytoplasmic inclusions (aggregates of intermediate filaments) and vesicular nuclei with prominent nucleoli. We present the histological and immunohistochemical features of a rhabdoid melanoma as a metastatic tumor of the lung.

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Corresponding Author: Raluca-Margit Szilveszter e-mail: ralucaszilveszter@gmail.com **Material and methods.** A 62-year-old female patient, without any history of nevi or melanoma, presented with a 4.4/3/3 cm lung mass for which atypical right inferior lobe resection was performed. Frozen sections were taken and revealed a poorly differentiated malignant tumor.

**Results.** Histological sections revealed a malignant proliferation of large cells, with epithelioid and plasmacytoid/rhabdoid features, uni- or binucleated, with vesicular nuclei, large nucleoli, with moderate nuclear pleomorphism, eosinophilic, abundant cytoplasm, with solid, nested, papillary pattern, focally with angiocentric growth. The tumor cells were positive for vimentin, HMB45, S100, Melan-A, SOX10, BRAFV600E, CD56 and negative for p63, TTF-1, Chromogranin, panCK, CK7, SMA.The histological aspect and immunochemical profile were consistent with pulmonary malignant melanoma with rhabdoid features, more likely metastatic.

**Conclusion.** The rhabdoid subtype of melanoma with pulmonary localization is a rare entity and differential diagnoses like rhabdoid variant of metastatic renal cell carcinoma, primary PEComa, epithelioid hemangioendothelioma, sarcoma or poorly differentiated carcinoma, are to be considered; it is imperative to recognize this entity in order to properly administer a treatment.

# Beyond the jaw: exploring biomarkers for temporomandibular dysfunction

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Corresponding Author: Romana Vulturar e-mail: romanavulturar@yahoo.co.uk **Introduction.** The field of biomarkers in temporomandibular disorders (TMD) has gained significant attention. The overall prevalence of TMD is 31% for adults/ elderly and 11% for children/adolescents. These biomarkers are quantifiable indicators for biological status, existence, classification and progression of TMD. They can assist in early diagnosis and development of tailored treatment plans of TMD patients.

**Material and methods.** A critical review of the literature using the keywords 'Temporomandibular Disorders' AND 'biomarkers' (dated June 2014 to June 2023) was conducted to identify biomarkers that are associated with the development and the progression of TMD.

**Results.** TMD is characterised by a complex etiology wherein biochemical, bio-mechanical, neuromuscular, and bio-psychosocial variables all contribute to its manifestation. Notably, biomechanical variables, such as occlusal overloading and parafunctional habits, often feature prominently. Additionally, research had found an association between TMD and a number of chemical biomarkers. This personalized approach can yield more efficacious treatment strategies. Ongoing research is dedicated to the identification and validation of specific gene biomarkers for TMD, i.e. association with mutant genotypes related to degradation of extracellular matrix components, pain, inflammation peculiarities. This entails a comprehensive exploration of the genetic, biochemical, and molecular pathways that are intricately linked with TMD in order to enhance understanding of this complex condition.

**Conclusion.** Biomarkers associated with the presence of TMD were DNA variations in specific genes (MMP1 -16071G/2G (P=.042), COMT Val158Met (P=.030), and TNF $\alpha$  -308 (P=.016)), proteomic biomarkers (NGF, CGRP, BDNF), imaging biomarkers (MRI or CT scans), and salivary biomarkers (cortisol, IL-1, glutamate, serotonin). The use of biomarkers in TMD management may help for more accurate diagnoses and improved treatment outcomes.

# The comparative effects of probiotics in dexamethasone-induced metabolic disorders - an experimental murine study

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Corresponding Author: Maria Adriana Neag e-mail: maria.neag@umfcluj.ro **Introduction.** Glucocorticoids are effective therapeutic agents used mainly due to their anti-inflammatory and immunosuppressive properties. However, during long-term administration, multiple side effects are noticed, particularly regarding glucose and lipid metabolism. Probiotics have been associated with modulatory effects regarding metabolism and inflammation due to their ability to restore gut microbiota composition. The aim of this study was to evaluate the comparative effects of probiotics containing Saccharomyces boulardii versus Lactobacillus paracasei in dexamethasone-treated rats.

**Methods.** A total of 20 rats were randomly divided into 4 groups: group 1 served as control, group 2 received dexamethasone, group 3 received dexamethasone and Enterol, a Saccharomyces boulardii- based probiotic, and group 4 received dexamethasone and Enterolactis Plus (EntPlus), a Lactobacillus paracasei- based probiotic. On the last day of the experiment, the animals were sacrificed; blood samples and liver tissue samples for histopathological examination were collected. We determined the serum concentration of glucose, total cholesterol, triglycerides, tumor necrosis factor-alpha (TNF- $\alpha$ ), interleukin-6 (IL-6) and interleukin-10 (IL-10). The administration of glucocorticoids in the form of dexamethasone increased the serum concentration of glycolipid metabolism parameters and inflammation cytokines.

**Results and conclusion.** Treatment with probiotics containing Saccharomyces boulardii or Lactobacillus paracasei decreased serum glucose and TNF- $\alpha$  in dexamethasone-treated rats. Moreover, rats treated with Lactobacillus paracasei exhibited increased IL-10 and improved liver histological aspect. These observed results suggest that probiotics could impact the metabolic disturbances induced by glucocorticoids.

### Hyperspectral microscopy offers new insights in characterizing hepatic stellate cells in hepatocellular carcinoma: a pilot study

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2) Research Center for Advanced Medicine MedFUTURE, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Hepatic stellate cells, the pericytes of the liver represent the hallmarks of liver fibrosis and hepatocarcinogenesis. Over the years these cells were examined by different methods including culture cells, immunohistochemistry, flow cytometry, real-time quantitative polymerase chain reaction, confocal imaging, genetic tests and Raman spectroscopy. Hyperspectral microscopy represents a new, innovative method of examination, which measures the photons elastically scattered by the investigated object, beyond the visible spectrum, creating a three-dimensional image.

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Corresponding Author: Lavinia Patricia Mocan e-mail: lavinia.trica@gmail.com In this study, we used hyperspectral microscopy in order to characterize hepatic stellate cells in hepatocellular carcinoma (HCC) cases.

**Material and methods.** We included hepatic resection specimens from 8 HCCs and 6 benign hepatic tumors (hemangiomas and angiomyolipomas). We highlighted hepatic stellate cells with immunohistochemistry, using the anti  $\alpha$ -SMA antibody. The liver samples were afterwards evaluated with a hyperspectral microscope, enhanced with dark field examination mode (Olympus BX53 CytoViva). We analyzed  $\alpha$ -SMA immunolabeled hepatic stellate cells within three specific areas of hepatocellular carcinoma and benign liver tumors: tumoral capsule, tumoral stroma and adjacent hepatic parenchyma. For statistical analysis, we used the R 4.3.0 program and the statistical Wilcoxon rank sum test, with Holm correction.

**Results.** We observed statistical significance (p=0.01) and very statistically significant spectral differences (p<0,001) between hepatic stellate cells in both HCC and benign liver tumors, as well as between the examined areas.

**Conclusions.** Hyperspectral microscopy detected different spectral features of hepatic stellate cells within HCC and benign tumors, thus facilitating differential diagnosis between these entities. These findings support the integration of hepatic stellate cells examination using hyperspectral microscopy in the diagnostic and therapeutic conduct of HCC.

### The importance of NGS technology in the diagnosis of rare neurological disorders

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Corresponding Author: Eleonora Dronca e-mail: nora\_dronca@yahoo.com **Introduction.** Neurological disorders secondary to single gene mutations are an extremely heterogeneous group of diseases, individually rare, and often associated with progressive and severe disability. Given the degree of both clinical and genetic heterogeneity, next-generation sequencing (NGS) has become an important diagnostic tool.

**Patients and methods.** Although single-gene testing remains an important first tier test for disorders with clear phenotype-genotype correlation, NGS is used for the identification of rare mutations in genes known to be associated with genetically heterogeneous diseases. Here we present the case of a six-year old female patient, with microcephaly, spastic paraparesis, delayed speech and language development, and spina bifida occulta. The patient had no specific family history and no issues were detected during the pregnancy. Parents were of Caucasian origin and not related. Initial genetic testing showed normal (negative) SNP-array and spatial orientation disorders genetic test. The whole genome sequencing identified the c.760C>T [p.(Arg254Trp)] heterozygous mutation in the KIF1A gene; this mutation is classified as a missense pathogenic (class 1) mutation. Due to the early onset (in infancy) and clinical/ neurological features, it was diagnosed as NESCAV syndrome.

**Results and discussion.** NESCAVS is caused by de novo heterozygous mutations in the Kinesin family member 1A (KIF1A) gene. The KIF1A gene is located on chromosome 2q37.3 and is expressed mainly in the brain and spinal cord. Pathogenic

variants in the KIF1A gene are responsible mainly for three phenotypes: autosomal recessive and dominant spastic paraplegia 30, autosomal recessive hereditary sensory and autonomic neuropathy type 2 and autosomal dominant neurodegeneration and spasticity with or without cerebellar atrophy or cortical visual impairment syndrome NESCAVS. Most identified KIF1A variants associated with NESCAV syndrome are heterozygous and de novo.

#### Limiting factors in evaluating the bactericidal efficacy of Ag/ PDMS active textured substrates on Staphylococcus aureus

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 Research Institute for Renewable Energies, Politehnica University Timişoara, Timişoara, Romania

Corresponding Author: Pavel Şchiopu e-mail: pavelschiopu@gmail.com **Introduction.** This study aims to manufacture and test an advanced membrane with electrically stimulated self-disinfection properties that allow for the controlled release of metal ions.

**Material and methods**. The membrane was fabricated by casting 2 mm thick polydimethylsiloxane in 46x56 mm silicon molds, fabricated by photolithographic methods. Silver nanowires and silver microcrystals were placed in the membrane's channels. The morphology of the substrates was characterized by optical and electron microscopy and the optical properties by UV-VIS spectrometry. On the surface of the substrates,  $5\mu$ l agar spots were deposited and inoculated with  $5\mu$ l 2 McFarland S. aureus suspension. The durations of exposure to the membrane were tested in duplicate - 3, 9, 27, 81 seconds and a control. Afterward, the agar was peeled and vortexed in 1 mL of 0.9% saline. Three serial dilutions were plated and colonies were counted after 24 h incubation.

**Results.** Temperature and polymerization time drastically influenced membrane transmittance in the UVB region. SEM images revealed the homogeneous distribution of metallic nanowires. At the same time, the hydrophobic nature of the PDMS substrate does not allow an efficient wetting of the channels with the agar solution. Apart from the experimental data points obtained after 3 seconds, which are dominated by stochastic experimental errors, a proportional decrease in the concentration of bacteria on the agar is observed with increasing exposure time, particularly in channel B samples.

**Conclusion.** Quantitative differences in bactericidal effect between channels may be due to the different distribution of electric field lines in different areas of the membrane due to the hydrophobic nature of PDMS or the non-polarization of some microelectrodes in channel A.

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### Zoonotic parasitic elements in environmental samples from the emerging urban ecological niche of dog parks in Cluj-Napoca

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Corresponding Author: Alina Mihaela Baciu e-mail: alinabacium@gmail.com **Introduction.** Infections caused by parasites, which can have life cycles involving stages in humans, animals, and in some cases a phase of environmental embryonation, fit aptly within the One Health approach, yet often only the human aspect gets addressed. This study aims to investigate the presence of zoonotic parasitic elements in environmental samples, as well as Public Health measures found in the emerging niche of dog parks in Cluj-Napoca.

**Material and methods.** Seven locations where dog parks were situated in the proximity of playgrounds were identified throughout Cluj-Napoca. A purposive sampling technique was employed to gather soil and sand samples from the seven locations. Data regarding park type, park vegetation, and Public Health measures currently in place were also collected. A concentration-flotation method was used for each of the 105 soil and sand samples. The resulting samples were observed under light microscopy.

**Results.** The results are in line with a prior study from Romania, which identified 12.5% of soil and sand samples from public areas as positive for parasite elements. In our study, 9.5% of the 105 soil and sand samples were positive for a nematode ova or larvae. Eggs of Toxocara spp., Toxascaris spp., Trichuris spp. and Ancylostomatidae family, as well as Strongyloides spp larvae were identified. While the observed soil contamination is comparable with other data from Romania, these results are relatively lower than studies from other European countries. These variations could potentially be attributed to disparities in methodology and timing of sample collection. No statistically significant results were found for the influence of Public Health measures, neighborhood density, or the type of park on the positive sample rate.

**Conclusion.** While limited in its scope, the current study could be a stepping stone in the development of a One Health framework that would allow the surveillance of parasitic elements in the new urban niche of dog parks.

# Antioxidative effect of propolis vs. propolis and ginseng, in intense physical effort

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**Introduction and aim.** Intense physical effort can be a source of oxidative stress. Propolis, a natural mixture of viscous resins, and Ginseng, could improve the antioxidant protection. The objective was to highlight the antioxidant effect of propolis vs. propolis and ginseng, on intense physical effort in young amateur fitness practitioners.

**Methods.** 51 young healthy, amateur fitness practitioners, were randomly blind divided into three groups: subjects who did not receive any product, before intense physical effort (control = C = 13); subjects who received propolis capsules for one

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Corresponding Author: Ramona-Niculina Jurcău e-mail: ramona\_mj@yahoo.com month, before intense physical effort (Propolis group = P = 19); subjects who received capsules with ginseng and propolis for one month, before intense physical effort (Propolis+Ginseng group = PG = 19). The evaluated parameters were: interleukin-6 (IL-6), superoxide dismutase (SOD), malondialdehyde (MDA), and total antioxidant capacity (TAC), before and after intense physical exercise.

**Results.** SOD and TAC serum concentration were upregulated, IL-6 and MDA serum concentration were down-regulated in P and PG, compared to C, after intense physical effort.

**Conclusions.** A month of treatment with propolis or propolis with ginseng, increased the antioxidant defense after the intense physical effort, in fitness amateur practitioners, the effect being much more intense after using the of propolis and ginseng combination.

# Can vitamin D make a difference? Analyzing its effects on COVID-19 hospital stay and mortality

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Corresponding Author: Alexandru Constantin Sîrbu e-mail: alexdak.sirbu@gmail.com **Introduction.** The COVID-19 pandemic, caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), escalated into an unprecedented global health emergency. This has intensified efforts to identify therapeutic interventions that can ameliorate patient outcomes. Vitamin D, recognized for its immunomodulatory functions, has been suggested as a potential adjunctive treatment for COVID-19.

**Material and methods.** In this systematic review and meta-analysis, we investigated the impact of vitamin D supplementation on the clinical trajectory of COVID-19 patients. We directed our analysis toward key outcomes: the length of hospital stay (LOS), intensive care unit (ICU) admission rates, and mortality. Thirteen randomized controlled trials (RCTs) were selected for inclusion in this study.

**Results.** Upon analyzing the data gathered from the selected randomized controlled trials, it seems that high-dose vitamin D supplementation may offer some benefits in reducing the length of hospital stays and decreasing the likelihood of intensive care admissions in COVID-19 patients (RR = 0.63, 95% CI [0.41, 0.99], p= 0.04). However, this supplementation did not demonstrate a statistically significant effect on mortality rates.

**Conclusions.** Our results suggest that high-dose vitamin D supplementation could help shorten hospital stays and reduce ICU admissions for COVID-19 patients. However, the significant variability across studies and various limitations call for careful interpretation. More rigorous, well-designed randomized controlled trials are essential to definitively determine the effectiveness of vitamin D treatment for COVID-19 outcomes.

### Comparative analysis of the biofilm produced by Enterococcus faecalis and Staphylococcus aureus in a microfluidic device

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Corresponding Author: Dan Alexandru Țoc e-mail: toc.dan.alexandru@elearn.umfcluj.ro **Introduction.** The Gram-positive bacteria Enterococcus faecalis and Staphylococcus aureus are well known for their ability to produce a large amount of biofilm on different surfaces. Thus, in a medical environment they become one of the most difficult to eradicate bacteria and are responsible for a large number of deaths each year. However, little is known about the way these two bacteria produce the biofilm in a microfluidic device.

**Material and methods.** The H-type microfluidic device was 3D-printed using a polylactic acid filament. A bacterial suspension of 3McF was prepared for each bacterium and 5 ml of that suspension was used in the microfluidic device. We confirmed the presence of the biofilm using optical coherence tomography (OCT), scanning electron microscopy (SEM) and Fourier Transform Infrared (FTIR) spectroscopy. The quantity of the biofilm was assessed using a modified crystal violet staining technique.

**Results.** The experiment was analyzed at 12h-24h-72h and showed that Staphylococcus aureus produced a larger quantity of biofilm. However, the trend was positive for Enterococcus faecalis too. The overall structure of the biofilm analyzed using the SEM appears similar in both species but Enterococcus faecalis seems to produce smaller microcolonies.

**Conclusion.** Staphylococcus aureus is able to produce a large quantity of biofilm in a microfluidic device but with a different overall structure compared to Enterococcus faecalis. Future articles should focus on means of eradication of the bacterial biofilm that is produced in a dynamic manner in order to tackle this emerging issue.

## The effectiveness of dietary antioxidants on stress and anxiety - a systematic review

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2) Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The objective of the systematic review was to evaluate the effectiveness of antioxidant-rich diet on anxiety (AOA).

**Material and method.** All selected studies were published between 2015 and 2022. Databases: Medline/PubMed and Embase. Keywords: "anxiety and dietary antioxidant". Inclusion criteria: human subjects, both adult genders; STAI, HADS-A and BAI questionnaires; plasma TAC and MDA; the control group is placebo in all selected

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Corresponding Author: Ramona-Niculina Jurcău e-mail: ramona\_mj@yahoo.com therapeutic trials; randomized controlled trials. 12 studies where included with a total of 715 subjects, adult men and women. Effects monitored: impact of AOA on anxiety via 3 anxiety self-assessment scores; impact of AOA on the antioxidant capacity of the body; impact of AOA on SO markers. Evaluation: AOA effect on the level of anxiety and manifestations of stress; comparison of the intervention group with a control group.

**Results.** 69 eligible studies; 12 studies were selected for this systematic review. Selection of studies by title. Characteristics of the studies include: authors and date of publication of the RCTs; characteristics of the populations studied, the total number of subjects (NS); numbers of the intervention (GI) and control groups (CG: all placebos); protocol of the intervention, criteria of interest (psychological and biological) and results were described for each study.

**Conclusion.** Although anxiety is very widespread today, uncertainty persists about the effectiveness of AOA as anxiety modulators. On the one hand, AOA significantly improves somatic symptoms of anxiety and the level of plasma antioxidant defense, but on the other hand they do not act significantly on SO, an important mechanism in the pathophysiology of anxiety. Carrying out new therapeutic trials precisely evaluating the effectiveness of AOA on anxiety is therefore strongly recommended. A better understanding of anxiety and associated excess mortality could help prevent deaths in anxious individual.

#### Ginseng effects in mental stress - review and research

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 "Ion Creangă" State Pedagogical University Chişinău, Republic of Moldova **Introduction.** Ginseng increases resistance to stressors, an organism's ability to adapt to environmental conditions. The objectives of the license thesis was to assess the interest in the relationship between Ginseng and stress.

**Materials and methods.** A) Studies published on PubMed were selected and analyzed on the basis of a literature review. Period studied was 1960 – 2021. Keywords used were: "Ginseng" (G); "Ginseng AND Stress" (G+S); "Ginseng AND Cortisol" (G+C); "Ginseng AND Salivary Cortisol" (G+SC). B) Clinical research. Evaluation of the antistress action of GSG in mental stress, in 24 male participants. The GSG consumption period was one month before the stress, daily. Parameters evaluated, before and after the physical effort: malondialdehyde (MDA), total antioxidant capacity (TAC) and salivary cortisol (SC). There were two groups, control (C-G), which received no therapy and which received GSG (GSG-G).

**Results.** The keywords combination of G+S was the first to have presented studies on PubMed (1964), in other words the interest in the relationship between Ginseng and stress is the oldest. The most recent interest is for the SC (2013). The total number of publications is the highest for G+S again, so the interest in the relationship between Ginseng and stress remains the most important. GSC determined the significant reduction of MDA and SC and significantly increased TAC.

Corresponding Author: Ramona-Niculina Jurcău e-mail: ramona\_mj@yahoo.com **Conclusion.** Interest in the relationship between Ginseng and stress was highlighted by publications that contain the keywords G+S, G+C, G+SC. The most numerous studies are those related to G+C. For all selected keyword combinations, studies with animals predominated over those with human subjects. The interest in the relationship between ginseng and stress, from a physiopathological point of view, is real and important, being towards a growing and constant evolution over time. GSG is an effective antioxidant and anti-stress modulator in mental effort.

**MEDICINE Medical Specialties** 

# The re-entry circuit in ventricular tachycardia. The experience of the Cluj-Napoca Rehabilitation Hospital

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Corresponding Author: Gabriel Cismaru e-mail: gabi\_cismaru@yahoo.com **Introduction.** Ventricular tachycardias (VT) are considered among the most severe types of arrhythmias, with a significant risk to the patient's life. In cases with no structural heart disease, the focal mechanism is the most frequent. In cases where the heart shows structural disease, re-entry is the fundamental mechanism. The objective of our study was to elucidate the underlying mechanism of the reentry circuit in patients diagnosed with VT, admitted for ablation procedures, utilizing a three-dimensional mapping technology.

**Material and methods.** Over a span of 10 years, between 2014 and November 2023, a total of 169 patients had electrophysiological study and ablation for sustained VT in the Rehabilitation Hospital using a three-dimensional mapping system. Seventy-one patients were excluded from the study due to the focal mechanism as the cause of: outflow tract VT or VT originating on the inferior wall of the right ventricle or crux cordis. The rest of 98 patients were analyzed in order to characterize the re-entry circuit of VT.

**Results.** Of the 98 patients, 81 had a figure-of-8 reentry circuit due to an old myocardial infarction scar. In 2 patients with arrhythmogenic right ventricular dysplasia, the reentry circuit had double loop: one around the tricuspid valve and one around the scar from the RVOT. In 3 patients with fascicular TV, the reentry was located at the level of the Verapamil-sensitive area and the posterior fascicle of the left ventricle (LV). In 2 patients with bundle branch reentry, the reentrant circuit included the left branch and the right branch of the conduction system. In 4 patients a scar was detected on cardiac MRI and the re-entry circuit depended on the area of fibrosis. Two patients with dilated cardiomyopathy and old myocardial infarction had a reentrant circuit localized in the papillary muscle of the LV. One patient with old myocardial infarction had a focal mechanism of the VT from the scar of the LV. In 5 patients with old myocardial infarction, the reentry circuit was localized inside the epicardium, confirmed by the radial activation of the endocaridum at the level of the scar.

**Conclusion.** In patients with structural heart disease the most common mechanism of VT is reentry at the level of the scar. In patients with old myocardial infarction, the reentrant circuit has a figure-in-8 shape.

# **Diastolic performance parameters - early markers of cardiotoxicity in high-risk cancer patients?**

Anca Daniela Farcaș<sup>1</sup>, Florin Petru Anton<sup>1</sup>, Diana Larisa Mocan-Hognogi<sup>1</sup>, Mirela-Anca Stoia<sup>1</sup>, Camil Horia Eusebiu Crișan<sup>2</sup>, Călin Căinap<sup>3,4</sup>

 Department of 1<sup>st</sup> Medical Clinic, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Survival after chemotherapy (CMT) in oncological patients can be affected by several factors, including cardiotoxicity. Identification of high-risk patients and early diagnosis of cardiotoxicity would allow preventive therapies that would

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Corresponding Author: Anca Daniela Farcaș e-mail: ancafarcas@yahoo.com mitigate its effect.

**Material and methods.** 68 middle-aged women (34.5±8.4) with breast cancer treated with trastuzumab, who underwent clinical, biological (NT-proBNP, hsTnI, Gal 3, GDF-15) and echocardiographic (systolic and diastolic) assessment at inclusion and after CMT (trastuzumab). The patients were followed-up for 1 year and cardiovascular events were noted.

**Results.** Echocardiography showed no significant change in ejection fraction (EF) and global longitudinal strain (GLS), but significant change in left ventricular end-diastolic filling pressure (LVEDP) estimated by the e/e' ratio. LVEDP positive correlated with NTproBNp (r=0.71) and Gal3 (r=0.44). Univariate analysis showed that only NTproBNP variability predicted 16.3% of the LVEDP variability between the two moments. The NTproBNP and LVEDP could predict the cardiovascular events during the 1 – year follow-up.

**Conclusion.** Changes in diastolic performance - e/e' ratio – occur early after CMT and correlate with the variability of serum natriuretic peptides.

# Striking a balance: treating pulmonary thromboembolism during COVID-19 and thrombocytopenia - the complex intersection - etiology, diagnostic and anticoagulant therapy dilemmas – a case presentation

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Corresponding Author: Florin Petru Anton e-mail: florinantonfr@yahoo.com We present the case of a 78-year-old patient from an urban environment who came to the emergency department with palpitations and dyspnea, symptoms that appeared a few days before admission. The patient was under anticoagulant treatment due to a recent cholecystectomy complicated with acute renal failure requiring hemodialysis, for the prevention of venous thrombosis, considering prolonged immobilization.

Given the clinical presentation and suspicion of a possible pulmonary embolism - 88% saturation of  $O_2$ , dyspnea, significant edema in the right lower limb with echocardiographic evidence of deep venous thrombosis in the common femoral vein, a decision was made to perform a pulmonary angiography via CT. The CT angiography revealed a pulmonary embolism with a thrombus in the main pulmonary artery trunk and involvement of both pulmonary branches and showed the presence o pulmonary infarction.

Considering this, oxygen, anticoagulant therapy with enoxaparin (Clexane 80mg twice/day) was initiated, and appropriate hydration was provided, considering the recent history of renal insufficiency that had required hemodialysis through a right femoral venous catheter.

In the presence of a thrombocytopenia of 52000/mm<sup>3</sup>, we discussed the risk and benefit of anticoagulant therapy and we decided to give the anticoagulant in the presence of the thrombus in the main pulmonary artery and in both pulmonary arteries.

Post-procedure, no increase in creatinine was noted, but there was a progressive decrease in platelet count from 52000/mm<sup>3</sup> at the admission to 25000/mm<sup>3</sup> after one day of treatment with Clexane 80 mg twice a day. In the context of persistent thrombocytopenia, a hematological consultation was performed, and a switch to fondaparinux was decided. Antiplatelet antibody testing was considered, along with the possibility of platelet transfusion and close monitoring.

With platelet counts dropping to 10,500/mm<sup>3</sup>, two units of platelets were transfused. Subsequently, in the context of a positive COVID-19 test, treatment with remdesivir was initiated, along with the administration of dexamethasone.

The patient's condition improved slowly, with a reduction in symptoms, a marked decrease in lower limb edema, and a gradual increase in platelet count. In the given context, it is dabetable if thrombocytopenia was induced by heparin therapy, considering possible changes related to thrombosis and thromboembolism in the context of SARS COVID-19 infection.

The special aspect of the case. This case is intriguing, considering the multitude of diagnostic and treatment challenges, especially related to the presence and exacerbation of thrombocytopenia, while considering the dilemmas associated with anticoagulant therapy in a patient with severe thromboembolism.

Additionally, the onset of SARS-CoV-2 infection raised additional treatmentrelated issues, including the possibility that this infection may have precipitated the thrombotic episode and even contributed to thrombocytopenia.

### Assessment through simulation of the medical staff response ability to practical request

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Corresponding Author: Maria Irina Brumboiu e-mail: ibrumboiu@umfcluj.ro **Introduction.** Correct execution of medical procedures avoids the occurrence of negative effects on the patient's health status and other events that may alter the doctor-patient relationship. Our aim was to analyse how medical personnel in training performs a task by simulating a practical activity.

**Material and methods.** A before-after study was conducted, with the first phase consisting of circling numbers on a specially created form, according to a set of rules that simulated the request to perform a medical act. The second phase consisted in providing the correct solution before performing the same act. The subjects were medical students in the 2nd and 6th year, and the activity was carried out during the practical activity scheduled for the Epidemiology module. The descriptive statistics were conducted on the following variables: correct, incorrect, and coinciding answers (which matched the correct numbers but were wrongly placed and ordered).

**Results.** A total of 262 forms were included for assessment. Completely correct answers were given by 17.9% of students in the first phase, which increased to 34.7% in the second phase. 72.1% of participants provided completely incorrect answers in the first phase, proportion that decreased to 64.9%, in the second phase. Among the answers given by each student, predominantly correct were initially 27.9% of them and 35.9% in the second phase. As far as performance evolution, 45.4% had an improvement in the second phase compared to the first, while 30.9% of participants performed worse.

**Conclusion.** There was a large proportion of the medical students which performed the task in an incorrect manner. After providing them the correct method of execution, we noticed that almost half of the participants had improved results. These simulations support the need of assuring the medical personnel the appropriate information to perform a medical act and open the discussion for further research.

# How big is the motor cortex of a surgeon? – A case report assessing the size of the motor area of a surgeon through TMS

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Corresponding Author: Nicoleta Jemna e-mail: nicoleta.jemna@brainscience.ro **Introduction.** The use of TMS (transcranial magnetic stimulation) as a noninvasive method of mapping the M1 (hand motor) area has been well established from the beginning among the methods emergence in the neuroscientific community. The size of the hand motor area has been known to be correlated to the use of the corresponding muscle group. We investigated this assumption by mapping the M1 area of a particularly hand-skilled participant – a surgeon.

**Methods.** The present paper is a case report, in which we mapped the motor area of a healthy volunteer, third year surgical resident. We used a single pulse TMS mapping protocol – linked to an ENG (electroneurography) machine in order to evaluate the obtained MEP (motor evoked potentials) in the APB (abductor pollicis brevis).

**Results.** In our surgically trained volunteer we detected MEP in the ABP as far as 11 centimeters anterior to the vertex line, and 12 centimeters lateral to the interhemispheric line.

**Conclusions.** We observed in our subject a significantly more extended hand motor area compared to the known literature data. The exceptionally larger M1 area identified could be due not only to the increased use of the hand for fine motor actions, but also to prefrontal circuits linked directly to the motor area through extended training. Randomized controlled studies using large sample sizes are needed to confirm this hypothesis.

### Between acute coronary syndrome and subacute myocarditis - diagnostic and therapeutic decisions – a case report

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Corresponding Author: Mirela-Anca Stoia e-mail: mirelastoia@yahoo.com We present the case of a male patient, 71 years old, who came to ER, Emergency County Hospital Cluj-Napoca for anterior chest pain with the characteristics of myocardial ischemia, which started a few hours ago, disappeared in the emergency room and increased BP values. The repeated ECG did not reveal ischemic-lesional ST-T changes, and the echocardiography shows a normal size heart, with no alteration of global or regional parietal kinetics, preserved systolic function (natriuretic peptides within normal limits), without pericardial collection. The first troponin (Tn) value in emergency was normal, but the 2nd value was increased, the patient being hospitalized with unstable pectoral angina secondary to increased BP values. Optimal medical management included: sartan, calcium blocker, dual antiplatelet agents, statin, cardioselective beta blocker, nitrates, colchicine. During the first days of observation, although the patient had no longer angina, the Tn value increased (2 values>4000 pg/ ml) disproportionately compared to the normal values of creatine kinase (CK) and CK-MB isoenzyme. The patient mentions a recent episode of respiratory infection, treated with antibiotics and anti-inflammatory drugs. Suspicion of subacute myocarditis was raised in a patient who also presented major cardiovascular risk factors (male, age>70 years, HTN, hypercholesterolemia). Coronary angiography showed LAD II (left anterior descending coronary artery) sub-occlusion and 70% IVA III stenosis and there were resolved by angioplasty and implantation of 2 DES stents. The patient remained asymptomatic at discharge and at follow-up. The particularities of the case were related to the discrepancies between the clinical picture and the dynamics of the biomarkers of myocardial injury: first normal Tn, then exponentially increased (an aspect encountered more frequently in the context of subacute myocarditis), discordant with the absence of angina and the normal values of CK, CK-MB, compared to the unchanged electrocardiographic and echocardiographic appearance also, and respectively the severe IVA lesions, solved interventionaly.

### Management of heart failure in a frail patient with multiple comorbidities - a challenge beyond limits – case report

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We present the case of a male patient, 61 years old, who came to ER, Emergency County Hospital Cluj-Napoca with clinical manifestations of chronic aggravated and acute congestive heart failure, significant peripheral and visceral congestion and alteration of the general condition, with tachyarrhythmia and tendency to hypotension. The initial evaluation reveals increased values of biomarkers (atrial natriuretic peptides, troponin and d-dimers), anemia, alteration of liver and renal function tests. Echocardiography shows dilated cardiomyopathy, with a restrictive diastolic profile and altered systolic function, 1 year after biological valve prosthesis intervention for aortic bicuspid valve, replacement of the ascending aorta and multiple aorto-coronary bypass, in a poly-arterial patient with carotid endarterectomy and unilateral femoralpopliteal arterial bypass also. Although the initial chest radiology visualizes bilateral pleural collections, without pneumonia, the patient's management was difficult due to frailty and associated comorbidities along the way: bronchial and skin infection, aggravated anemia, hydration and electrolytes troubles, acute renal and additional liver functional alterations. The management was extremely complex, addressing the congestive and low flow cardiac output compensation, respectively the severe comorbidities, administering diuretics in triple combination (furosemide up to 280 mg iv, spironolactone, hydrochlorothiazide, mannitol), positive inotropic (dobutamine in renal doses), 2 stages of broad-spectrum antibiotics, MER transfusion, ferric carboxy-maltose. The patient was discharged compensated and stable after 25 days of hospitalization. The particularities of the case consist in the difficulty of compensating congestive and low flow cardiac output heart failure with complex comorbidities, that required associated and difficult treatments under strict monitoring, as well as the introduction with perseverance and success of innovative therapies to maintain cardiac compensation and increase survival and quality of life.

### Stem cells – an alternative therapeutic method for patients with knee osteoarthritis

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Corresponding Author: Titus Vari e-mail: titusvari@yahoo.com **Introduction.** Knee osteoarthritis is characterized by a progressive loss of cartilage, bone edema, subchondral bone sclerosis, synovitis and marginal osteophyte formation. Stem-cell therapy represents a novel direction regarding the nonsurgical treatment of knee osteoarthritis. Whereas bone marrow as a source of stem cells has been extensively studied for the treatment of knee osteoarthritis, human umbilical cord-derived stem cells as therapeutic agents for osteoarthritis of the knee are a relatively new source of study.

**Objective.** Assessing the efficacy of human umbilical cord-derived stem cells compared to those obtained from bone marrow in the treatment of patients diagnosed with knee osteoarthritis.

**Methods.** We searched the PubMed database to identify systematic review studies, published in the last three years, which analyzed the efficacy of stem-cell treatment for knee osteoarthritis and compared the efficacy of those obtained from human umbilical cord and bone marrow. The search mode was umbilical cord stem cells and (versus or comparison) and bone marrow stem cells and ("knee osteoarthritis" or "osteoarthritis of knee"). We found 6 eligible studies. After screening titles and abstracts, 3 studies were included in our analysis.

**Conclusion.** Stem-cell therapy, regardless of the site of harvest, showed significant improvement of both pain and function. Umbilical cords are considered medical waste, therefore an abundant supply of these types of cells exists. Compared to other sites, human umbilical cord-derived stem cells possess the advantage of having a higher proliferation and differentiation potential, as well as a higher production of type II collagen. Also, human umbilical cord-derived stem cells show higher chondrogenesis potential and lower lipogenic and osteogenic capacity. Additional well designed studies with a higher number of patients could bring this treatment method among those recommended by guidelines for the treatment of patients with osteoarthritis of the knee.

#### Clinical and imaging correlations of peripheral vascular anomalies

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Corresponding Author: Alexandru-Ronald Poeană e-mail: alexandruronaldpoeana@gmail.com **Introduction.** The objectives of this educational poster are: to highlight the importance of anamnesis and clinical examination in peripheral vascular anomalies detection, to stress the crucial role of radiology and imaging in vascular malformations diagnosis and describing their anatomy in detail and to exemplify the differential diagnosis of vascular anomalies with pathologies which have similar signs and symptoms.

**Material and methods.** We aim to present three particular cases with similar clinical findings, which include: low intensity pain of the forearm and hand, which is accentuated when the limb is positioned downwards and is not influenced by antiinflammatory medication; difference of skin color between hands, subtle engorgement of superficial veins of the affected limb and slight size difference of the hands.

These patients were diagnosed using radiology and imaging investigations such as: conventional radiography, 2D and Doppler ultrasonography, computed tomography

angiography and magnetic resonance angiography.

**Results.** By correlating information from clinical examinations with radiology investigations, the diagnoses of the patients were established. Two patients were diagnosed with vascular anomalies, one with venous malformation of the distal radial epiphysis and one with arteriovenous fistula of the median nerve. The diagnosis of the third case was thoracic outlet syndrome caused by the compression of scalene muscles.

**Conclusion.** Subtle clinical findings (engorgement of superficial veins, slight size or skin color difference between hands) are crucial in rising suspicion of a peripheral vascular anomaly. Radiology and imaging investigations are essential in establishing the diagnosis and describing the architecture of the vascular anomalous communications, but also in making differential diagnosis with pathologies which have similar signs and symptoms.

### An electrical storm hook the brain and the heart of a new born babycase presentation

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5) 2<sup>nd</sup> Medical Clinic Department, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Mutations in the KCNQ2 gene are associated with various phenotypes of neonatal epilepsy. We report a case of neonatal epileptic encephalopathy linked to KCNQ2, which also presents with ventricular extra systolic arrhythmia discovered incidentally.

Case Presentation. A newborn, 4 days old, second child, born via cesarean section from a physiologic pregnancy, weighing 3890 g, length 56 cm, Apgar score 8/9, artificially fed, with a family history of neonatal seizures in a 5-year-old sibling, presented to the pediatric emergency department in Cluj-Napoca for two episodes of tonic-clonic seizures involving the left hemibody, lasting <1 minute, with spontaneous resolution. Clinically, cardiac arrhythmia was detected, and electrocardiography revealed organized ventricular extrasystoles (trigeminy). Sleep EEG showed changes suggestive of benign neonatal seizures. Ambulatory ECG monitoring detected 35% organized ventricular extrasystoles and short episodes of unsupported ventricular tachycardia. Remission of seizure episodes was achieved under treatment with Phenobarbital 5mg/kg/day. Ventricular arrhythmia persisted despite oral Propranolol therapy and improved after introducing Flecainide therapy (10% arrhythmic burden). Considering the neurological symptoms and the association with the observed arrhythmia, genetic testing confirmed the presence of the KCNQ2 gene mutation (Potassium Voltage-Gated Channel Subfamily Q Member 2). With treatment, the arrhythmic burden reduced to less than 1% ventricular extrasystoles. Neurologically, the prognosis is reserved for the possible development of epileptic encephalopathy.

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# Heart failure: pitfalls in clinical assessment of non-congenital heart disease in pediatric patients. A five case-series presentation

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Corresponding Author: Alexandra Popa e-mail: alexindra.popa@gmail.com **Introduction.** In the pediatric population, the most common cause of heart failure (HF) is represented by congenital cardiac anomalies. The diagnosis of the underlying cause in HF can be delayed when clinicians focus on elements that overshadow the standard clinical picture.

**Material and method.** This observational, retrospective study includes a series of 5 cases recorded between 2018-2023 in the Pediatric Cardiology department, Cluj-Napoca.

**Results.** 1. Premature newborn, 34 weeks gestational age, presented with cyanosis, respiratory distress, and cardio-circulatory insufficiency. Suspicion of congenital heart malformation was ruled out; echocardiography revealed changes suggestive of a cerebral vascular malformation. Cerebral CT angiography confirmed the diagnosis of Galen vein aneurysm.

2. A 6-month-old infant was referred for evaluation of high blood pressure values and hepatomegaly. Coarctation of the aorta was ruled out through echocardiography. Left ventricular hypertrophy, coupled with hepatosplenomegaly detected by abdominal ultrasound, raised suspicion of Niemann-Pick disease, genetically confirmed.

3.A 7-year-old patient with a history of poorly controlled type 1 diabetes, was admitted for severe ketoacidosis and acute left pneumonia, shows unfavorable progression. Emphasis was placed on the respiratory etiology of the manifestations. Clinical and imaging findings led to the diagnosis of acute cor pulmonale. The patient later succumbed to angioinvasive mucormycosis.

4.A 15-year-old patient admitted for digestive complaints and suspected pancreatitis, experienced a syncope episode during which ventricular tachycardia was captured on the ECG, subsequently converted pharmacologically to sinus rhythm. Systolic dysfunction and tachycardiomyopathy, consequences of arrhythmia, were interpreted in the context of energy drink consumption.

5.A 5-year-old patient was admitted for evaluation of anemia. Clinical presentation: extreme pallor, tachycardia, and hepatomegaly. Echocardiography revealed dilated cardiomyopathy and reduced ejection fraction. Anamnestic and laboratory data allowed the diagnosis of HF secondary to iron-deficiency anemia triggered by excessive cow's milk consumption.

**Conclusion.** In daily practice, we often encounter clinical clues that are hidden at first glance when evaluating patients with HF, obscured by manifestations other than congenital cardiac causes.

### Trajectories of care model for pediatric patients with congenital heart disease from the family, nurse and general practitioner perspective

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**Introduction.** Congenital heart diseases (CHD) represent the most common cardiac pathology in newborns, infants, and young children. The survival of these patients correlates with substantial progress in the diagnosis and treatment of the condition.

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Corresponding Author: Alexandra Popa e-mail: alexindra.popa@gmail.com Families and primary healthcare providers are essential partners in recognizing and managing cases of these patients.

**Material and method.** An observational, retrospective study was conducted on 49 respondents who completed a specific questionnaire for their respective groups, as follows:

Group 1: Parents of 20 children with CHD under the care of the 1st Pediatrics Clinic, Pediatric Cardiology Department, Cluj-Napoca, between 2017-2021, randomly selected.

Group 2: 23 medical assistants from the Pediatric Cardiology departments (1st Pediatrics Clinic and Heart Institute, Cluj-Napoca, Cardiovascular Surgery section).

Group 3: 6 family doctors from Cluj County who have patients with CHD in their care.

**Results.** The suspicion of diagnosis, almost equally, was reported by medical staff in 45% of cases, and 55% by family members. 95% of patients seek specialized pediatric cardiologist care. Family doctors report the majority of presentations unrelated to cardiac pathology (67%). The need for psychological support among patients was observed by medical assistants in 100% of cases, while family doctors did not consider psychological intervention necessary in 67% of cases. 75% of cases do not have access to psychological support groups. The doctor-patient and doctor-nurse relationship is good in 65% of cases. 16% of family doctors report a deficient relationship with the pediatric cardiologist.

**Conclusion.** Pediatric congenital heart disease is a subject of growing interest concerning both the medical management of cases and their management in a non-medical environment and social integration. The study highlights a predominantly beneficial relationship between family members and specialist doctors, while it is slightly deficient between family members and family doctors. Regarding the relationship between family members and contributes to the improvement of the quality of life for patients with congenital heart diseases.

# Neonatal supraventricular tachycardia: clinical and therapeutic challenges

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Corresponding Author: Anamaria-Claudia Sitaru e-mail: dr.sitaruanamaria@gmail.com **Introduction.** Supraventricular tachycardia represents the most frequent arrhythmia in newborns. Despite this, it is difficult sometimes to diagnose it due to the fact there are no specific symptoms to recognize it. Signs and symptoms of cardiogenic shock can occur during a prolonged episode of tachycardia. Pharmacological management is frequently challenging in these patients.

**Material and methods.** In our center, we followed retrospectively the evolution of twelve infants diagnosed with supraventricular tachycardia.

**Results.** Out of twelve patients, nine were males and three were females. The first episode was diagnosed in the first three days of life in seven patients, whereas the other five were diagnosed during the first four weeks of life. None of these patients responded to vagal maneuvers. Sinus rhythm was successfully obtained by the use of Adenosine in three patients, the other antiarrhythmics used being Digoxine and Amiodarone. Four patients required administration of a second antiarrhythmic and only one needed triple therapy. Regarding prophylactic treatment, five patients were treated with only one antiarrhythmic such as Propranolol, Digoxine, and Amiodarone whereas six of them needed a combination of two antiarrhythmics, the most used being

Propranolol and Amiodarone. Throughout follow-up, four patients had no recurrence of supraventricular tachycardia under treatment, two of them had two recurrences in the first 24 h, four of them during the first weeks.

**Conclusions.** Supraventricular tachycardia is difficult to diagnose in newborn babies. Thus, most of them require immediate medical intervention due to the risk of becoming hemodynamically unstable. The most frequent mechanism is the reentrant mechanism via the accessory pathway. Pharmacological treatment is the most efficient. Recurrences after one year are rare.

### Metabolic risk factors outweigh sanitation-related risks as the primary health concern in Romanian rural Roma communities

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Corresponding Author: Dana Crișan e-mail: crisan.dc@elearn.umfcluj.ro **Introduction.** Romanian rural Roma communities are characterized by a high burden of poverty, limited access to resources, and a variable degree of social and cultural isolation. The current study aimed to assess the prevalence of environmentalrelated risk factors that are traditionally linked to poor health.

**Material and methods.** Field trips were organized to 25 rural Roma communities. At-risk behaviors (alcohol consumption, smoking, hypercaloric diet) were collected using a standardized questionnaire adapted to the cultural and educational norms of the target population. The health status of the patients was assessed using physical exams, blood pressure measurement, random blood glucose testing, stool collection for coproparasitological testing, and a portable ultrasound-based screening for hepatic steatosis.

**Results.** 253 patients were screened during the visits, with a median age of 49 years old. The rate of a stable professional occupation was 9.5%. The prevalence of parasitosis was 4.5%, the most common infection being Giardia Lamblia. The prevalence of smoking was 50.2%, at-risk alcohol consumption was encountered in 10.5% of the subjects, while 53.3% reported at-risk consumption of high-fructose beverages. Regarding the health-related outcomes, 77.6% of the patients were overweight, with a prevalence of morbid obesity of 17.3%. While 10.8% of the patients had previously documented type 2 diabetes, an additional 11.2% of the patients had a random glucose level >200 mg/dL. The prevalence of hepatic steatosis was 70.3%, while 21.3% of the patients had elevated blood pressure levels.

**Conclusion.** The study reveals that metabolic risk factors and associated conditions in rural Roma communities far surpass the burden of sanitation-related infectious diseases traditionally associated with poverty. The primary contributing factors are poor diet and the adoption of high-risk behaviors.

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### Glycated albumin and glycated hemoglobin in type 2 diabetes

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Corresponding Author: Dana Mihaela Ciobanu e-mail: danam\_b@yahoo.com **Introduction.** Type 2 diabetes is a long-term metabolic disorder characterized by insulin resistance and hyperglycaemia. Glycated hemoglobin (HbA1c) evaluates mean glycemia in the preceding 2-3 months and is the gold standard for assessing glycaemic control, while glycated albumin (GA) is considered a short-intermediate term glycaemic control marker since it reflects glycaemic status over the last 3 weeks.

**Material and methods.** We aimed to investigate the response and adherence to antidiabetic treatment based on prospective evaluation of both HbA1c and GA in type 2 diabetes patients (n=28) randomly selected from Clinical Centre of Diabetes, Emergency Clinical County Hospital, Cluj-Napoca, Romania.

**Results.** HbA1c and GA levels were measured at days 21 and 90 from the first visit. We found that 11 out of 28 patients had a good HbA1c decrease (< -0.5%), being confirmed as good responders at day 90 for both GA and HbA1c. In addition, our data showed that 9 out of 11 patients could be addressed as good responders by GA at day 21, suggesting that GA at day 21 predicted HbA1c results at day 90. Changes in GA measured from initial visit and days 21 and 90, respectively, significantly correlated with changes in HbA1c measured at initial visit and days 21 and 90, respectively (p<0.001). These correlations confirm that GA is an indicator of protein glycation as good as HbA1c.

**Conclusion.** Compared to HbA1c, GA might be a more reliable glycaemic control marker in early estimating the effectiveness of ongoing antidiabetic treatment since changes in GA occurring 21 days could predict the change in HbA1c expected 3 months later.

Acknowledgement. The measurement of glycated albumin was funded by Medist S.A, Romania.

### Autoimmunity in children: a case of autoimmune hepatitis with sclerosing cholangitis, ulcerative colitis and autoimmune hypothyroidism

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Corresponding Author: Alina Grama e-mail: gramaalina16@yahoo.com **Introduction.** The association of several immune diseases has been frequently reported in the literature. The overlap syndrome of autoimmune hepatitis (AIH) with autoimmune sclerosing cholangitis (ASC) is often met. Extra-hepatic immunemediated disorders such as ulcerative colitis (UC), celiac disease, or autoimmune hypothyroidism in children with autoimmune liver disease might also be possible. Three or more concurrent autoimmune diseases are rare.

**Case report.** We describe the case of a 13-year-old girl known in our service with AIH and overlap syndrome with ASC from the age of 10. The diagnosis was based on the clinical aspects (asthenia and jaundice) and the laboratory studies (high transaminases and GGT, high IgG, and positive anti-neutrophil cytoplasmatic and anti-nuclear antibodies). Her evolution was undulant toward liver cirrhosis. Two years after



diagnosis, the patient was hospitalized for fever, aphthous stomatitis, diarrhea with Bristol type 4-5 stools, and lower gastrointestinal bleeding. The laboratory studies revealed an important inflammatory syndrome and a poor evolution of AIH despite the therapy with prednisone, azathioprine, and ursodeoxycholic acid. Based on the colonoscopic aspect and the biopsy, the diagnosis of UC E4S0, Mayo score 1 was established. At that moment, thyroid function tests were also abnormal, with normal thyroid stimulating hormone, low thyroxin levels, and positive anti-thyroid peroxidase antibodies, which suggested autoimmune hypothyroidism. In contrast with the favorable evolution of UC on 5-aminosalicylic acid, an increasing stage of treatment for AIH was necessary. Upper digestive hemorrhage as an adverse reaction to mesalazine and unfavorable evolution of AIH required multiple changes in immunosuppressive medication. The remission of the inflammatory processes was obtained with biological therapy with infliximab.

**Conclusion.** Concurrent autoimmune diseases are common in AIH, but the presence of two or more autoimmune diseases makes the patients' management more difficult. The screening of autoimmune diseases must be done regularly in patients with AIH.

# **Congenital thrombocytopenia - differential diagnosis of thrombocytopenia in pediatrics**

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Corresponding Author: Cristina-Mihaela Bujor e-mail: ella\_sirbu@yahoo.com **Introduction.** Although very rare, congenital thrombocytopenia must be part of the differential diagnosis for children with isolated thrombocytopenia. This is a genetical disorder, therefore proper and early genetic diagnosis is essential for the treatment.

**Case report.** We report the case of a 1 year and 11 months old boy with recurrent episodes of epistaxis and cutaneous hemorrhagic syndrome. Following hematological investigations and bone marrow aspiration, he was diagnosed with immune thrombocytopenia (ITP) and underwent multiple treatment attempts with corticosteroids and immunoglobulins. Regardless of the treatment used he only had transitory responses, with relapses after several days. After approximately 2 years, treatment with thrombopoietin receptor agonist (Romiplostin) was initiated, with favorable evolution. At this point, congenital thrombocytopenia was suspected, because of the microplatelets that were observed on the peripheral blood smear. Therefore the patient was genetically evaluated by sequence analysis, and a pathogenic WAS gene variant was detected. Given the positive response to Romiplostin, the patient remained under this treatment, which was approved by the ANMDM.

**Conclusion.** Early recognition of congenital thrombocytopenia might often be difficult, many patients being misdiagnosed as ITP and treated consequently, but is of great importance for future monitoring and therapeutical options in these patients.

# Frequency of chromosomal abnormalities in malignant hemopathies. Retrospective study

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Corresponding Author: Mariela Sanda Militaru e-mail: dr.mariela.militaru@gmail.com **Introduction.** Malignant hemopathies represent a heterogeneous group of clonal hematological neoplasms that includes myeloproliferative syndromes, lymphoproliferative syndromes, acute leukemias and myelodysplastic syndromes. The American Cancer Society estimates that in the United States in 2023 there will be about 61,000 new cases of leukemia (of all types) in adults and children and about 24,000 deaths.

**Methods.** The current study was carried out between January 2020 and May 2023 on a number of 1492 samples from the marrow. The genetic techniques used for the analysis of these samples were: karyotyping techniques with G bands and molecular biology techniques (PCR and RT-PCR).

**Results.** 727 marrow samples were karyotyped identifying 251 chromosomal abnormalities representing 35.3%. The distribution of chromosomal anomalies was as follows: numerical anomalies 64%, structural anomalies 25% and complex anomalies 11%. The Philadelphia chromosome was identified in 28% of the cases. Molecular biology tests were performed on 765 marrow samples, and abnormal results were identified in 117 cases representing 15%. The most common gene fusion was BCR-ABL p210 in about 69 cases.

**Conclusions.** Genetic tests are useful in malignant hemopathies for diagnosis, for establishing prognosis and for monitoring treatment. Karyotype remains the basic technique in the evaluation of malignant hemopathies.

# Hereditary breast cancer in Romania - molecular particularities and genetic counseling challenges in an Eastern European country

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 Breast Cancer Tumour Center, "I. Chiricuță" Institute of Oncology, Cluj-Napoca, Romania

 Medical Genetics, University of Medicine and Pharmacy "Victor Babes", Timişoara, Romania In Romania, breast cancer (BC) is the most common malignancy in women. However, there is limited data on the prevalence of predisposing germline mutations in the population in the era of precision medicine, where molecular testing has become an indispensable tool in cancer diagnosis, prognosis, and therapeutics. Therefore, we conducted a retrospective study to determine the prevalence, mutational spectrum, and histopathological prediction factors for hereditary breast cancer (HBC) in Romania.

A cohort of 411 women diagnosed with BC selected upon NCCN v.1.2020 guidelines underwent an 84-gene NGS-based panel testing for breast cancer risk assessment during 2018–2022 in the Department of Oncogenetics of the Oncological Institute of Cluj-Napoca, Romania.

A total of 135 (33%) patients presented pathogenic mutations in 19 genes. The prevalence of genetic variants was determined, and demographic and clinicopathological



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Corresponding Author: Andreea Cătană e-mail: catanaandreea@gmail.com characteristics were analyzed. We observed differences among BRCA and non-BRCA carriers regarding family history of cancer, age of onset, and histopathological subtypes. Triple-negative (TN) tumors were more often BRCA1positive, unlike BRCA2 positive tumors, which were more often the Luminal B subtype. The most frequent non-BRCA mutations were found in CHEK2, ATM, and PALB2, and several recurrent variants were identified for each gene.

Unlike other European countries, germline testing for HBC is still limited due to the high costs and is not covered by the National Health System (NSH), thus leading to significant discrepancies related to the screening and prophylaxis of cancer.

# Indicators of impact of a diabetic neuropathy awareness campaign

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Corresponding Author: Cornelia Bala e-mail: corneliabala@gmail.com **Introduction.** Diabetic neuropathy (DN) is one of the most common chronic complications of diabetes. Considering that approximately 50% of patients affected by DN are asymptomatic, the degree of awareness of this complication is low, which can lead to serious consequences. The "Stand up for your feet!" initiative was a hybrid-digital and carried out through medical offices and pharmacies- information and awareness campaign. The objective of the research is to evaluate the results of this awareness campaign.

**Material and methods.** The target population of this study was people with diabetes with/without DN and people caring for a person with diabetes who were interviewed by a specialist company using a structured questionnaire. This report presents data obtained from interviews collected from people with diabetes either face-to-face or by telephone.

**Results.** 760 people with diabetes were interviewed, with a mean age of 69.5 years, 52% women. Only 20% have heard of DN, while only 21% report the absence of any symptoms suggestive of neuropathy. The most commonly reported symptoms are tingling (61%), with 54% attributing these symptoms to DN. When looking for information about specific symptoms, patients turn mainly to the doctor (>90%), pharmacists (24-36%) and the Internet (23-37%) being rather secondary sources of information.

Regarding foot care behaviors, those with diabetes or DN do the bare minimum wearing proper shoes, trimming nails, and not protecting feet from cold temperatures. 50% go to the doctor to check their feet, while self-examination is not an option for 1 in 5 sufferers. Media consumption is mostly represented by TV (97%), the use of the Internet being less frequent and limited to social networks and YouTube. 26% of respondents recognized the campaign logo, and 10% were able to identify the name of the campaign. 77% of respondents said they liked the campaign, 65% that it was credible and informative, and 50% that they would recommend it to others, Of all the materials used in the campaign, "The 10 Commandments" had the greatest impact, followed by the advertorial and the calendar.

**Conclusions.** The campaign was visible more in the doctor's office and it was credible and informative but had a rather limited impact on motivating patients to have a conversation with the doctor about symptoms.

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### Subdural empyema - a rare complication of frontal sinusitis

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Corresponding Author: Alina Grama e-mail: gramaalina16@yahoo.com **Introduction.** Subdural empyema is the most common intracranial complication of sinus origin, consisting of a purulent collection between the dura mater and the arachnoid. Often represents a neurosurgical emergency, which, if not recognized in time, can lead to serious neurological sequelae. It has a predilect origin at the level of the frontal sinus and occurs most frequently in boys between 7 and 18 years of age.

**Case presentation.** We present the case of a 15-year-old boy who presented with fever, vomiting, and abdominal pain. Clinically, the patient presented affected general condition, hypotension, and tachycardia. At the right frontal level, an area of fluctuating and painful edema was noted without meningeal clinical signs. From the history, we noted a dental abscess that was not adequately treated. A significant inflammatory syndrome was detected. The diagnosis of sepsis with sinus/possible intracerebral starting point was made, and volume resuscitation and empiric intravenous antibiotic therapy with meropenem were initiated. Brain MRI was performed, which revealed acute maxillary and right frontal sinusitis with the appearance of epi- and subdural empyema. The case management was carried out in a multidisciplinary team (pediatrics, neurosurgery, ENT, and BMF) with a slow favorable subsequent evolution after antibiotic therapy, drainage of the epicranial empyema, endoscopic surgery of the sinuses, and cleaning of dental foci.

**Conclusions.** The presented case aims to highlight the preventable nature of CNS infections due to odontogenic causes within regulated oral health programs, possibly carried out at the level of educational institutions. One of the particularities of the case is the rapid diagnosis and the favorable evolution, even if most patients have an unfavorable prognosis, especially neurologically.

#### **BalneoMap** - The digital map of balnear resources

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Corresponding Author: Gabriela Bombonica Dogaru e-mail: dogarugabrielaumf@gmail.com **Introduction.** Romania has a great variety of natural resources in the balnear resorts in our country and their value is redeemed through prevention and medical rehabilitation programmes in chronic diseases. A part of these resources have been assessed and studied in the course of time regarding their mineralogical, physicochemical, microbiological and pharmacodynamic properties. The upgrade of the treatment installations in the balnear resorts and the entering of new medical rehabilitation technologies require the identification of new appropriate competences and digital solutions in balneology.

**Material and methods.** A unique digital monograph was developed for an improved function and quality of the updated information in the teaching activity (students, medical residents, graduate students). It is called BalneoMap and it is a digital interactive map of the balnear resources, with easy and free access. The localities with balnear potential, natural resources (mineral waters, lakes, mofettes, muds, salines) and their composition, indications and contraindications are accounted on this platform.

**Results.** The moment, 121 localities and 500 balnear spots are added on this digital map, but this is a constantly growing project (balneomap.ro)

**Conclusion.** The purposes of this platform are educational, informational and to stimulate the research activity of these natural resources, which contribute to the rebuilt of the balnear culture, but also to empower balneology as a field of excellence.

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### What are the barriers stopping patients to tell their family doctor that they think they have cancer? - the study of the Örenäs group in Cluj

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Corresponding Author: Aida Puia e-mail: draidapuia@gmail.com In September 2023, the Orenas group, a prominent member of the EGPRN, met in Cluj for a three-day workshop, the members of the family medicine discipline and resident colleagues in this specialty being the hosts of the event supported by our University, the Association of Family Physicians and the College of Physicians Cluj. The group's interest is mainly focused on the early diagnosis of cancer in primary care, an interest embodied in numerous specialist publications. Membership of a European working group opens up opportunities for valuable medical practices.

More than 30 participants, 25 from 14 European countries and 7 members of the Romanian group formulated a current research theme in primary care related to the perception and fears of patients when it comes to cancer.

The research question posed was "What are the barriers stopping patients to tell their GP that they think they have cancer?" and a study protocol began to take shape. We want to develop a European primary care/family practice survey of patients who have/had and ask an open question "When did you first see your GP with your cancer symptoms, did they - did you tell them about your concerns? Why/why not?" The data obtained will be analyzed through thematic analysis by coding the qualitative data and by iterative comparison with the information obtained about barriers to cancer communication in family medicine. What we could find is the lack of awareness of ,,red flag" symptoms, prejudices related to the fear of cancer, fatalism, and stigma related to cancer, some bad experiences of cancer in family members, limited involvement of the family doctor in the diagnosis of oncological diseases, social media misinformation.

We hope that our study confirms the importance of knowing the barriers in communicating concerns about a possible oncological pathology, as an important factor in improving the early diagnosis of cancer in primary care.

#### Flurona: the first autopsied case

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**Introduction.** COVID-19-associated coinfections increase the patient's risk of developing a severe form of the disease and, consequently, the risk of death. The term

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Corresponding Author: Bogdan Alexandru Gheban e-mail: ghebanbogdan@yahoo.com "flurona" was proposed to describe the coinfection of the influenza virus and SARS-CoV-2.

**Case Report.** This report is about a case of a 7-month-old female infant who died due to flurona coinfection.

**Results.** A histopathological exam showed activation of microglia (becoming CD45 positive), bronchial inflammation, diffuse alveolar damage in proliferative phase with vasculitis, a peribronchial infiltrate that was predominantly CD20-positive, and a vascular wall infiltrate that was predominantly CD3-positive.

**Conclusion.** The aggressiveness of the two respiratory viruses added up and they caused extensive lung inflammation, which led to respiratory failure, multiple organ failure, and death. Tissues injuries caused by both the influenza virus and SARS-CoV-2 could be observed, without the ability to certify the dominance of the aggression of one of the two viruses.

# The importance of a correct differential diagnosis of liver steatotic disease in children: a case report

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 2<sup>nd</sup> Pediatric Clinic, Emergency Clinical Hospital for Children Cluj-Napoca, Romania **Introduction.** Steatotic liver disease (SLD) is a common chronic liver condition with an increasing incidence in the pediatric population in the last decade. Usually a hallmark feature of insulin resistance and dyslipidemia, hepatic steatosis can also be indicative of a wide range of conditions, including Wilson's disease (WD) or other rare inborn errors of metabolism, autoimmune liver disease, viral hepatitis, alpha-1-antitrypsin deficiency or celiac disease. Neither of these conditions should be missed



#### Annual Meeting Iuliu Hațieganu University of Medicine and Pharmacy 2023

Corresponding Author: Alina Grama e-mail: gramaalina16@yahoo.com from the differential diagnosis of SLD.

**Case report.** We present the case of a 6-year-old male patient with no prior history of liver disease who was admitted for abnormal liver function tests with a normal lipid profile. Subsequent laboratory tests ruled out a viral or autoimmune hepatitis. The abdominal ultrasound detected hepatic steatosis, which prompted further investigations. Additional laboratory tests revealed low serum ceruloplasmin (10.6 mg/dL) with high 24-hour urinary copper excretion (272  $\mu$ g/24h), suggestive for WD. Genetic testing was performed. The liver elastography indicated no fibrosis (Liver Stiffness Measurement 3.3 kPa corresponding to F0 Metavir) with a CAP score of 281 dB/m, suggesting severe steatosis. Administration of d-penicillamine resulted in progressive improvement of the liver function tests.

**Conclusion.** Hepatic steatosis in children can be the mask of a variety of chronic liver diseases, with particular treatments and distinct prognostic ramifications. In most conditions, the progression to cirrhosis can be prevented by early diagnosis and suitable therapy. A thorough evaluation of all these diseases is required to have a correct diagnosis in children with SLD, even if there are features of metabolic syndrome.

### Can the symptoms and gender of the patient identify the form of paroxysmal supraventricular tachycardia: AVRT versus AVNRT?

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Corresponding Author: Diana Andrada Irimie e-mail: gurzaudiana@yahoo.com **Introduction.** Paroxysmal supraventricular tachycardia (PSVT) is one of the most common supraventricular arrhythmias with a fast, regular rhythm, characterized by the sudden onset and end of the arrhythmia. Depending on the electrophysiological mechanism, it is divided into 2 subtypes: atrioventricular reentrant tachycardia (AVRT) and atrioventricular nodal reentrant tachycardia (AVNRT). Establishing the subtype is essential for the electrophysiologist in order to perform the ablation procedure, which is the gold standard treatment. The differential diagnosis can be made based on the resting ECG by analyzing the RP interval, but most of the time, the P wave is not visible on the ECG, an aspect that practically makes it impossible to establish the tachycardia subtype before performing the electrophysiological study (EPS). The purpose of the current study is to identify if other factors, such as the patient's symptoms or gender, can be correlated with the subtype of PSVT.

**Material and method.** 103 patients diagnosed with PSVT were included in the study, of which 67 (65%) were women, admitted to the Cardiology Department of the Clinical Rehabilitation Hospital, during 2021-2022. All patients included, underwent an EPS (through which the form of the supraventricular arrhythmia was determined: AVRT or AVNRT) and later radiofrequency ablation. The patients were divided into two groups according to sex.

**Results.** Regarding the main characteristics of the patients included in the study, no significant differences were recorded related to the presence of comorbidities, such as hypertension, diabetes, obesity etc. Biologically, a statistically significantly lower value of HDL cholesterol ( $48 \pm 9.9$  vs  $45 \pm 9.3$ , p=0.0112) and significantly higher triglycerides

 $(107.5\pm69.8 \text{ vs } 145.5\pm67.5, p=0.0499)$  was observed in men, while the value of ESR  $(12.10\pm13.1$ vs  $6.56\pm8.4$ , p= 0.0023) was higher in women. From the point of view of the symptomatology given by the tachycardia episodes, symptoms such as: palpitations (65.67% vs 77.77%), dyspnea (10.44% vs 11.11%), dizziness (2.98% vs 5.55%), fatigue (13.43% vs 8.33%) or syncope (7.46% vs 2.77%), there were no significant differences between the two groups. At the same time, the mode of onset and termination of tachycardia, the response to the Valsalva maneuver or Adenosine administration, the duration of symptoms or the frequency of PSVT episodes, did not show significant differences between the two groups. However, when we correlated the type of PSVT with the gender of the patient, we observed a predominance of AVNRT arrhythmia in women (64.5%), especially the typical form, but also the AVRT arrhythmia (5 women vs 2 men). Also, when we correlated the patient's gender with the symptoms and the type of PSVT, we observed a statistically significant association between the presence of syncope (p-0.0491) and fatigue (p-0.038) and the AVNRT form in males. Dizziness was statistically correlated with the AVRT form (p-0.0128), but in the entire study population, and not according to gender. Although palpitations are the most common and frequent symptom in patients with PSVT, this was not correlated with gender or form of tachycardia.

**Conclusion.** The form of supraventricular arrhythmia: AVRT versus AVNRT, is often difficult to differentiate based on clinical or paraclinical elements, but female gender seems to be a predictor of the AVNRT arrhythmia. At the same time, the presence of syncope and fatigue in men can be highly suggestive of the AVNRT form in them, while dizziness is correlated with the AVRT arrhythmia. Of course, although gender and symptoms can be suggestive for the type of arrhythmia, only the electrophysiological study can establish with certainty the form of the PSVT.

#### Factors that raise concerns after implantable cardioverterdefibrillator placement

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Corresponding Author: Dana Pop e-mail: pop67dana@gmail.com **Introduction.** Implantable cardioverter-defibrillator (ICD), has saved countless lives through prompt cessation of the life-threatening arrhythmias. Despite these benefits, there are some potential complications of the device implantation or of its inappropriate functioning.

The study aimed to assess the ICD related complications in a single center along a given time period and to identify possible correlations with the patient's comorbidities and treatment.

**Material and methods.** 60 consecutive ICD - implanted patients between 2016 and 2018 in Clinical Rehabilitation Hospital were followed up along a mean period of 5.5 years; the device related complication were counted and possible risk factors were assessed. The data regarding the implantation procedure and early complications was collected from the implantation registry and from the hospitalization files of the patients. The follow-up data was obtained from the device interrogation reports and from the clinical assessment.

**Results.** The study population consisted of 15 female (25%) and 45 male (75%) with a mean age of 61.2 years. The ICD was implanted for secondary prevention in 38 patients (63%) and for dilative cardiomyopathy in 25 patients (41.6%) among which 19

patients (31.6%) with ischemic heart disease. The complications occurred as following: device infection - 2 patients (3.3%), lead failure - 3 patients (5%), small pericardial effusion - 6 patients (10%), inappropriate shocks - 9 patients (15%). Device infection was correlated with diabetes mellitus and age and inappropriate shocks with atrial fibrillation. During the follow-up period a number of 16 patients died (26.6%). This was more prevalent among secondary prevention (44%) and decreased LVEF subgroups (36.3%).

**Conclusion.** During a 5.5 years follow up period, there were a decreased prevalence of complications related to ICD implantation, these were more prevalent in old patients, in those with diabetes and with atrial fibrillation.

#### The relationship between atrial fibrillation and diabetes mellitus

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Corresponding Author: Dana Pop e-mail: pop67dana@gmail.com **Introduction.** Patients with atrial fibrillation and diabetes mellitus (DM) often bear a greater burden of complications and experience a worse quality of life than those with the arrhythmia alone. The aim of the study is to investigate the impact of diabetes on the burden of atrial fibrillation, both silent and symptomatic.

**Material and methods.** A cohort consisting in 103 pacemaker careers were taken into account. The data was collected from the pacemaker implant registry and hospitalization files from Clinical Rehabilitation Hospital-Cardiology Department. A matching process created two groups of 19 patients each, with and without DM respectively, with a similar risk factor profile and comorbidities (NYHA Class, ischemic heart disease, hypertension, moderate or severe valve regurgitation, chronic kidney disease, COPD). The two groups were compared in terms of atrial fibrillation burden.

**Results.** The study population consisted of 37 female (36%) and 66 male (64%) with a mean age of 73 years.

The mean burden of atrial fibrillation in the non DM group was 13.05% (95% CI, 8.37-17.74) compared to 18.42% (95% CI, 12.18-24.67) in the DM group. The difference - 5.37% - was statistically significant (p=0.045). The prevalence of silent atrial fibrillation in the DM grup was 29% compared to 7% in the non-DM group (p=0.012).

**Conclusion.** Patients with diabetes have a greater burden of atrial fibrillation and are more likely to have silent atrial fibrillation episodes.

### **Overview of the clinical experience in primary immunodeficiencies at the Allergy and Clinical Immunology Department during 2022-2023**

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**Introduction.** Primary immunodeficiency disorders (PID) or inborn errors of immunity (IEI) encompass a heterogeneous group of conditions characterized by the deficient or absent function in one or more components of the immune system. These

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Corresponding Author: Irena Pintea e-mail: irennedelea@gmail.com conditions predispose individuals to frequent and severe infections, autoimmunity, alterations in immune homeostasis, autoinflammatory diseases, lymphoproliferative diseases, neoplasias, and bone marrow failure.

It is estimated that over 6 million individuals worldwide have PID, with 70-90% of the cases still undiagnosed. Moreover, this group of disorders has a current median delay of diagnosis between 6 and 9 years. Early diagnosis and treatment of PID has been associated with improved patient outcomes.

For unelucidated reasons, more than 50% of all IEIs are associated with abnormalities in humoral immunity, making antibody deficiency the most common PID in both adults and children. Common variable immunodeficiency (CVID) is an umbrella name for the most common symptomatic primary antibody deficiency, estimated to occur in approximately 1 in 25,000. CVID results from impaired B cell differentiation that leads to defective immunoglobulin production. Clinical phenotype is heterogeneous and includes recurrent infections, chronic lung disease, gastrointestinal disease, autoimmunity, and malignancy.

**Material and methods.** In this paper, the authors aim to summarize the clinical experience of the Immunology and Allergy Discipline of the "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania. This is a retrospective overview of patients with Primary Immunodeficiency in our care included in the National Program of Rare Diseases, Immunoglobulin replacement therapy, between 2022 and 2023.

**Results.** A number of 77 patients aged 20-80 years old (median age of 54.46) were in our evidence in the 2022-2023 timeframe. The median age of clinical onset was 34.34 (3-45), while the median age at the time of the diagnosis was 48.06 (11-69), showing a diagnostic delay of 13.38 years (age range of 1-50). Most patients are females (n=49, 64 %) with 28 male patients (36 %). Most patients are diagnosed with CVID (n=65), followed by hereditary angioedema types I and II (n=11), selective IgG deficiency (n=6), hyperIgM (n=1), Job's syndrome (n=1), Kabuki type II (n=1), Muckle-Wells syndrome (n=1), undefined primary immunodeficiency (n=2). In patients with predominantly antibody deficiency (n=72) most patients had the clinical phenotype of infections with non-infectious complications (n=53), which included autoimmunity, lymphoproliferation including persistent splenomegaly and lymphadenopathy and atopy, allergic asthma and rhinitis, pulmonary fibrosis, gastrointestinal nodular lymphoid hyperplasia and malignancy (solid organ and haematological disease, mostly lymphomas). With regards to the infectious complications, most patients experienced recurrent infections of the upper and lower respiratory tract, followed by gastrointestinal infections and of other sites (osteomyelitis, arthritis, meningoencephalitis, endocarditis, skin, urinary tract). Severe COVID-19 disease was seen in two of the patients, with no lethal cases. Genetic testing for Primary Immunodeficiency panel (407 genes), performed with the support of the Jeffrey Modell Foundation, SUA, was useful in 3 (21% of the tested patients). With regards to the treatment, patients received intravenous immunoglobulins (n=11, 14%), subcutaneous immunoglobulins (n=31, 40%), facilitated subcutaneous immunoglobulin (n=30, 39%), while the remaining 5 patients (6%) were monitored and they did not require immunoglobulin replacement treatment.

**Conclusions.** PIDs remain largely undiagnosed, and a delay in treatment exponentially increases the risk of complications. Life-long treatment with immunoglobulin replacement is required in humoral PIDs to reduce the search for PIDs in cases with a high index of suspicion.

#### A rare case of glycogenosis type VI

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Corresponding Author: Alina Grama e-mail: gramaalina16@yahoo.com **Introduction.** Glycogen storage disease type VI (Hers Disease) is caused by a deficiency in hepatic glycogen phosphorylase, resulting in glycogen excess storage. The onset is usually during early childhood, with hepatomegaly, increased transaminases, hypoglycemia, and hyperlipidemia. The disease evolution is less severe than in other types of glycogen storage disease.

**Case report.** A 2-year-old girl without significant medical history was initially admitted for increased transaminases levels. Physical examination revealed mild growth retardation, "dolly face", and hepatomegaly. Laboratory data revealed high transaminases (ASAT 1471 UI/l, ALAT 1474 UI/l), hyperlipidemia (cholesterol 394 mg/dl, triglycerides 215 mg/dl) and fasting hypoglycemia (34 g/dl). The abdominal ultrasound showed hepatomegaly and steatosis. Due to the association of hypoglycemia, dyslipidemia, and hepatomegaly, we considered fatty-acid oxidation disorder or glycogen storage disease as a possible diagnosis. Genetic testing confirmed the diagnosis of type VI glycogen storage disease as a compound heterozygous status of variants of the PYGL gene: c.1726C>T, p.(ARG576\*) / c385\_386delinsCT, p.(Asp129Leu). We recommended a specific diet (eating frequent meals, using extended-release cornstarch and complex carbohydrates with slow absorption). The evolution was favorable, with normal growth, normal serum levels of transaminases, and a good control of glycemia.

**Conclusions.** This case report underlines the importance of early diagnosis of storage disorders in children, including genetic tests and proper management to decrease the incidence of hypoglycemia-associated complications and prevent chronic hepatopathy.

### Efficacy of Levetiracetam monotherapy in controlling sleep and awake epileptic seizures – a case report

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3) "RoNeuro" Institute for Neurological Research and Diagnostic, Cluj-Napoca, Romania **Introduction.** Epileptic seizures can manifest during both sleep and waking states, with some generalized seizures having a focal origin and subsequently spreading bilaterally. Proper evaluation of epilepsy in such cases should begin with an awake EEG and a brain MRI with contrast, complemented by a sleep EEG examination.

**Case report.** A 29-year-old woman sought medical attention in May 2019. She had experienced five tonic-clonic seizures between August 2018 and May 2019, three occurring during sleep. After the third episode, the anticonvulsant therapy with Levetiracetam (500 mg, twice daily) was initiated. The two waking state seizures were characterized by brief tonic mouth contractions and a 20-minute postictal confusion. The first waking state seizure followed voluntary treatment withdrawal, alcohol consumption, and sleep deprivation, while the second occurred after consuming cola and coffee.

An initial brain CT scan with contrast in October 2018 suggested an M1 segment aneurysm in the right middle cerebral artery. A subsequent Brain MRI Angiography 4) Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

Corresponding Author: Livia Livinț Popa e-mail: livintz@yahoo.com with contrast in June 2019 determined that the pseudoaneurysm was actually the origin of a cortical blood vessel, and there was a small hypoplasia of the right hippocampus.

Two awake EEG examinations conducted in August 2018 and May 2019 revealed low-voltage alpha and beta rhythms without epileptiform activity. The sleep EEG performed in May 2019 detected interictal epileptiform discharges in the left frontal and temporal areas during the N2 stage of NREM sleep, indicative of a left frontotemporal epileptic focus.

The patient's Levetiracetam dosage was gradually increased to 1000 mg twice daily, with no further recurrence of epileptic manifestations reported.

**Conclusion.** Frontotemporal focal epilepsy (most likely responsible for focal seizures with rapid secondary generalization) can be identified through EEG sleep examination and may respond well to a single antiepileptic drug when administered at an appropriate dosage.

### Higher functional connectivity metrics in alpha band of traumatic brain injury patients treated with Cerebrolysin and rTMS - the CAPTAIN-rTMS randomized controlled trial

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Corresponding Author: Livia Livinț Popa e-mail: livintz@yahoo.com **Introduction.** Quantitative encephalography (QEEG) is a non-invasive method of objectively measuring brain electrical activity data. We analyzed the differences in weighted Phase Lag Index (wPLI) averaged across pairs of electrodes from specific brain zones in a subset of patients with traumatic brain injury (TBI) from the CAPTAIN-rTMS randomized controlled trial.

**Material and methods.** 50 patients assigned to three groups (Cerebrolysin - CRB+rTMS; CRB+sham; placebo - PLC+sham) underwent two 32-electrodes EEG recordings, at 30, respectively 180 days post TBI. QEEG features were computed with Brainstorm, and data aggregation and statistical analysis were done using a custom platform using R. QEEG features, from each visit, as well as their corresponding differences across visits, were analyzed.

**Results.** We found statistically significant differences between groups in the alpha-band wPLI averages corresponding to all possible pairs of electrodes, values at the last visit being significantly higher in the CRB-rTMS group than both CRB-sham (p=0.002, Cohen's  $\delta$ =0.642) and PLC-sham (p=0.018,  $\delta$ =0.467). This was also true for pairs of electrodes from the same hemisphere (p=0.001,  $\delta$ =0.65 respectively p=0.02,  $\delta$ =0.461), as well as for mirrored pairs of electrodes (p=0.015,  $\delta$ =0.508 respectively p=0.044,  $\delta$ =0.401). Differences were higher in the frontal (p<0.001  $\delta$ =0.675, p=0.018  $\delta$ =0.467) and parietal (p<0.001  $\delta$ =0.7, p=0.008  $\delta$ =0.52) rather than central (p=0.002  $\delta$ =0.642, p=0.024  $\delta$ =0.447), temporal (p=0.012  $\delta$ =0.525, p=0.008  $\delta$ =0.52) or occipital (p=0.892  $\delta$ =0.033, p=0.545  $\delta$ =0.125) electrode pairs.

**Conclusion.** Cerebrolysin and rTMS have a synergic effect on maintaining physiological electrical brain activity synchronicity. This effect is most visible in the frontal and parietal lobes.

# Primary and secondary prophylaxis of ischemic stroke in patients with diabetes mellitus and atrial fibrillation

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Corresponding Author: Livia Livinț Popa e-mail: livintz@yahoo.com **Introduction.** Stroke is a leading cause of global disability and the fourth leading cause of death, with 85% of cases preventable by managing risk factors like diabetes mellitus (DM) and atrial fibrillation (AF).

**Method.** We reviewed the literature on stroke mechanisms in diabetic patients, the link between type 2 diabetes and atrial fibrillation, and prevention strategies, along with a case presentation.

**Results.** Both DM and AF contribute to ischemic stroke through factors like coagulation system activation, reduced fibrinolysis, and endothelial dysfunction. DM patients face twice the risk of ischemic stroke, whereas AF increases stroke risk fivefold and doubles mortality, especially in cases of embolic strokes.

The pathophysiology of AF in DM involves complex structural, electrical, electromechanical, and autonomic remodeling.

Blood glucose-lowering therapies have varying effects on AF risk, with Metformin and Thiazolidinediones reducing risk, while insulin increases it.

In analyzing Phase III trials comparing direct oral anticoagulants (DOACs) and Warfarin, we found that DOACs generally performed similarly, regardless of diabetes status. However, DM patients on DOACs experienced a 20% reduction in stroke and systemic embolic events, a 43% decrease in intracranial bleeding, and a 17% reduction in cardiovascular death compared to Warfarin. Notably, DM presence in Warfarin users correlated with a narrower therapeutic range, potentially reducing safety and efficacy.

**Recommendations.** DM patients with a CHA2DS2-VASc score of 2 should consider DOACs over Warfarin. For AF patients with DM and a CHA2DS2-VASc score of 1, the need for oral anticoagulation is uncertain.

**Conclusion.** Diabetic patients require multidisciplinary care, and specific oral antidiabetic drugs can reduce AF risk. Screening for diabetes in AF patients is vital for appropriate anticoagulation therapy, as diabetes is a key factor in CHA2DS2-VASc risk scores for stroke assessment and treatment guidance.

# Errors of metabolism in newborns – diagnostic challenges in disadvantaged populations

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 2<sup>nd</sup> Pediatric Department, Faculty of Medicne, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Inborn errors of metabolism (IEM) result from the absence or abnormality of an enzyme or its cofactor, leading to either deficiency or accumulation of a metabolite. The majority are autosomal-recessive disorders, but some are X-chromosome-linked or due to a de-novo mutation.

**Case presentation.** We present the cases of two brothers, born in a family of 7 children (three healthy sisters and two brothers deceased in the first months of life –

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Corresponding Author: Alina Grama e-mail: gramaalina16@yahoo.com of unknown causes), with consanguinity (parents are 1st-grade relatives). They were admitted at 9 and 15 days (2 years apart). The first newborn presented hypotonia, intermittent apnea, and vomiting, while the second child presented positive screening tests. We noticed metabolic acidosis and hyperammonemia in both cases. Considering the family history and the clinical and paraclinical features, urea cycle disorder was already suspected as a possible X-linked disease in the first case. The metabolic profile (plasma amino acids, urine organic acids, acylcarnitine profile, and molecular genetic testing) did not establish a particular diagnosis until now. Further monitoring, investigations, and counseling are being continued in this case.

**Conclusions.** IEMs are rare diseases, but they can lead to significant health concerns (especially in some ethnic groups), eventually life-threatening events, diagnostic challenges, and high medical care costs. As practitioners, we aim to rapidly recognize a potential IEM, take immediate measures to avoid complications, and diagnose, support, and educate the family. The lack of education and poor comprehension of the parents from vulnerable populations make our goals challenging to achieve in this case, especially concerning genetic counseling.

# 28-day sepsis and septic shock mortality prediction of Interleukin-6 in the Emergency Department

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Corresponding Author: Sonia Luka e-mail: sonia.luka@umfcluj.ro **Introduction.** Sepsis is a critical global health challenge marked by its vast variability, complex diagnostic criteria, and the challenge of late-stage treatment. It is a life-threatening condition triggered by the body's response to infection, resulting in self-inflicted tissue damage. With sepsis carrying high mortality and morbidity rates, there is an urgent need for innovative diagnostic tools and prognostic indicators to address its multifaceted nature. Early diagnosis, monitoring, and prognosis for high-risk patients are crucial for achieving effective treatment and reducing mortality rates. Hence, there is a pressing demand for simple techniques for early prognosis.

This study aimed to investigate the prognostic value of Interleukin-6 (IL-6) in septic patients, particularly in predicting 28-day mortality in an emergency department (ED) setting. IL-6, a pro-inflammatory cytokine produced in response to inflammation, plays a pivotal role in modulating immune responses. However, its precise role in predicting sepsis outcomes, particularly in terms of 28-day mortality, remains the subject of debate. Variability in results published so far needs further evidence to define the clinical significance of IL-6 in sepsis prognosis.

**Material and methods.** A prospective observational, single-centre study was conducted in the ED from November 2020 to December 2022. 67 septic patients were enrolled within the first hour after their admission, based on the Sepsis-3 Criteria. After the patient's or legal representative's written informed consent, clinical parameters, blood tests, and demographic data, were collected and patients were followed 30 days after admission.

**Results.** 67 patients completed the follow-up. The group was divided into survivor (n=34) and non-survivor (n=33). The median age of surviving patients was 72, while non-survivors had a median age of 78. A Glasgow Coma Scale <=11 at arrival in ED and the need for mechanical ventilation, were the most important risk factors for 28-day mortality (P $\leq$ 0.001).

Interleukin-6 serum levels [median 290.4, 25th-75th percentile (76.3,529.22) vs. median 694, 25th-75th percentile (346.5,858.3) pg/ml, P=0.001]. IL-6 displayed an AUC (Area Under the Curve) of 0.73 for predicting 28-day mortality, with a cutoff value >538 pg/ml. This cutoff value yielded a sensitivity of 63.64% (95%CI 45.1% - 79.6%) and a specificity of 79.41% (95%CI 62.1% - 91.3%).

**Conclusion.** Interleukin-6 may be a useful marker in predicting 28-day mortality for septic patients in the Emergency Department.

### **Chronic Hepatitis B Virus infection - current challenges in pediatric practice**

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Corresponding Author: Alina Grama e-mail: gramaalina16@yahoo.com **Background.** Chronic hepatitis B virus (HBV) infection still stands as a significant cause of global mortality and morbidity despite improvements during the last decades due to vaccination programs. Diagnosis in the pediatric population is infrequent, partly attributed to the nonspecific symptomatology and the lack of data collected from endemic regions for HBV infection. Deficient public awareness programs regarding the dissemination and diagnosis of hepatitis B contribute to this substantial public health issue, leading to chronic hepatic impairment over time.

**Case report.** We present the cases of 7 siblings, all born to a mother carrying hepatitis B surface antigen (HBsAg) with active viral replication. These siblings, institutionalized both within the state service and under the care of social assistants, sought our clinic for further investigations, with the certainty that their mother was infected with HBV. Prenatal care was absent in these instances, and periodic check-ups and laboratory analyses were not performed throughout gestation. Consequently, no prophylaxis was administered at birth, culminating in HBV transmission. Additionally, shortly after birth, the children were institutionalized. Due to the absence of specific symptoms or diagnosis, they were treated as healthy individuals, devoid of supplementary investigations into their family history, hence leading to a delayed diagnosis postnatally. Paraclinical investigations revealed positive HBsAg's, elevated viremia and mildly elevated transaminase levels across all patients. Upon diagnosis, initiation of treatment was considered, but none of the patients were conservatively managed, undergoing regular follow-ups and exhibiting excellent progress.

**Conclusions.** Our objective as medical practitioners is to prevent, diagnose and analyze treatment options for each patient with HBV infection, curbing the course of the disease and preventing subsequent complications associated with chronicity. These cases underscore the challenges in long-term case management, as each patient was institutionalized. The necessity for medical education programs and screening campaigns against infectious diseases within disadvantaged settings remains a genuine public health concern that could be combated over time with heightened awareness about the significance of vaccination and proper care for pregnancies at risk.

#### Purpura fulminans in a 6-month-old infant - differential diagnosis

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Corresponding Author: Alina Grama e-mail: gramaalina16@yahoo.com **Introduction.** Purpura fulminans (PF) is a possible clinical manifestation of disseminated intravascular coagulation (DIC), a widespread microvascular thrombosis, including cutaneous small vessels as the histological substrate of purpuric lesions and skin necrosis. DIC is a severe and life-threatening disease that can rapidly progress to multiorgan failure and death. Along with supportive care, identifying the triggering factor of DIC and administering specific therapy are essential steps in patient management.

**Case presentation.** We report the case of a 6-month-old infant who presented a rapidly extensive purpuric rash one week after the onset of fever, cough, and loose stools. At presentation, he was febrile, with signs of severe dehydration, respiratory distress, neck stiffness, and focal skin necrosis. Laboratory studies showed elevated inflammatory parameters (CRP 11 mg/dL, procalcitonin 90 ng/mL), severe anemia, thrombocytopenia, prolonged prothrombin time and aPTT, low fibrinogen and elevated D-dimers. The patient was started on empirical broad-spectrum antibiotics, given the diagnosis of severe sepsis, possibly meningococcemia. Cerebral MRI was normal, while blood, urine, and stool cultures came out negative. SARS-CoV-2 IgG antibodies were positive, so Multisystem Inflammatory Syndrome (MIS-C) was also suspected to cause DIC. Given this presumption, intravenous immunoglobulins and methylprednisolone were added to the treatment plan. The disease evolution was with the resolution of respiratory and digestive symptoms, improvement of skin lesions, normalization of inflammatory markers, and remission of coagulation abnormalities.

**Conclusions.** DIC is a hazardous complication of various systemic diseases, and its first sign can be the development of PF. Although the most common cause in children is sepsis, other causes should be considered to guide medical judgment. However, precisely establishing the underlying cause is not always possible.

### Comparative effects of transcutaneous electrical nerve stimulation and ultrasound therapy in patients with low back pain

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Corresponding Author: Ileana Monica Borda e-mail: monicampop@yahoo.fr **Introduction.** Low back pain (LBP) is a very disabling musculoskeletal disorder, with high prevalence in the general population. Although electrical therapy is largely used, studies trying to prove its benefits are very few up to now and they often have contradictory results. The aim of this study was, therefore, to evaluate the short-term effectiveness on pain relief, mobility and functional improvement of transcutaneous electrical nerve stimulation (TENS) versus ultrasound (US) therapy in patients with LBP.

**Material and methods.** 58 patients with LBP (age between 32 and 73 years, 33 women and 25 men) participated in this prospective randomized clinical trial. Patients were assigned to TENS group (n=29) or to US group (n=29). Study participants received 10 sessions of TENS or US therapy, 5 days / week, for 2 weeks. All patients were assessed on the first and on the last day of treatment, by: visual analogue scale



(VAS) for pain, Schoeber index for mobility, Roland-Morris Disability Questionnaire (RMDQ) for function.

**Results.** There was no difference between groups in any of the parameters at baseline. At the end of treatment, patients in both groups obtained significant improvement in all parameters: pain (VAS decreased from  $7.3\pm1.9$  to  $4.5\pm1.7$ , p<0.001 in US group, and from  $7.7\pm1.7$  to  $3.2\pm1.6$ , p<0.001 in TENS group), mobility (Schoeber index increased from  $14.1\pm2.7$  to  $15.2\pm3.3$ , p<0.001 in US group, and from  $14.6\pm1.3$  to  $15.8\pm2.2$ , p<0.001 in TENS group), function (RMDQ decreased from  $14.6\pm4.8$  to  $3.9\pm1.6$ , p<0.001 in US group, and from  $13.2\pm6.8$  to  $3.1\pm1.4$ , p<0.001 in TENS group). No significant difference was found between the final results of the 2 groups (p>0.05) in any parameter.

**Conclusion.** TENS and US therapy had similar effects in LBP. Both were effective in relieve pain, increase mobility and reduce disability, representing promising therapeutic options for rehabilitation of LBP.

## Pulsed electromagnetic field in the rehabilitation of distal radial osteoporotic fractures

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Corresponding Author: Ileana Monica Borda e-mail: monicampop@yahoo.fr **Introduction.** The study aims to assess the effects of Pulsed Electromagnetic Field (PEMF) on pain, edema, range of movement and functional performance in patients with distal radial osteoporotic fractures.

**Material and methods.** 53 women ( $61.8 \pm 7.3$  years) with distal radial osteoporotic fractures, treated by reduction and immobilization, were included (after cast removal) in a prospective randomized controlled study. Osteoporosis was confirmed by dual-energy X-ray absorbtiometry (DXA) method. Patients were randomly assigned to either PEMF (31 patients) or control group (22 patients). PEMF therapy or sham therapy (in the control group) was applied 10 minutes / day, for 10 days. Patients from both groups received a standard exercise programme. Parameters assessed on the first and on the last day of treatment were: pain (SAV), edema (displacement method), range of motion (goniometry), function (patient-rated wrist evaluation score – PRWE).

**Results.** After the rehabilitation programme, improvement of all measured parameters was recorded in both groups, but with constant significant differences in favour of PEMF group: pain (p< 0.01), edema (p<0.001), range of motion (p<0.05), PRWE (p<0.05).

**Conclusion.** PEMF provided important additional benefits in the rehabilitation of patients with distal radial osteoporotic fractures.

### Clinical and immunological profiles of patients with anti-synthetase syndrome: a retrospective cohort study from a tertiary centre

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Corresponding Author: Oana-Mihaela Resteu e-mail: resteumihaela@yahoo.com **Introduction.** Anti-synthetase syndrome (ASS) is a rare and highly variable condition, both clinically and immunologically. Our aim was to evaluate the clinical characteristics of ASS patients with different anti-ARS antibodies from a tertiary rheumatology center.

**Patients and methods.** We conducted a retrospective observational study on consecutive patients diagnosed with ASS according to Connors' criteria from January 1, 2015, to July 31, 2023. We obtained demographic, clinical, and serologic data from the hospital's records.

**Results.** Sixty-five patients (46 females) with a mean age of 53.9 (13.9) years were included. The most frequently reported clinical manifestation was interstitial lung disease (ILD) (70.7%), followed by Raynaud's phenomenon and arthralgia (67.7%), muscle weakness (66.2%), proximal myalgias (49.2%), mechanic's hands, and arthritis (41.5%). Only 26.1% had the classic ASS triad. Thirty (46.1%) patients were PL7+, 22 (33.9%) were Jo1+, 3 (4.6%) were PL12+, and 2 (3.1%) were OJ. The most frequently found myositis associated antibodies (MAA) was anti-Ro52 (36.9%). Of the 65 patients included, 45 were diagnosed in the last 3 years (the COVID-19 pandemic). The most frequently myositis specific antibodies (MSA) in ASS patients diagnosed during the COVID-19 pandemic was anti-PL7, while anti-Jo1 was the most common MSS before 2020 (p<0.05). Anti-Jo-1 patients had an earlier onset, more myalgia, and higher CK levels than anti-PL-7 patients (p<0.05). ILD was more common in anti-Ro52 positive ASS patients (p<0.05).

**Conclusions.** ASS patients have heterogeneous manifestations, and different types of anti-ARS antibodies are associated with distinct clinical and immunological features. The COVID-19 pandemic led to an increase in the prevalence of ASS cases and a remarkable shift in the anti-ARS antibody profile, with an increased frequency of anti-PL7 antibodies. Further studies are needed to investigate the link between SARS-CoV2 infections and myositis.

# Diagnosing Muckle-Wells syndrome in the absence of fever or family history of autoinflammatory disease

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1) Department of Rheumatology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Muckle-Wells syndrome (MWS) is a rare autoinflammatory disease (AID) caused by a mutation in the CIAS1/NLRP3 gene and represents the moderate phenotype of cryopyrinopathies. It manifests from early childhood with febrile episodes, urticarial rash, arthralgias, progressive eye and hearing involvement, with amyloidosis being the most severe complication that can occur. Targeted biological therapies, such as

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Corresponding Author: Rebeca Bărbulescu e-mail: rebecabarbulescu@gmail.com IL-1β inhibitors like Canakinumab, are available for treating this condition.

**Patients and methods.** We identified four patients with MWS in the time frame 2018-2023 through the electronic archive of the Cluj-Napoca Rheumatology Clinic.

**Results.** A 12-year-old girl with a family history of neurosensory deafness, developed arthritis, cold urticaria, and recurrent conjunctivitis.

A 29-year-old male with recurrent marginal keratitis and cold hives, reported similar skin manifestations as his paternal uncle.

A 30-year-old patient who had recurrent conjunctivitis, urticarial rash, febrile syndrome and polyarthritis, developed bilateral neurosensory deafness at 10 years of age.

A 46-year-old patient presented with urticarial rash, chorioretinitis, bilateral neurosensory hypoacusis and febrile episodes.

The diagnosis of MWS was based on clinical and biological evidence, with genetic testing as a prospective investigation. Two patients didn't present fever, while the adult female patients had no family history of AID. Hearing impairment is uncommon in children, but it can develop later in the disease course. Although TNF inhibitors had limited effects on mild symptoms, IL-1 inhibitors, especially Canakinumab, determined a quasi-complete resolution of symptoms.

**Conclusions.** MWS manifestations are diverse and often nonspecific, leading to diagnostic delays. Genetic testing is not always conclusive. While TNF inhibitors relieved fever and skin rash, IL-1 inhibitors (particularly Canakinumab) demonstrated remarkable efficacy in treating cryopyrinopathies. Further studies are needed to confirm the sustained response to IL-1 inhibitors in this rare condition.

### Progressive fibrosing interstitial lung disease in a young woman with rheumatoid arthritis and anti-PL-7 antisynthetase syndrome

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Corresponding Author: Oana-Mihaela Resteu e-mail: resteumihaela@yahoo.com **Introduction.** Interstitial lung disease (ILD) represents a significant complication of rheumatoid arthritis (RA) and antisynthetase syndrome (ASS). We present a case of severe ILD in the context of overlapping RA and ASS, a rarely reported association in the literature.

**Case presentation.** A 37-year-old female presented with a 6-month history of symmetric polyarthritis, inflammatory syndrome, a high titer of RF, and positive anti-CCP antibodies, resulting in a seropositive RA diagnosis. Physical examination revealed fine crackles at lung bases, dyspnea on exertion, dry cough, and an accentuated interstitium on chest radiograph. Pulmonary function tests showed a restrictive pattern, and a HRCT demonstrated a UIP-type ILD. Initial treatment included corticosteroids and Cyclophosphamide, followed by combinations of conventional DMARDs with an unfavorable outcome. The patient's respiratory symptoms worsened after Tocilizumab therapy, leading to consideration of an overlapping pathology. Laboratory tests revealed elevated transaminases, a mild increase in CK and LDH levels, without myalgia, and normal EMG. An extended myositis panel detected anti-PL-7 antibodies, leading to a diagnosis of overlapping RA and anti-PL-7 ASS. Over time, despite immunosuppressive therapy, the pulmonary symptoms worsened. Functional respiratory tests and HRCT indicated the progression of pulmonary fibrosis, prompting the initiation of Nintedanib.

Anti-PL-7 ASS is associated with a UIP pattern, poor prognosis, and a significantly lower response to immunosuppressive therapy. Pulmonary involvement typically dominates the clinical picture and is often associated with amyopathic forms of the disease.

**Conclusion.** The presence of pulmonary involvement at the time of an RA diagnosis should raise suspicion of an overlapping pathology. This case highlights the importance of a multidisciplinary team for the optimal management of ILD patients.

#### **MODY diabetes - a challenging diagnosis**

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Corresponding Author: Alexandra Mititelu e-mail: perta\_alexandra@yahoo.com **Introduction.** Maturity Onset Diabetes of the Young (MODY) is a distinct type of monogenic diabetes, which differs from the other two more common forms (type 1 and 2) both by clinical manifestations and therapeutic approche. To date, 14 subtypes of MODY are known, with the diagnosis usually being established before the age of 35. Among the pediatric population, MODY represents approximately 1-5% of cases diagnosed with diabetes mellitus. Among the subtypes of MODY, the most common forms are 2 and 3, type 9 being extremely rare. Considering the rarity of cases and the heterogeneity of the clinical manifestations of MODY forms, these forms are often classified, at least initially, as type 1 or 2 diabetes.

**Case presentation.** We present the case of a 16-year-old patient who came to our service for polyphagia, polydipsia that started about 1 month before admission. Clinical examination revealed normal weight patient, BMI=20 kg/m2, without any other changes.

Laboratory parameters indicated glycemic profile with normal values (except for a single fasting value of 130 mg/dl), pH parameters within normal limits. However, increased values of HbA1c and fructosamine were detected, ketonuria, as well as the alteration of glucose tolerance following the performance of OGTT. We determined C peptide, insulinemia which were within normal limits and anti GAD2, ICA, IA2 antibodies were negative. Additionally, lipid profile, HOMA-R index were normal, but abdominal ultrasound highlighted the pancreas with a slightly inhomogeneous structure. Thus, we considered a MODY diabetes, which was confirmed after genetic testing: double heterozygous mutation at the level of the PAX gene (Paired Homeobox 4). Also, we have confirmed the heterozygous status of both parents for this mutation. Both parents have a heterozygous mutation in the PAX gene. The patient presented normal glycemic values and the decrease of HbA1c values under 250 g CH diet.

**Conclusions.** The present case illustrates a very rare form of diabetes, namely MODY 9. This form usually manifests with slightly/moderately elevated blood sugars associated with ketosis, manifestations also seen in our patient. Usually, the evolution is favorable with diet and oral antidiabetic drugs, but on the log term it may be necessary to initiate insulin therapy, so careful monitoring is required.

# Integration of respiratory rehabilitation and impact on the quality of life in patients with COPD

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Corresponding Author: Ruxandra Râjnoveanu e-mail: ruxandra.rajnoveanu@umfcluj.ro **Introduction.** Respiratory rehabilitation represents a comprehensive and integrated approach of care for patients with chronic or acute lung conditions. Through tailored exercise, education, nutritional interventions, psychological counseling and social support, pulmonary rehabilitation aims to improve patients' quality of life, optimize their lung functional capacity and reduce respiratory symptoms. Therefore, pulmonary rehabilitation plays an essential role in the care and management of lung conditions, helping to promote the health and well-being of patients. The aim of the research was to provide a systematic review of the available evidence on the effectiveness of integrated pulmonary rehabilitation and its impact on quality of life in patients with COPD.

**Material and methods.** The electronic search in PubMed, MEDLINE and Embase databases included studies published between 01.01.2020 and 07.10.2023. The search keywords were: "COPD", "pulmonary rehabilitation", "respiratory rehabilitation", "integration pulmonary rehabilitation", "integration respiratory rehabilitation", "quality of life". From the total of 8,708 articles initially identified, after applying filters, according to the inclusion and exclusion criteria set in the methodology and after removing duplicates, 8 articles suitable for inclusion in this qualitative analysis were finally identified.

**Results.** Cycle ergometer and Qigong exercises significantly improved lung endurance and quality of life. Aerobic and strength exercises improved health status in patients with COPD. Early rehabilitation programs resulted in significant improvements in the 6-minute walk test.

**Conclusion.** Individualizing respiratory rehabilitation programs according to the needs of COPD patients can play an essential role in optimizing outcomes and improving their quality of life.

# Prevalence of interatrial block in the Rehabilitation Hospital of Cluj-Napoca

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2) Department of Pharmacology, Toxicology and Clinical Pharmacology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Interatrial block is a distinct electrocardiographic pattern associated with atrial dilatation, atrial arrhythmias such as atrial fibrillation, and cerebral embolic events. It is defined as prolonged P wave duration  $\geq 120$  ms due to a conduction delay between the right atrium and the left atrium. The association between interatrial block and supraventricular arrythmias is known as Bayes syndrome. The aim of this study was to determine the prevalence of interatrial block in a large non-selected population of patients admitted to the Cardiology department of the Rehabilitation Hospital Cluj-Napoca.

Material and methods. 82,266 electrocardiograms belonging to patients hospitalized between 1989 and November 2017 were reviewed. Only patients in sinus

Corresponding Author: Sabina Istratoaie e-mail: sabina.istratoaie@gmail.com rhythm were included, while those who had atrial arrhythmia were excluded due to the impossibility of measuring the P wave duration. Partial interatrial block was defined as a P wave duration of more than 120 ms and advanced interatrial block was defined as prolonged P wave duration associated with a biphasic P wave configuration in the lower leads: DII, DIII, aVF.

**Results.** Of the 82,266 electrocardiograms, 9,289 were excluded because it recorded atrial fibrillation or atrial flutter. 1280 recordings showed interatrial block, which corresponds to a prevalence of 1.75%. Most of them were men (57.5%), the mean age of the men with interatrial block was 70.6 years, while for women was 65.8 years (p<0.001).Most ECG recordings of interatrial block had a P wave duration between 120 and 129 msec (38.3% equivalent to 491 patients). No patient under 30 years of age presented interatrial block.

**Conclusions.** The prevalence of interatrial block in Rehabilitation Hospital Cluj-Napoca was 1.75%, more common among men, but no patient under 30 years of age presented this electrocardiographic pattern. Considering the association with atrial fibrillation, left atrial dilation and atrial electrocardiogram, and clinicians should closely follow these patients for atrial arrhythmias or cerebral embolic episodes.

#### Cutis laxa syndrome: a case report

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Corresponding Author: Adrian Baican e-mail: adrianbaican@yahoo.com **Introduction.** Cutis laxa (CL) is a rare disorder of unknown cause characterized by progressive looseness of the skin associated with abnormalities of other organs containing elastic tissue such as the lungs, blood vessels and gastrointestinal tract. Both inherited and acquired forms of CL exist. The diagnosis of CL syndrome is based on clinical assessment of typical skin features and the associated extracutaneous findings.

**Case report.** P. R. an 11 months old boy, a child of related parents, presented with an acute respiratory disorder in the department of pediatrics. Upon admission, physical examination revealed that the patient had psychomotor retardation, generalized hypotonia, joint hypermobility and ligamentous laxity. Assessment of the patient's facial features revealed craniofacial dysmorphia with microcephaly, hypertelorism and epicantus. Skin examination showed loose and extensible skin, lacking elasticity. Laboratory tests, skin biopsy with histologic examination and genetic testing were performed.

**Discussion.** Cutis laxa is a rare connective tissue disorder characterized clinically by loosely hanging skin folds. Histologically, there are changes in dermal elastic fibers. Skin changes may be associated with variable systemic involvement. Neurological involvement is very common in CL syndromes, pointing to the importance of the underlying genes in neurodevelopment and positioning this group of disorders to neurocutaneous syndromes. There are several overlapping symptoms of the diverse types of CL syndromes. The mode of transmission can be autosomal recessive (OMIM 219100) with the severest clinical manifestations.

# Paraneoplastic dermatomyositis or induced by checkpoint inhibitors? – a case report

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Corresponding Author: Mihaela-Maria Tamşa e-mail: tamsa.mihaela@gmail.com **Introduction.** Dermatomyositis is often associated with neoplasms such as breast, lung, or gastrointestinal cancers, but myositis can also be caused by treatment with checkpoint inhibitors. We present a clinical case of a bronchopulmonary neoplasm which developed muscular symptoms after treatment with checkpoint inhibitors.

**Case report**. A 60-year-old smoker female diagnosed with stage IV small cell bronchopulmonary neoplasm, treated with Nivolumab for 3 months, presents with heliotrope rash and facial edema, predominantly periorbital, erythema on the neck, myalgias, and muscular asthenia at shoulder and hip girdle, arthralgias in the small joints of the hands with morning stiffness of 30 minutes. Biologically - no inflamatory syndrome, significant muscle cytolysis syndrome, immunologic - negative ANA and myositis profile, EMG - myogenic pattern predominantly in the upper limbs.

**Discussion.** The differential diagnosis between paraneoplastic dermatomyositis and checkpoint inhibitors-induced myositis can be challenging, especially when a neoplastic patient presents muscular manifestations after checkpoint inhibitor administration. Both conditions cause myalgias and muscular asthenia with a proximal pattern. Paraneoplastic dermatomyositis is accompanied by specific skin manifestations, whereas checkpoint inhibitors treatment does not induce such manifestations and also affects the ocular and paravertebral muscles, which do not occur in dermatomyositis.

**Conclusions.** Subclinical paraneoplastic dermatomyositis may manifest after Nivolumab treatment. The pattern of muscular involvement and the persistence of symptoms after discontinuation of Nivolumab support the diagnosis of paraneoplastic dermatomyositis.

#### Typhoid fever – low incidence, high likelihood of misdiagnosis

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Corresponding Author: Mihai-Aronel Rus e-mail: aronelrus@gmail.com **Introduction.** Typhoid fever is still a public health problem in developing countries. Within the E.U. it has seen increasing incidence in recent years, and immigration from high-prevalence countries continues to further increase the number of imported cases. Clinically, patients will generally present with fever, diffuse abdominal pain, constipation, diarrhea, asthenia and anorexia, all of them non-specific.

**Case report.** We report the case of a 30-year-old patient, who was admitted to our hospital after 3 weeks of persistent fever associated with nausea, vomiting, constipation, dry cough, and marked asthenia; he was prescribed different treatment, without improvement. After admittance in our hospital, careful history taking revealed he recently immigrated from Bangladesh, significantly changing the diagnostic spectrum; blood cultures are positive for *Salmonella typhi*, thus confirming the diagnosis of typhoid fever. After the identification of the etiological agent and the antibiogram, the therapeutic scheme was changed to 3rd generation cephalosporins, under which the clinical evolution was favorable. We will discuss the diagnostic problems raised by the described case, as well as the methods of diagnosis, treatment, prevention of enteric fevers.

### **Re-emerging infections: clinical and epidemiological** characteristics of children hospitalized with measles in 2023

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Corresponding Author: Raluca-Elena Tripon e-mail: rhorge@yahoo.com **Introduction.** Measles is an acute, highly contagious viral disease caused by the measles virus that can produce huge epidemics and serious consequences. People who have not been immunized or have just been partially immunized are the most vulnerable. The vaccine against this disease, which is included in the Rubella-Mumps-Measles (MMR) vaccine, is highly efficient in preventing and controlling the disease.

Our country leads Europe in the number of measles cases, and vaccination rates are significantly below the WHO objective of 95%.

**Material and method.** Between January and September 2023, we conducted a statistical study on the clinical and epidemiological characteristics of Cluj County children hospitalized with measles at the Clinical Hospital for Infectious Diseases Cluj-Napoca.

**Results.** There were 136 children enrolled, with 126 cases confirmed by serology. Fever, oculo-nasal catarrh, and the distinctive rash predominated clinically. Children under the age of one year were the most afflicted (44.1%), followed by children aged one to four years (25%). The majority (72 cases) were unvaccinated; 13 children had two doses of the vaccine; and in the case of 24 children, the immunization status was unknown by the relatives. The most prevalent complication (73 cases) was pneumonia. All of the cases had a positive outcome.

**Conclusions.** Measles is a vaccine-preventable disease. It is estimated that roughly 140,000 children die each year as a result of measles complications; thus, preventative initiatives are critical for disease control.

#### Enteroviral meningoencephalitis – a case series

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Corresponding Author: Lorand Magdo e-mail: lorand.magdo@gmail.com **Introduction.** Enteroviral meningoencephalitis can be a major public-health provocation among neonatal population and immunosuppressed patients, both in terms of morbidity and mortality. Taking into consideration the unspecific and broad spectrum of clinical findings, most of the time, contact tracing becomes challenging and unsuccessful. In the last period, there has been a surge of novel diagnostic tests on the market, multiplex syndromic testing being one such example. These methods prove to be useful both when it comes to accurately identifying infection etiology and also for the control of outbreaks.

**Material and methods.** The case series presents the admissions of confirmed enteroviral meningoencephalitis in the Clinical Hospital of Infectious Diseases from Cluj-Napoca after the alert on the rise of severe cases of enteroviral infections among neonates had been published by the European Centre for Disease Prevention and Control (ECDC), in June 2023.

**Results.** Between July and August 2023, 5 cases of confirmed enteroviral meningoencephalitis in the pediatric population have been admitted in the clinic. Although contact tracing has been difficult to conduct (no epidemiological link being found in 3 cases) and the clinical findings unspecific, the final diagnosis has been made using

molecular testing with a multiplex syndromic testing kit for the evaluation of cerebrospinal fluid. After the identification of the etiology of infection and rapid etiological treatment, the evolution was rapidly favorable, with the cessation of clinical symptoms.

**Conclusions.** The 5 cases underline the importance of molecular testing in everyday clinical settings, offering benefits both for the patients (immediate de-escalation to an etiological treatment and avoiding a prolonged useless empirical treatment) and for public health (contact tracing with adequate prophylaxis and better epidemiological surveillance of outbreaks).

#### **COVID-19** in children

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Corresponding Author: Mihaela Lupșe e-mail: sorina.lupse@umfcluj.ro **Introduction.** The SARS-CoV-2 infection has had a significant impact on our lives for approximately 3 years. The severe evolution of COVID-19 in adults has raised multiple concerns about how children will be affected. Fortunately, the initial statistical data showed mild involvement in most cases, with symptoms resembling those of an upper respiratory tract infection, with a few peculiarities. According to available data, out of the total reported global infection cases (696,943,378 cases), 17.9% of them represent pediatric patients. Our study aimed to analyze the progression of children admitted to the Clinical Hospital of Infectious Diseases and compare the results with the data from the literature.

**Material and method.** Patients under the age of 18, admitted to the Clinical Hospital of Infectious Diseases between September 1, 2021, and April 30, 2023, with a diagnosis of SARS-CoV-2 infection, were included in this retrospective observational study aimed at evaluating the clinical aspects and progression of SARS-CoV-2 infection in children, comparing two cohorts corresponding to the Delta and Omicron waves. Information was collected from observation sheets, and the database was processed using Microsoft Excel, corresponding to the two waves (September 1, 2021, to January 15, 2022, for the Delta variant, and January 16, 2022, to April 30, 2023, for the Omicron variant).

**Results.** The study included 657 patients aged between 1 month and 18 years. Demographically, the two groups are characterized as follows: the average age is 109 months (approximately 9 years) for the Delta wave group (Group D) and 33 months (approximately 3 years) for the Omicron wave group (Group O). The majority of patients come from urban areas (72% of Group D patients and 66% of Group O patients), and boys slightly outnumber girls (60% boys in Group D and 51% in Group O).

In terms of disease severity, both groups are predominantly composed of mild cases: Group D had 217 mild cases (92%), 16 moderate cases, and one severe case, while Group O had 243 mild cases, 76 moderate cases (18%), and 4 severe cases.

We analyzed the prevalence of symptoms and signs that make up the clinical picture specific to each form. From a biological standpoint, it's worth mentioning that vitamin D levels were within a sufficient range in most cases where measurements were taken.

**Conclusion.** Most of the patients included in the study presented mild forms of the disease with favorable outcomes, consistent with expectations based on literature data. Although it represents the optimistic aspect of this pathology, SARS-CoV-2 infection in children can be surprising due to severe post-infection reactions. Conditions such as

MIS-C, long COVID, skin lesions, or the onset of diabetes are life-threatening pathologies that affect children, and their development is not necessarily correlated with the severity of the initial illness. Experience gained over time and the scientific perspective on these pathologies will provide us with answers to the current concerns.

### Electrocardiographic predictors of right ventricular dysfunction in patients with heart failure

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Corresponding Author: Madalina Patricia Moldovan e-mail: madalina.patricia.moldovan@gmail. com **Introduction.** Right ventricular (RV) dysfunction is an important predictor of survival in patients with heart failure (HF) with both preserved (HFpEF) and reduced ejection fraction (HFrEF). The complex geometry of the RV makes accurate assessment of its function at times imprecise. These limitations affect all indices of RV function that are based on geometric assumptions. Recently, artificial intelligence-based assessment of left ventricular function using the 12-lead electrocardiogram (ECG) and not using geometric assumptions about ventricular cavity, was shown to be highly accurate. To date there are no studies assessing the value of ECG in predicting RV function. Given these considerations the aim of our study was to assess the possible relationship between several electrocardiographic parameters and right ventricular function evaluated by echocardiography. We focused our attention on ECG lead V1, which is in the vicinity of the RV.

**Material and methods.** We included 107 patients (age  $61\pm14$  years, 67men) of whom 87 had HF (HFpEF N=61 and HFrEF N=26) and 20 patients without HF. Twelve-lead ECG and echocardiograms were performed in all patients. We assessed echocardiographic parameters of global and regional RV function.

**Results.** Time to Intrinsicoid deflection in lead V1 (TID-V1) and the QTc interval measured in lead V1 (QTc-V1) were significantly more prolonged in patients with HF vs. patients with no HF ( $35\pm24$ ms vs  $24\pm15$ ms; p value 0.03 and  $449\pm40$ ms vs.  $427\pm20$ ms Pvalue=0.05 respectively). TID-V1 correlated significantly with the tricuspid annulus systolic excursion (TAPSE) and RV fractional area change (FAC; r=-0.31; p=0.02 and r=-0.35; p=0.029). QTc-V1 correlated significantly with the RV diameter in the subtricuspid and midventricular areas, RV longitudinal dimension (r=0.31 p 0.009, r=0.30 p 0.01, and r=0.27 p=0.03). QTc-V1 also correlated with parameters of global and regional RV function including FAC, RV apex longitudinal strain, RV free wall strain, and global RV strain (r=-0.42 p=0.0004, r=0.35 p=0.0032, r=0.21 p=0.045, and r=0.41 p=0.0005). RV dysfunction as defined by RV-FAC<35% was predicted by TID-V1 > 30ms with and sensitivity of 60% and specificity of 72%, AUC 0.735 and by QTc-V1>440ms with a sensitivity of 80% and specificity of 52% AUC=0.814. TID-V1 and QTcV1 predicted RV-FAC<=35% independent of age, TAPSE, and LV ejection fraction.

**Conclusions.** Lead V1 time to intrinsic deflection and QTc-V1 predict RV dysfunction independent of echocardiographic parameters of RV function in patients with HF.

**MEDICINE** Surgical Specialties

### Fetal "gallstones" are still an unsolved mystery

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Corresponding Author: Dan Boitor-Borza e-mail: danboitor@yahoo.com **Introduction.** It is uncommon to find echogenic content in the fetal gallbladder. This condition's etiology, natural progression, and prognosis remain unclear. In addition to providing a systematic review of the literature on this subject, we also propose a plan for patient follow-up.

**Material and methods.** There were one hundred database entries found in PubMed, EMBASE, and ICTRP reviews. Out of these, thirty-four studies investigating the ultrasound features and outcomes of this condition were included.

**Results.** There were 226 infants identified with gallbladder echogenic content. Seventy-two fetuses had biliary sludge; thirty cases had a solitary hyperechogenic focus; and one hundred fetuses had multiple hyperechogenic foci in the gallbladder. There were sixteen cases of distal shadowing, thirty-seven fetuses with a comet tail and twinkling, and twenty-six cases without acoustic artifacts. There have been nine documented cases of spontaneous resolution before birth, nine infants with no echogenic content at birth, and 138 cases of resolution of echogenic content within the first year of life.

**Conclusion.** The echogenic content in the fetal gallbladder typically resolves spontaneously during the postnatal period. After reassuring the parents adequately, the patients should be observed for spontaneous resolution; medical or surgical intervention is not indicated. Patients who are asymptomatic can be managed using a wait-and-see approach.

# Accessory cavitated uterine mass (ACUM): a new Müllerian anomaly

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Corresponding Author: Dan Boitor-Borza e-mail: danboitor@yahoo.com A 35-year-old female presented with worsening dysmenorrhea and dyspareunia that were resistant to medical treatment. The patient requested a subtotal hysterectomy, which was subsequently performed laparoscopically because of dyspareunia, an inadequate response of the dysmenorrhea to medical therapy, and an unsatisfactory quality of life. On the second day following surgery, the patient was discharged. There were no intraoperative or postoperative complications, and at the 3-month follow-up appointment, the patient did not complain of dyspareunia.

ACUM is presently thought to be a new Müllerian anomaly that might be linked to dysfunction of the female gubernaculum. In this rare condition, there is a uterine mass located in the broad ligament, close to where the round ligament attaches, but the rest of the genital tract is normal. The correlation between MRI findings and surgical and pathological characteristics is significant. The MRI can rule out endometriosis and adenomyosis. Differential diagnoses include Robert's uterus, degenerated leiomyomas, noncommunicating cavitated rudimentary uterine horn, and cystic adenomyosis. Surgical excision by laparoscopy or laparotomy is the most effective treatment for this condition.

#### Young woman with abdominopelvic tuberculosis

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Corresponding Author: Dan Boitor-Borza e-mail: danboitor@yahoo.com **Case.** An 18-year-old female presented to the hospital with a temperature of 40.5 degrees Celsius, chills, generalized chronic abdominal pain, loss of appetite, and diarrhea. Laboratory tests performed revealed an inflammatory syndrome, with an erythrocyte sedimentation rate of 49 mm/hour, C-reactive protein of 20 mg/dL, fibrinogen of 496 mg/dL, ferritin of 759 ng/mL, and procalcitonin of 2.6 ng/mL. CA125 levels were raised to 214.9 U/mL. Because of persistent fever and severe exhaustion, an emergency diagnostic laparoscopy was performed, which was subsequently converted to a laparotomy. An amorphous inflammatory pelvic mass encasing the uterus, adnexa, and urinary bladder was discovered during the laparotomy. Pathologic examination revealed granulomas and acid-fast bacilli, and PCR proved Mycobacterium tuberculosis. An antituberculosis treatment was initiated.

**Comment.** Tuberculosis is one of the world's significant problems of health, and the second biggest infectious killer after COVID-19 (above HIV/AIDS), according to the WHO (1). Even in developed countries, the disease's prevalence has recently increased (2). Female genital tuberculosis is more prevalent in immunocompromised patients, such as those with HIV, COVID-19, diabetes, and chronic renal disease (1, 3, 4). The decreased immune response after COVID-19 enhances the chance of Mycobacterium tuberculosis coinfection or latent tuberculosis activation (5). Female genital tuberculosis should be considered as a potential cause of tubo-ovarian abscesses, particularly in young, sexually inactive women.

#### An aggressive primary neuroendocrine liver tumor: a case report and literature review

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Corresponding Author: Mihaela Berar e-mail: mihaella.berar@gmail.com **Background.** Primary hepatic neuroendocrine tumors (PHNT) are very rare malignancies, consisting of less than 0.3% of all neuroendocrine tumors. While the 10-year survival rate is high, most tumors being less aggressive, there is no clear consensus regarding the management of these entities. However surgical resection appears to be the appropriate treatment.

**Case presentation.** We present the case of a 49-year old female patient who was incidentally diagnosed with a large PHNT located in the forth liver segment. Initial preoperative imaging raised the suspicion of a liver hemangioma associated with chronic gallbladder lithiasis. Surgical resection was performed and the pathology examination revealed a primary hepatic neuroendocrine tumor with a high mutation rate (Ki67 rate of 90%) invading the gallbladder.

**Conclusion.** The hepatic location of neuroendocrine tumors is exceptionally rare. Since the tumors do not secrete any biologically active molecules, they can go undetected for a long period of time, reaching large dimensions. A definitive diagnosis is based on immunohistochemistry.

### A quality assessment and systematic review of clinical practice guidelines on hormone replacement therapy for menopause using the AGREE II instrument

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Corresponding Author: Răzvan Ciortea e-mail: mpr1388@gmail.com **Introduction.** Variations in guidelines can impact treatments and health outcomes. Our goal was to assess Clinical Practice Guidelines (CPG) on hormone replacement therapy (HRT) for menopause, systematically reviewing their quality and compiling recommendations for HRT usage.

**Material and methods.** A search of Embase, Scopus, MEDLINE and GFMER databases from inception to December 2022 was conducted. Nine CPG were included. A team of four researchers evaluated the quality of the selected CPG using the Appraisal of Guidelines for Research and Evaluation (AGREE II) tool and extracted recommendations.

**Results.** According to the AGREE II evaluation, three CPG were deemed of high quality and were endorsed without need for modifications. The included CPG received the lowest ratings in the domains "Applicability" and "Editorial Independence". Agreement among raters measured by Kendall's W varied between 0.28-0.67. More than 300 recommendations were organized into categories such as diagnosis and treatment, patient information, alternative treatments, relation with cancer and safety and efficacy. All the CPG agreed on the use of estrogen without progesteron only in women without an uterus, the use of estradiol for vasomotor symptoms, the use of vaginal low dose estrogen without an associated progestogen for genitourinary syndrome, the use of HRT for the prevention and treatment of dementia. No consensus was reached on the use of continuous / cyclical HRT for peri- and postmenopausal women, the safety of a progesting intrauterine device during HRT, the safety of low doses of estrogens without progestogen or the risk of breast cancer attributable to HRT.

**Conclusion.** Most CPG demonstrated a moderate quality level, with significant variations in their recommendations. Integrating universally accepted recommendations from existing CPG into daily practice is likely to enhance clinical outcomes.

### Evaluation of the correlation between the anxiety induced by childbirth perineal trauma and associated vaginal symptoms in primiparous women: preliminary data

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 2<sup>nd</sup> Obstetrics and Gynecology, Department, Faculty of Medicine, Iuliu HatieganuUniversity of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Perineal trauma, occurring during childbirth in about 90% of primiparous patients, can significantly impact a woman's overall well-being and her experience of vaginal symptoms. This study aims to explore the interplay between anxiety induced by childbirth perineal trauma and how it relates to the scoring of vaginal



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Corresponding Author: Răzvan Ciortea e-mail: mpr1388@gmail.com symptoms in primiparous women.

**Methods.** The conduct of this research was approved by our Institutional Ethics Committee. Each patient reported their anxiety score related to childbirth trauma at birth and at 6 months postpartum. At six months after birth all women completed the validated International Consultation on Incontinence Questionnaire - Vaginal symptoms (ICIQ – VS). The questionnaire included information on vaginal symptoms, sexual matters and quality of life. The scores for each of those domaines were compiled. Graphpad Prism 9.1.0 was used to assess correlations.

**Results.** Ninety-five primiparous women were enrolled in the study. Significant positive correlations were found between the anxiety scores at birth and at 6 months postpartum (p=0.0016, r= 0.4019) as well between anxiety scores at birth and the quality of life (QoL) at 6 months postpartum (p=0.0496, r=0.2505). A significant negative correlation emerged between the anxiety scores at 6 months postpartum and patients' age (p=0.0332, r= - 0.2754). The other parameters did not yield significant correlations.

**Conclusions.** These preliminary data provide valuable insights into the intricate relationship between anxiety induced by perineal trauma during childbirth and the subsequent experience of vaginal symptoms, sexual matters and quality of life in primiparous women. Our findings reveal significant positive correlations between anxiety scores at various time points, highlighting the enduring nature and emotional impact of perineal trauma. This study also highlighted a potential age-related factor in how anxiety manifests in the context of childbirth perineal trauma.

#### Parvovirus B19 in pregnancy – do we screen for fifth disease or not?

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Corresponding Author: Cristina Ormindean e-mail: cristina.mihaela.prodan@gmail.com **Introduction.** Infections during pregnancy have become a serious public health problem worldwide. The agents most commonly responsible for these infections can be viruses, bacteria, protozoa or fungi. Although much less common than bacterial infections, the occurrence of congenital and perinatal viral infections can have serious consequences for the newborn, some with important sequelae during childhood and later in adult life. Parvovirus B19 infection is known as erythema infectiosum, the "fifth disease" or "slapped cheek disease" a common childhood illness. The aim of this article is to summarize the existing data in the literature on the effects of parvovirus B19 infection during pregnancy and to assess if there is a need of screening in pregnant patients.

**Material and methods.** For data collection we searched the available online databases PubMed, Cochrane library, Google Scholar using the keywords: Parvovirus B19 infection, fetal transmission, congenital infection, pregnancy, fetal effects, screening, diagnosis, management, non-immune hydrops, fetal anemia, miscarriage, fetal death and selecting publications from the last 10 years.

Parvovirus B19 vertical transmission rate ranges from 17% to 30%, most seen between 9- and 20-weeks' gestation. Maternal-fetal effects of Parvovirus B19 infection: Maternal- asymptomatic, erythema infectiosum, arthropathy, anemia, myocarditis, Fetal- fetal death, anemia/hydrops, myocarditis. Currently, there is no formal recommendation for routine antenatal serologic screening of the immune status for parvovirus B19. Diagnosis of maternal infection is based on antibody detection,

although viremia detection through PCR (Polymerase Chain Reaction) is also available. Diagnosis of fetal infection: detection of B19V DNA in the amniotic fluid collected by performing amniocentesis is the most used method when attempting to establish the etiology of fetal hydrops of unknown cause.

**Results.** Intrauterine transfusions (IUT) of red blood cells were the life-saving treatment for fetal hemolytic disease due to Rhesus alloimmunization and are now the standard treatment for a variety of causes of fetal anemia.

**Conclusions.** Should parvovirus B19 infection be included in routine screening of pregnant patients? Screening should only be offered if a condition is common and/ or causes diseases with a significant impact on health for which treatment and/or prevention is possible. Parvovirus B19 is generally a mild disease.

## Fibrous dysplasia of the sphenoid bone - case report and review of literature

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Corresponding Author: Sever Pop e-mail: sever.pop@umfcluj.ro **Introduction.** Fibrous dysplasia is a rare, benign, slowly growing bone disease characterized by the replacement of normal bone with various degrees of fibrous tissue and immature woven bone. The patients can present with single-bone involvement (monostotic form) or multiple-bone involvement (polyostotic form). Craniofacial involvement occurs in 50-100"% of polyostotic forms and 10% of monostotic variants. The disease usually affects the craniofacial bones, and the fibro-osseous tissue compression can influence the clinical picture. Patients are usually asymptomatic, although headaches or other symptoms of cranial nerve compression can occur.

**Case report.** We report the case of a 61-year-old male patient who presented in our Department with no symptoms but with a left sphenoid sinus opacity detected on an on-demand head and neck CT scan.

Endoscopic examination of the nasal cavities revealed no pathologies except for a mild septal deviation. We recommended an MRI with contrast which revealed a mass within the left sphenoid sinus suggestive for a benign fibro-osseous lesion.

On June 12, 2023, under general anaesthesia, we performed an endoscopic approach of the sphenoid sinus. After drilling the anterior wall, we found the sinus cavity filled with a fibrous trabecular mass. We performed a tumoral debulking, with surgical specimens delivered to the histopathology department. The postoperative evolution was favorable, the patient was discharged on the second day after surgery. The HP result confirmed the diagnosis of fibrous dysplasia of the sphenoid bone.

We recommended a regular follow-up with another MRI examination every 6 moths after the surgical procedure.

**Conclusion.** Fibrous dysplasia must be considered in the differential diagnosis of isolated sphenoid sinus opacities. If non-symptomatic, the best management is a regular follow-up.

#### The complicated bronchogenic cyst

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Corresponding Author: Ioana Medeea Tițu e-mail: medeea.titu@gmail.com **Introduction.** Bronchogenic cyst is a congenital, relatively rare condition, mostly located in the middle mediastinum. Extra-mediastinal locations (intrapulmonary, subdiaphragmatic) are extremely rare. It represents a dysembryoplasia of the respiratory tract, typically occurring between the  $26^{th}$  and  $40^{th}$  days of intrauterine life, with a frequency of 10-15% of mediastinal tumors and 50-60% among all mediastinal cysts. It is more common in men, predominantly diagnosed in the 3rd and 4th decades of life. The paper presents the therapeutic management of 3 cases of complicated bronchogenic cyst treated in the Thoracic Surgery department.

**Case report.** Between February and November 2022, 3 patients aged between 36-42 years (2 men, one woman), with suspected bronchogenic cyst (2 intrapulmonary, 2 mediastinal) based on computer tomography were treated in our clinic. Patient symptoms included fatigue, chest pain, productive cough, and hemoptysis. Surgical treatment, consisting of cyst excision and, when necessary, fistula closure, was performed in all cases. Histopathological examination confirmed the diagnosis of bronchogenic cyst.

**Discussion.** Up to 45% of bronchogenic cysts can be complicated without necessarily increasing morbidity and mortality. The incidence of complicated bronchogenic cysts has increased with the use of EBUS-TBNA and EUS-FNA, as a result of superinfection in partially evacuated cysts through these methods. Surgical treatment remains the only method to prevent recurrence or superinfection by removing both the cyst's contents and mucosa simultaneously.

**Conclusions.** Treating complicated cysts presents a high level of difficulty due to tight adhesions that form as a result of inflammation between the cystic wall and adjacent tissues. Puncturing and evacuating bronchogenic cysts via transbronchial, transtracheal, or transesophageal routes, which often lead to superinfection and recurrence, should be strictly avoided.

# Laparoscopic intracorporeal ileal conduit after radical cystectomy

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Corresponding Author: Matei Maximilian Buzoianu e-mail: maximilian.buzoianu@yahoo.com **Introduction.** Ileal conduit is the most common urinary diversion performed after radical cystectomy providing less long-term complications and a better quality of life for the patients, as compared to the historic cutaneous ureterostomies. An intracorporeal minimally invasive approach for this urinary diversion can lead to improved postoperative outcomes, particularly in highly comorbid patients. However, it is a technically challenging procedure which is usually done only in experienced centers.

**Objectives.** To assess the outcomes of laparoscopic intracorporeal urinary diversion after radical cystectomy, as a feasible alternative to the robotic approach in centers with limited access to robotic surgery.
**Materials and methods.** 58 consecutive patients who underwent 3D laparoscopic radical cystectomy with intracoporeal ileal conduit for muscle-invasive bladder tumors in our department were included in the current study. For ileal conduit, a 15 cm bowel loop was used, 20 cm from the ileocecal valve. The exclusion of the bowel loop and bowel reanastomosis was performed using laparoscopic staplers in all cases. The left ureter was transposed on the right side. The implantation of the ureters was Wallace in 35 cases and Bricker in 23 cases. The uretero-ileal suture was performed using 3/0 Vicryl. Mono-J ureteral stents were used in 52 cases, whereas in 6 cases double-J stents were inserted.

**Results.** Median intracorporeal urinary diversion time was 150 (min 90, max 250) minutes. There were no significant intraoperative complications. The nasogastric tube was removed in the first postoperative day. Bowel movements resumed at a mean of 3 days. The ileal conduit drainage was removed after a mean of 4 days. In the immediate postoperative period, 15 patients (25.8%) had Clavien 1-2 complications, while 4 patients (6.8%) presented Clavien  $\geq$ 3 complications: two patients presented urinary fistula (one case managed conservatively, the other case requiring excision of the ileal conduit), one patient presented postoperative bleeding that required reintervention and one patient died due to aspiration pneumonia.

The ureteral stents were removed after a mean of 4 weeks after surgery. At a mean follow-up of 12 months, 13.7% patients presented uretero-ileal stenosis (unilateral 6 cases, bilateral 2 cases), which was managed by ureteral stent or nephrostomy.

**Conclusion.** The 3D laparoscopic approach is feasible for intracorporeal urinary diversions, ensuring complete minimally invasive approach in radical cystectomies, in centers that do not benefit from Da Vinci system. Once the learning curve is overcome, performing a laparoscopic intracorporeal urinary diversion offers significant advantages to the patient with a less economic burden.

#### Racial differences in non-arteritic anterior ischemic optic neuropathy unravel its pathophysiology

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4) Department of Neurology, Emory University School of Medicine, Atlanta, GA **Introduction.** Non-arteritic anterior ischemic optic neuropathy (NAION) is a devastating cause of visual loss considered to have a mechanical pathophysiology (crowded optic disc) in addition to a vascular component (systemic vascular risk factors). Despite well-known racial differences in optic disc topography, racial differences in NAION are unknown. The aim of this study was to describe these differences.

**Material and methods.** Retrospective cross-sectional study in two tertiary neuro-ophthalmology services (states of Georgia and New York) of consecutive adult NAION patients seen between 2014 - 2022. We collected self-reported race, and ocular and systemic clinical features. We compared race data to the US Bureau of Census for each region. To demonstrate that both neuro-ophthalmology services evaluated diverse populations, we also collected racial data in idiopathic intracranial hypertension (IIH).

**Results.** Of 1,006 total NAION patients seen, 852 (84.7%) were White, 51 (5.1%) were Black, 37 (3.6%) were Asian. The percentage of White NAION patients

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Corresponding Author: Ana Banc e-mail: ana.banc@umfcluj.ro was higher than the percentage of White population in the respective states (Georgia: 91.06% vs 55.7%; New York: 78.9% vs 60.5%). The percentage of White NAION patients was significantly higher than the percentage of White IIH patients (91.06% vs 33.6% and 78.9% vs 35.7%). The majority of Black NAION patients had multiple systemic risk factors. Mean cup-to-disc ratio in Black NAION patients was 0.19±0.18.

**Conclusion.** NAION is rare in people of Black race. The relatively small cupto-disc ratio noted in our Black NAION patients is significantly lower than has been reported for the normal eyes. Even though NAION appears to mostly occur in patients with multiple systemic risk factors, optic disc crowding is likely the most important risk factor for NAION, regardless of race.

Acknowledgement. This study was conducted during a 1-year neuroophthalmology fellowship undertaken by the first author at Emory University in Atlanta, GA.

### The role of surgical experience in the management of malignant gliomas

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Corresponding Author: Lehel Beni e-mail: lehelbenimd@gmail.com **Introduction.** High-grade gliomas (HGG) remain a challenging medical condition, and despite numerous advancements in treatment modalities, their prognosis remains relatively unchanged. This study aims to investigate the impact of surgical experience on the management of malignant gliomas, with a focus on patient survival.

**Methods.** The study analyzed data from 1591 patients with pathologically confirmed glial tumors operated on between 2000 and 2020, with the surgeries performed by the same neurosurgeon. The patients were divided into two time intervals: 2000-2009 and 2012-2020. The study assessed the impact of surgical experience on patient outcomes by comparing overall survival (OS) and other factors.

**Results.** *Patient cohort:* out of the 1591 patients, 42.8% had low-grade gliomas (LGG), and 57.1% had HGG. Within the HGG cohort, glioblastoma (GBM) was the most common histological subtype, representing 68.2% of HGG cases. *Histological features:* among HGG patients, 27.9% had WHO grade III tumors, and 72.1% had WHO grade IV tumors. GBM was the most common subtype, accounting for 68.2% of HGG cases. *Survival analysis:* the study analyzed survival at 12, 18, and 24 months. Patients treated between 2012 - 2020 had better OS, with an additional survival time of 2.441 months on average. Survival varied by pathology, age groups, and extent of resection.

**Conclusions.** Surgical experience plays a crucial role in the management of HGG, significantly impacting patient survival. Patients treated by the same surgeon during the 2012-2020 period showed improved survival compared to those treated between 2000-2009. The study highlights the importance of surgical competence in neuro-oncology and emphasizes the need for patient-tailored therapies.

## Da Vinci XI nephron sparing surgery - techniques for optimizing functional results

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Corresponding Author: Eliza Cristina Bujoreanu e-mail: bujoreanucristina@yahoo.com **Introduction.** Nephron sparing surgery for renal cell carcinoma can be challenging in complex high PADUA cases.

**Material and methods.** Different techniques are explored to minimize or exclude warm ischemia during Da Vinci XI partial nephrectomy using a video collage-ICG dye, intraoperatory ultrasound and ZERO ischemia technique.

**Results.** 113 ZERO ischemia technique cases are reported, peri- and postoperatory complications, functional and oncologic results.

**Conclusion.** ICG presents a safe usage profile and along with intraoperative ultrasound, it offers guidance for selective clamping and safe tumoral excision. Zero ischemia technique is feasible within oncologic safety for complex cases, offering optimal functional results.

# Da Vinci XI robotic radical prostatectomy - extraperitoneal approach

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Corresponding Author: Eliza Cristina Bujoreanu e-mail: bujoreanucristina@yahoo.com **Introduction.** Surgery remains the gold standard treatment for localized prostate cancer and robotic surgery stretches the limits of functional results.

**Material and methods.** Using a video collage, extraperitoneal technique is presented for DA Vinci XI radical prostatectomy. Key surgical aspects for optimizing functional results are discussed.

**Results.** Peri- and postoperative results (last 4 years) are presented along with Clavien-Dindo complications.

**Conclusion.** Robotic surgery offers on point dissection and precise tissue manipulaton, enabling oncologic surgery to become functional surgery- with prezerved continence and erectile function. Extraperitoneal approach is ideal in cases with previous abdominal surgery or high BMI.

### **HOLEP Holmium laser enucleation of the prostate - initial 100** cases

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Corresponding Author: Eliza Cristina Bujoreanu e-mail: bujoreanucristina@yahoo.com **Introduction.** Prostatic adenoma challenges the life quality of almost all men as their hair turns grey, bringing low urinary tract symptoms and secondary urinary tract complications.

**Material and methods.** Using an intra operative video collage, technical aspects are discussed regarding HOLEP Holmium laser enucleation of the prostatic adenoma, the standard treatment for BPH benign prostatic hyperplasia used in the last 18 months in our hospital.

More than 100 cases are reported along with technique adjustments and up to date functional results and Clavien-Dindo complications - adapted to prostate volume.

**Conclusion.** HOLEP is a feasible treatment for BPH for different prostate sizes, with optimal functional results and minimal surgical related complications.

#### Iterative surgery for ovarian peritoneal carcinomatosis

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Corresponding Author: Corneliu Lungoci e-mail: lungocicorneliu@yahoo.com **Background.** In the past, second look (third-look) was clearly defined as an optimal procedure in the management of ovarian cancer, due to its known regional dissemination and risk of peritoneal carcinomatosis. Today, multimodal procedures combining cytoreductive surgery and intraperitoneal chemotherapy (with or without hyperthermia) are becoming the gold standard treatment for peritoneal carcinomatosis in highly selected patients, which include many ovarian cancers. Still, the treatment of isolated recurrence after multimodal approach for patients with ovarian peritoneal carcinomatosis has not been thoroughly explored.

**Methods.** We present 8 patients with such isolated tumor recurrences in whom iterative radical surgery was performed. They were selected from a dataset of 57 patients who have had optimal cytoreductive surgery and intraperitoneal chemotherapy for ovarian peritoneal carcinomatosis, between 2017 and 2022.

**Results.** The diagnosis of the recurrences was possible due to the adequate follow up of the patients, including CA 125, CT and MR imaging. Median disease-free survival was 13 months after the first procedure. Surgery was addressed to the tumor relapse in the abdominal wall, pelvic and retroperitoneal lymph nodes, around the ureter and ureterovesical junction. Despite previous extensive surgery and intraperitoneal chemotherapy, there were no significant adhesions and the complete exploration of the abdomen and pelvis was facile. Because radical surgery was achieved, no intraperitoneal chemotherapy was required. There was no significant morbidity and no mortality.

**Conclusions.** This series of patients has shown that iterative radical surgery is feasible with acceptable morbidity and mortality rates in selected patients. Selection of good candidates implies a careful follow-up after initial procedures, an accurate assessment of the extent of recurrence and of the likelihood of achieving an optimal cytoreduction.

#### Case reports of toe-to-hand transfer

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Corresponding Author: Alma Corpodean e-mail: corpodean.alma@gmail.com **Introduction.** In 1967 Yang and Gu became the pioneers in using the second toe for thumb reconstruction in humans. Nowadays, due to expanding microsurgical techniques the indication and technique for toe-to-hand transfer procedure continues to evolve from acquired injuries to congenital hand defects. There are various classification systems that take in consideration the level of finger amputation, involvement of the thumb and provide guidelines for reconstruction options. The toe transfer can be performed in a delayed or immediate manner with similar success rates.

Microsurgical transfer of toe-to-hand can restore acceptable level of function with insignificant morbidity at the donor sites. In the decision making for multiple finger amputations an important factor is represented by the specific occupational and cosmetic needs of the patient. In our cases an important factor was the restoration of hand grip and the ultimate aim was to provide at least a pattern of tripodal pinch. There are a few important principles for free transfer of toe to hand that were observed during our procedure. Although free toe transfer techniques continue to evolve, these procedures are lengthy, technically demanding and require fine microsurgical skills.

**Methods.** We present a series of two cases with a toe-to-hand transfer after trauma with finger amputation. A 40 years old male who was involved in an accident implying a table saw and lost all fingers except the thumb from the left hand. The fingers had been amputated at the level of the meta-carpo-phalangeal joint and replantation was attempted without success. A double toe transfer was done using the second and third toes of the left foot to reconstruct the third- and fourth-digits using microsurgical techniques. Another case of a 23 years old patient who suffered an injury with partial thumb amputation. The patient was working in computer science department and was in need to restore the function of the hand. We performed a single second toe transfer to the amputation stump of the left pollicis.

**Results.** After follow-up of the two patients we observed no complications, stable digits, with very good outcome in terms of mobile, pain free, good sensory feedback and aesthetic appearance.

**Conclusion.** Today the indication for toe-to-hand transfer continues to evolve but it is still a demanding surgery that requires microsurgical skills. Toe-to-hand transfer is a good option of treatment for congenital or traumatic injuries. There are some important surgery principles that should be followed during the procedure, with the transfer success implying a cumulus of outcomes.

#### Rehabilitation programs in the laryngectomized patients: impact on patients' quality of life

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 Department of ENT, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania Laryngeal cancer is the second most frequent head and neck cancer in the world. Total laryngectomy is a radical method reserved for the treatment of advanced laryngeal carcinoma or as a salvage therapy. Total laryngectomy has devastating consequences that



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Corresponding Author: Cristina Țiple e-mail: cristinatiple@yahoo.com affect the quality of life and involves numerous problems for the patient: loss of voice, difficulty swallowing, greater risk of respiratory tract infection, loss of smell, reduction of taste and alteration of social life. Loss of voice, altered swallowing and a permanent tracheostomy have a negative effect on the patient's physical and psychological status. The rehabilitation of laryngectomized patients should be approached by a multidisciplinary team as soon as possible postoperative. Comprehensive rehabilitation after total laryngectomy, with psychological support for the patient and family-caregivers, has a positive impact on the quality of life of the laryngectomized patient. Rehabilitation after total laryngectomy remains critical to optimal patient care, as well as the development of rehabilitation programs and patient education.

## Synchronous cervical sympathetic chain schwannoma, parathyroid adenoma and hypofunctional nodular goiter - a case report

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Corresponding Author: Flaviu Mureşan e-mail: flaviumuresan@gmail.com Simultaneously diagnosing cervical sympathetic chain schwannoma, nodular goiter and parathyroid adenoma is a very rare occurrence in clinical practice. We had the opportunity to find this unusual association on a female patient. While nodular goiter and parathyroid adenoma are more common diseases and easier to diagnose, identifying the etiology of a parapharyngeal space tumor remains a challenge and requires multiple imaging studies such as computed tomography scan, magnetic resonance imaging or angiography. A cervical sympathetic chain schwannoma, a carotid body tumor, a paraganglioma or a vagal schwannoma must be taken into account as possible diagnostic variants. Complaints such as Horner's syndrome, hoarse voice or dysphagia may suggest a nerve originating tumor, but this is a rare situation. Only surgical exploration is successful in detecting the tumor origin from the cervical sympathetic chain. The pathology report of the specimen finally confirms the schwannoma diagnosis.

# Management of diabetic foot ulcer in a 75-year-old woman using negative pressure wound therapy: a case report

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4<sup>th</sup> Surgery Clinic Department, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania This case presentation outlines a compelling clinical case involving a 75-yearold female patient with diabetes who developed a severe diabetic foot ulcer. The patient was treated successfully using negative pressure wound therapy (NPWT), leading to Corresponding Author: Ioan Şimon e-mail: Ioan.Simon@umfcluj.ro significant improvements in wound healing and overall quality of life.

The case begins with a comprehensive assessment of the diabetic foot ulcer, including its size, depth, and associated risk factors such as neuropathy and peripheral vascular disease. A multidisciplinary care team evaluated the patient and determined that NPWT could offer substantial benefits in facilitating wound closure.

The presentation provides a detailed account of the NPWT procedure, including the techniques used, treatment duration, and the patient's progress throughout the therapy. Before-and-after images are included to visually illustrate the remarkable changes in wound appearance and tissue healing.

The final results of the treatment demonstrate a marked reduction in the size of the ulcer, improved local vascularization, and enhance nerve function. The patient also reported a significant reduction in pain and an improvement in the ability to walk.

This presentation highlights the efficacy of NPWT in managing diabetic foot ulcers, emphasizing the importance of a multidisciplinary approach for optimal patient care. It underscores the significance of continuous monitoring and prompt management to prevent sever complications in diabetic foot cases, particularly in elderly patients. This case serves as a valuable example of successful NPWT application in the context of diabetic wound management.

### Multiparametric ultrasound in the management of breast cancer patients

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Corresponding Author: Ioana Bene e-mail: ioanaboca90@yahoo.com **Introduction.** Patients with dense breasts have an increased risk of developing breast cancer compared to patients with fatty breasts. Furthermore, for this group of patients, mammography has a low sensitivity in detecting breast cancers, especially if it is not associated with architectural distortion or calcifications.

**Material and methods.** Automated breast ultrasound (ABUS) represents a new imaging technique approved by the Food and Drug Administration (FDA) in 2012 as a supplemental screening tool for women with heterogeneously and extremely dense breasts. ABUS tends to be increasingly used as a supplementary technique in the evaluation of patients with dense glandular breasts.

Contrast-enhanced ultrasound (CEUS) in breast pathology is used for various purposes, from differentiating benign from malignant lesions and evaluating the extent of the disease to assessing the response to neoadjuvant chemotherapy (NAC)

**Results.** The hybrid images obtained at the CEUS represent an overlap of the tumor in grayscale over the enhancement pattern, which allows an appropriate evaluation of the entire lesion without including in the analysis the peritumoral area. The association of ABUS with full-field digital mammography (FFDM) and digital breast tomosynthesis (DBT) can reduce the recall rate in breast cancer screening.

**Conclusions.** ABUS is suitable as additional diagnostic imaging techniques to FFDM and even DBT in women at an intermediate risk of developing breast cancer through the presence of dense breast tissue. In this study, hybrid CEUS radiomic features might have the potential to provide a noninvasive, easily accessible and contrast-agent-safe method to assess tumor biology before and during treatment.

#### The impact of prehospital emergency medicine service volunteering experience on the healthcare students' choice of specialty

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 Emergency Department, Clinical County Hospital, Cluj-Napoca, Romania

Corresponding Author: Eugenia-Maria Lupan-Mureșan e-mail: dr.eugenia.muresan@gmail.com **Background and aim.** Volunteering in prehospital emergency medicine services (EMS) has long been recognized as a valuable learning experience for healthcare students (HS). These opportunities expose students to high-stress emergency situations and allow them to work alongside skilled medical teams. The objective of this study is to examine how volunteering in prehospital medical services influences the professional development of medical students and shapes their career choices.

**Methods.** An online survey was conducted among former volunteers of a prehospital EMS that regularly engaged HS as volunteer paramedics on intensive care mobile units. The survey focused on motivations, organizational experiences, and the perceived impact of the program on personal and professional growth.

**Results.** A total of 87 responses were collected and analyzed. The majority of respondents (85%) remained active volunteers throughout their university studies. Most volunteers worked more than six shifts per month and participated in additional activities (providing medical assistance, fundraising campaigns, and first aid teaching programs). The impact of these experiences was overwhelmingly positive, with volunteers reporting enhanced medical knowledge, decision-making skills, and work ethic. Interestingly, the proportion of volunteers who initially aspired to pursue clinical surgical specialties decreased significantly, with one in three HS pursuing a career in intensive care. However, only 9.5% of the volunteer HS ultimately chose Emergency Medicine as their profession. Many cited a desire for a better work-life balance and less demanding work hours as reasons for choosing other specialties.

While the overall impact of volunteering was positive, this study also identified areas for improvement. Continuous training, addressing workload concerns, and ensuring that academic activities are not neglected were identified as areas needing attention. The study also analyzed career choice trends among volunteers. Despite HS' dedication towards EMS volunteering, it was only a minority who chose EM for their residency training.

**Conclusions.** This research emphasizes the importance of prehospital EMS volunteering experiences for HS. To address the challenges identified, recommendations for optimizing the EMS volunteering experience include incorporating ongoing training and finding solutions to workload issues.

#### Frontal sinus mucocele with ocular complications

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Department of ENT, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Paranasal sinus mucocoele is an accumulation of mucoid secretion and desquamated epithelium within the sinus, causing the dilation of its walls, and it is considered a cystic, expansive, and destructive lesion. The frontal

Corresponding Author: Mădălina Blaga e-mail: madalina.blaga@yahoo.com sinus is the most commonly involved among the sinuses; however, frontal sinus mucocoeles represent rare causes of unilateral exophthalmos. The objective of this case presentation is to review the ocular complications arising from frontal sinus mucoceles and their management.

**Methods.** We present the case of a 54-year-old patient with a history of chronic rhinosinusitis with nasal polyps operated on multiple occasions, who presented to our service with left eye exophthalmos. Nasal endoscopy revealed completely altered anatomy, with the absence of the middle turbinates bilaterally and the absence of the medial wall of the maxillary sinus. A CT scan revealed an isodense mass in the left frontal sinus extending into the left orbit, causing mass effect on the orbital contents. Surgical intervention was performed, including a maxillary antrostomy and bilateral anterior-posterior ethmoidectomy. The frontal sinus ostium was not found, leading to the decision perform an external approach and trepanopuncture of the frontal sinus, followed by mucocoele extraction.

**Results.** Due to the lack of communication between the left frontal sinus and the nasal cavities, a second surgical intervention was performed, including a Draf III frontal sinusotomy to restore the natural drainage of the frontal sinus.

**Conclusion.** Although a small number of patients develop ocular complications from frontal sinus mucocoeles, these can have serious consequences, necessitating rapid diagnosis and knowledge of the therapeutic approach.

#### Malignant tumors of the temporal bone

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Corresponding Author: Mădălina Blaga e-mail: madalina.blaga@yahoo.com **Introduction.** Malignant tumors of the temporal bone are extremely rare entities, representing approximately 2% of all head and neck neoplasms. They can originate from any region of the temporal bone and rapidly extend to adjacent structures or can result in distant metastasis.

**Methods.** This paper presents a series of cases treated at the ENT Clinic of the Emergency County Hospital Cluj-Napoca and the therapeutic approach for these cases. The primary surgical strategy for malignant conditions of the temporal bone is the resection of the temporal bone. This resection can be limited to the ear canal and tympanic membrane or may involve the otic capsule and its contents and/or the petrous apex. The management of adjacent neurovascular structures should be considered during surgical planning. Additionally, adjuvant procedures such as parotidectomy and neck dissection may be necessary depending on the tumor stage.

**Results.** Surgical treatment was recommended and successfully performed in all mentioned cases, leading to a significant increase in patient survival rates.

**Conclusion.** Malignant conditions involving the temporal bone are becoming increasingly common and require specialized multidisciplinary care, with temporal bone resection being one of the leading techniques in the treatment of lateral malignancies of the skull base.

#### **Eosinophilic granulomatosis with polyangiitis with endonasal manifestation - a case presentation**

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Corresponding Author: Mihai Şaişuc e-mail: mihai\_saisuc@yahoo.com **Introduction.** Churg Straus syndrome – renamed as eosinophilic granulomatosis with polyangiitis (EGPA) – is a specific variant of the group of diseases characterized by necrotizing vasculitis of small and medium-sized systemic blood vessels. Other subtypes within the broad group include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and polyarteritis nodosa. Eosinophilic granulomatosis with polyangiitis can be distinguished from the others disease by the coexistence of asthma, rhinosinusitis and the presence of eosinophilia in the peripheral blood (>10% of total leukocytes count). The primary trigger in the pathogenesis of this disease, at the cellular level, seems to be an aberrant development of T-helper cells. Early recognition of the pathology and the ability to start the treatment with corticosteroids and immunosuppressants have significantly changed the natural history of EGPA, improving prognosis, and overall survival. The motivation of this article is to raise the awareness of ENT doctors about the chronic inflammatory nassal diseases.

Material and methods. We present the case of a 26-year-old female patient whose symptoms began approximately 2 years ago with swelling of the medial angle of the right eye, later noticing the appearance of nasal symptoms, such as bilateral nasal obstruction and clear rhinorrhea. In the past, the patient has undergone a lobectomy of the lower left lobe for a lung abscess. Nasal endoscopy of the right nasal fossa reveals an ulcerative tumor, which includes both nasal fossae, with the nasal septum being amputated by the tumor, in both cartilage and bone area, multiple areas of ulceration and necrosis in both nasal fossae, the upper nasal turbinates being amputated and the middle nasal turbinates being partially amputated by the tumor, with intensely modified anatomical landmarks. CT imaging demonstrates the presence of pansinusitis with destructive osteocartilaginous changes at the ethmoidal level and osteolysis of the right lateral wall. In this case, surgery is performed and multiple biopsies are taken from the affected areas of the nasal fossa, along with a total middle left mucotomy and a left maxillary antrostomy. Afterwards, a bilateral lower partial mucotomy is performed, with progression into the nasopharynx where adenoid hypertrophy is observed and biopsy fragments are taken from that area. The result of the histopathological examination pleads in favor of an eosinophilic granulomatosis with polyangiitis (Churg-Strauss Syndrome), without pathological changes at the level of the nasopharyngeal mucosa. Immunological tests reveal the presence of a positive ANCA vasculitis, and a hyper IgG4 syndrome, which is why Cyclophosphamide and Methylprednisolone therapy is initiated.

**Results.** Periodic evaluation of the patient showed improved upper respiratory tract symptoms, with improved nasal breathing, better sleep and improved quality of life. Although a close monitoring of the patient is needed with periodic nasal evaluation and monitoring of biological samples to obtain the remission of the disease.

**Conclusion.** Eosinophilic granulomatosis with polyangiitis is a rare inflammatory pathology characterized by increased blood and tissue eosinophil values, with the production of granulomatous-type inflammatory changes that result in the necrosis of small and medium-sized blood vessels. These changes often occur in the respiratory tract, being often associated with the presence of asthma. The diagnosis is based on clinical evaluations along with histopathological examinations and laboratory tests. Treatment is represented by corticosteroid therapy and immunosuppressants which have significantly changed the natural history of EGPA, improving prognosis, and overall survival. ENT physicians must recognize and understand this pathology for an adapted diagnosis and treatment planning.

### The role of inflammatory ratios in the identification of acute or complicated cases of lithiasic cholecystitis

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Corresponding Author: Vlad-Ionuţ Nechita e-mail: nechita.vlad@umfcluj.ro **Introduction.** The aim of our study was to evaluate the diagnostic value of the inflammatory ratios (NLR - neutrophil-to-lymphocyte ratio, PLR - platelet-to-lymphocyte ratio and LMR - lymphocyte-to-monocyte ratio) for acute or complicated cases of lithiasic cholecystitis without biliary obstruction.

**Material and methods.** In this study, 3247 patients with cholecystitis were evaluated after undergoing cholecystectomy at The Regional Institute of Gastroenterology and Hepatology Cluj-Napoca between January first, 2018 and December 31, 2020. After excluding non-eligible patients, 2152 patients were considered for statistical analysis. Among those patients, 606 exhibited acute cases and 1583 chronic cases of lithiasic cholecystitis without biliary obstruction.

**Results.** In acute or complicated cases of lithiasic cholecystitis, significantly higher values were observed for the absolute number of neutrophils [9.52; 95%CI (7.01-12.32)] vs. [4.45; 95%CI (3.55-5.49)]; p<0.001 – Mann-Whitney Test; for NLR [5.93; 95%CI (4.1-9.18)] vs. [2.18; 95%CI(1.7-2.8)]; p<0.001 – Mann-Whitney Test) and for PLR [168.93; 95%CI (126.02-226.3)] vs. [125.77; 95%CI (99.05-157.72)]; p<0.001 – Mann-Whitney Test. The LMR values were higher in the group with chronic cases. For the absolute number of neutrophils the ROC curve (Receiving Operating Characteristics) indicated a cut off value of 6.87 ( $10^3/\mu$ L), for which the AUC (Area Under the Curve) equaled 92%, 95%CI (90%–93%) and Se (Sensitivity)=77%; Sp (Specificity)=92%. For NLR, at a cut off value of 3.58, the AUC was 94%, 95%CI (93%–95%); while Se=83% and Sp=93%. For PLR, at a cut off value of 173.37, the AUC was 71%, 95%CI (69%–74%); with Se=49% and Sp=84%.

**Conclusion.** A good differentiation capacity was observed for the NLR in the diagnosis of acute or complicated cases against chronic cases of cholecystitis without biliary obstruction.

Acknowledgement. This research was part of the Master Thesis "The role of inflammatory biomarkers in the identification of complicated lithiasic cholecystitis" under the supervision of Assoc. Prof. Dr. Horațiu Colosi.

#### Impact of distal vein ligation on minimizing venous-lymphaticreflux during lymphaticovenous anastomosis using a rat model

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1) Department of Plastic and Reconstructive Surgery, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Due to the relatively higher pressure gradient in the vein, the antegrade venous flow and occasional retrograde venous reflux (RVR) tend to enter the lymphatic lumen after lymphaticovenous anastomosis (LVA) which can lead to venous-lymphatic reflux (VLR). VLR has been associated with a higher rate of

2) Lymphedema Center, Division of Plastic and Reconstructive Surgery, Department of Surgery, Kaohsiung Chang Gung Memorial Hospital, Taiwan

Corresponding Author: Alex Orădan e-mail: alex.oradan@gmail.com anastomotic thrombosis. Distal vein ligation (DVL) has been performed in order to reduce VLR in certain LVA configurations but its efficacy has not been elucidated. By using a rat model, the aim of this study was to measure the venous pressure at the proposed site of anastomosis before and after DVL, as well as the pressure gradient in the event of RVR.

**Material and methods.** With four sprague-dawley rats, a blood pressure sensor was placed in the femoral veins pointing toward the distal vein. Changes in blood pressure were measured during sequential clamping/unclamping of microvascular clamps to mimic DVL and RVR.

**Results.** A significant reduction in the femoral venous pressure before and after DVL was identified from a total of eight measurements  $(21.09 \pm 4.51 \text{ mmHg vs. } 16.14 \pm 1.31 \text{ mmHg}$ , respectively, p = 0.007). No significant difference was found between normal femoral vein pressure and RVR ( $21.09 \pm 4.51 \text{ mmHg vs. } 19.15 \pm 2.00 \text{ mmHg}$ , respectively, p = 0.167).

**Conclusion.** DVL may help to decrease VLR, and RVR should be avoided to minimize VLR.

#### The usefulness of first-order radiomics features extracted from ADC maps in predicting metachronous metastases in rectal cancer: a preliminary study

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 Department of Oncology, Amethyst Radiotherapy Center Cluj, Romania **Introduction.** An early detection of rectal cancer patients with a higher risk of developing metachronous metastases (MM) could enhance treatment strategies and enable more precise, personalized management approaches. The Apparent Diffusion Coefficient (ADC) is a quantitative MRI biomarker capable of evaluating the diffusion properties of soft tissues by reflecting the microscopic water mobility, thereby providing insights into tissue cellularity. This study investigates the potential of first-order (FO) radiomics features extracted from ADC maps to predict the appearance of MM in rectal cancer.

**Material and methods.** We performed a retrospective analysis of 52 patients with rectal cancer, dividing them into two groups: those who developed metachronous metastases (n=15) and those who did not (n=37). From the pretreatment ADC maps, 17 FO radiomics features were extracted. Univariate statistical analyses were employed to assess the relationship between each FO feature and the presence of MM. Features that showed statistically significant differences were then integrated into a model using binary logistic multivariable regression. The diagnostic performance of individual parameters and of the combined model was evaluated using receiver operating curve analysis.

**Results.** The following FO features were significantly higher among patients with MM compared with the ones without metastases: 90th percentile, interquartile range, entropy, variance, mean absolute deviation and robust mean absolute deviation (p values between 0.002-0.01). Uniformity was lower in subjects with distant MM. The most effective diagnostic indicators for predicting MM were the 90<sup>th</sup> percentile

Corresponding Author: Bianca Boca e-mail: bianca.petresc@gmail.com and uniformity, with an area under the curve (AUC) of 0.74 [95% CI: 0.60–0.80]. The combined model achieved an AUC of 0.80 [95% CI: 0.66–0.90].

**Conclusion.** These findings suggest that ADC first-order features hold promise for predicting the occurrence of metachronous metastases in rectal cancer.

## Intracranial epidermoid cysts: anatomical localization and postoperative complication rates

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Corresponding Author: Maria Mihaela Pop e-mail: mihaela.d.pop@gmail.com **Introduction.** Epidermoid cysts are benign congenital inclusion cysts that in rare cases may occur intracranially, accounting for approximately 0.3–1.8% of primary intracranial tumors. Our retrospective analysis aimed to assess various aspects of these cysts.

**Material and methods.** The retrospective study was carried out on 36 cases, in which we evaluated the potential correlation between cysts located in the median or paramedian cisterns and clinical factors like recurrence risk, duration of hospitalization, and postoperative complications. Patients enrolled in this study had a pathologically confirmed diagnosis of an intracranial epidermoid cyst that was surgically resected.

**Results.** The overall postoperative complication rate was 38.9% and included persistent hydrocephalus (6 cases), aseptic chemical meningitis (2 cases), CN VII and VIII paresis (1 case), pseudomeningocele (1 case), dysarthria (1 case), acute subdural hematoma and seizure (1 case), transient hydrocephalus and subdural hygroma (1 case) and pulmonary embolus (1 case). Tumor localization analysis showed that these cysts were most frequently found in the paramedian cisterns (47.2%), followed closely by the median line cisterns (41.6%). Further analysis through multivariate assessment indicated that postoperative hydrocephalus and age under 40 years were significant prognostic factors for tumor recurrence. Additionally, tumors located in the median-like region were associated with a higher risk of symptomatic hydrocephalus both before and after surgery, which, in turn, increased the likelihood of an extended hospital stay exceeding ten days.

**Conclusion.** Despite their benign histopathological nature, these cysts hold clinical significance due to the relatively high rate of postoperative complications and an increased risk of recurrence, particularly in younger individuals with associated hydrocephalus.

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## Squamous cell carcinoma of the nail bed leading to arm amputation

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Corresponding Author: Ovidiu Fabian e-mail: fabianovidiu@yahoo.com Although a rare tumor, subungual carcinoma is the most common malignant nail tumor. The symptomatology is not characteristic, being a great imitator of other nail and periungual diseases, furthermore the diagnosis is established based on biopsy. With proper treatment it usually holds a favorable prognosis. Metastatic cases are rarely encountered, but have a poor outcome. Therefore, we present the case of a patient with a subungual carcinoma that developed metastases during the course of the disease which required amputation of the arm.

#### **PHARMACY Fundamental Research**

#### Validation of a rapid and portable electrochemical method for bacterial contamination detection in water samples

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Corresponding Author: Alexandra Canciu e-mail: alexandra.canciu@elearn.umfcluj.ro **Introduction.** Water quality testing is vital to ensure safety for the population and the environment. In situations with high bacterial load, such as untreated wastewater discharges during natural disasters, a rapid testing device can prove useful to alert the field operating teams and the authorities of the risk of contamination.

**Material and methods.** Portable electrochemical custom-made sensors were designed to achieve individual and simultaneous detection of E. coli and P. aeruginosa via their markers (enterobactin – Ent and pyocyanin – PyoC). Differential pulse voltammetry was used with an ultraportable potentiostat, connected to a smartphone for data registration and transmission. After the design and optimization, the sensors were evaluated on standard solutions containing Ent, PyoC, or both, followed by the intra-lab validation to correlate the electrochemical results with culture plate method. The inter-lab validation was carried out in Spain, the Netherlands, and Romania, on different water matrices (surface-, drinking-, and wastewater). Each partner lab tested the technology and compared the results with the standard methods (culture plate and Colilert test).

**Results.** The performance of the electrochemical sensors was evaluated, and their robustness, accuracy, precision, sensitivity, and specificity were determined for the detection of the two considered bacteria. The inter-laboratory validation performed on real water samples confirmed the intra-laboratory results, the values of the analytical parameters evaluated were satisfactory, with LODs in the range of 106 CFU/mL for E. coli and 105 CFU/mL for P. aeruginosa.

**Conclusion.** The electrochemical method proved feasible for the analysis of complex samples. A future step is the integration with a tailored software app to enable fast on-site detection of pathogen bacteria in real case scenarios.

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### Synthesis and antioxidant activity of new hybrid compounds with thiazolyl-polyphenolic structure

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2) Department of Pharmaceutical Technology and Biopharmacy, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Numerous recent studies in the field of antioxidant compounds are oriented towards synthetic molecules with a polyphenolic core. The objectives of this study were to develop a series of new hybrid thiazolyl-polyphenolic compounds with antioxidant activity and to optimize their structure in order to select hit/leader molecules.

Material and methods. In the present research, we put together the polyphenol fragment with a thiazole ring in order to increase the antioxidant activity. The

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Corresponding Author: Alexandra Cătălina Cornea e-mail: corneacatalina10@yahoo.com obtention of the thiazolyl-polyphenolic compounds was achieved through Hantzsch condesation, using various thioamides and 4-chloroacetyl-catechol.

**Results.** The compounds were characterized by mass spectrometry, IR spectroscopy and nuclear magnetic resonance. Their antioxidant activity was evaluated by the free radical scavenging assay (DPPH) and electron transfer test (FRAP) using ascorbic acid as a standard. The results obtained from the tests highlighted compounds with significant antioxidant activity.

**Conclusion.** New compounds with thiazolyl-polyphenolic structure with promising antioxidant activity were obtained.

### Electrochemical aptasensor for the impedimetric detection of HepG2 cells

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Corresponding Author: Alexandra Pusta e-mail: alexandrapusta@gmail.com **Introduction.** Hepatocellular carcinoma (HCC) is the most common type of liver cancer and has an increasing incidence and mortality rate. Because HCC is usually diagnosed in advanced stages, it is important to develop sensitive, quick and accessible techniques for HCC screening and diagnosis. The detection of circulating tumor cells, such as HepG2 cells, could represent a promising screening strategy for HCC. The aim of this work was the development of an electrochemical aptasensor for the impedimetric detection of HepG2 HCC cells.

**Material and methods.** Carbon screen printed electrodes were modified with a suspension containing chitosan, graphene oxide (GO) and polyaniline nanoparticles. The carboxyl groups were activated and aptamer TLS11a was covalently bound to the activated electrode using multipulse amperometry. Bovine serum albumin was used as a blocker. Lastly, the aptasensor was incubated with increasing concentrations of HepG2 cells. All modification steps were confirmed using cyclic voltammetry, electrochemical impedance spectroscopy (EIS) and microscopy techniques. The detection of HepG2 cells was carried out via EIS.

**Results.** An increase in the resistance to charge transfer after cell incubation was observed. This was proportional to the concentration of cells, which allowed the construction of a calibration curve and the detection of HepG2 cells on a wide concentration domain (10 - 200000 cells/mL) with a limit of detection of 10 cells/mL. Serum samples were spiked with known concentration of HepG2 cells and good recoveries were obtained.

**Conclusions.** In conclusion, a label-free electrochemical aptasensor was developed for the detection of HepG2 cells.

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### Development of an electrochemical aptasensor for the detection of Protein A

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Corresponding Author: Ana-Maria Tătaru e-mail: ana.mari.tataru@elearn.umfcluj.ro **Introduction.** A major health issue around the globe is represented by the spread of bacterial species highly resistant to the available antibiotics treatment. Staphylococcus aureus (S. aureus), along with its methicillin-resistant variant (MRSA), are the cause of various infections with a high rate of morbidity and mortality. In this context, rapid and sensitive detection of the pathogens would be a useful strategy in the healthcare systems. Using the wide range of virulence factors produced by S.aureus (such as the surface component – protein A), the aim of this study was to develop an electrochemical biosensor that can detect and quantify the presence of the bacteria.

**Material and methods.** The biosensor was developed on a gold screen-printed electrode (AuSPE), on which the specific SH-modified aptamer for protein A (PA#2/8 [S1-58]) was immobilized via multipulse amperometry (MPA), the remaining unbound sites on the electrode were blocked via MPA, using an agent containing a SH-group and the target, protein A, was incubated in time (30 min). After each step, the electrode surface was analyzed using the ferro/ferricyanide redox probe, by differential pulse voltammetry (DPV) and electrochemical impedance spectroscopy (EIS). The solutions used in the analysis were all prepared in TRIS buffer pH 7.2 and DNAase free water.

**Results.** The immobilization protocol of the aptamer sequence to the AuSPE was optimized in terms of procedure (incubation in time vs. MPA) and also in terms of parameters of the MPA procedure (pulse step and duration). Various blocking agents were tested (6-mercapto-1-henaxol and 11-mercaptoundecanoic acid) and different methods of blocking the SPE surface. The incubation of protein A was also optimized, choosing the most convenient temperature and time. A wide range of concentrations of the target were tested (25 nM-1000 nM). The selectivity of the sensor was also tested in the presence of other proteins (bovine serum albumine, interleukin-6) and by using different aptamers (for cortisol and gliadine) for the detection of the target (PrA).

**Conclusion.** An electrochemical biosensor using an aptamer sequence was developed for the fast detection of S.aureus and its specific marker (protein A). A linear correlation between the concentration of the target and the electrochemical signal was observed in both DPV and EIS analysis. Also, from the selectivity studies, the aptasensor showed a high recognition capacity for the target protein.

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#### Elaboration of dendronized iron oxide magnetic nanoparticles and the evaluation of their *in vitro* magnetic hyperthermia performances

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Corresponding Author: Cristian Iacoviță e-mail: cristian.iacovita@umfcluj.ro **Introduction.** The advancements in the synthesis of magnetic nanoparticles (MNPs) have developed magnetic hyperthermia (MH) techniques for cancer treatment, offering highly localized heating by activating MNPs using external alternating magnetic fields (AMF).

**Material and methods.** By means of modified thermal decomposition technique, using home-made magnetic precursors, spherical iron oxide MNPs were synthesized, which were further coated with a dendron layer. The MNPs were systematically investigated by using transmission electron microscopy, FT-infrared spectroscopy, vibration sample magnetometry and magnetic hyperthermia. The *in vitro* studies have been performed on the cell line MDA-MB-231 (breast cancer) by means of the Alamar Blue (AB) and Neutral Red NR) tests upon an incubation time of 24 h.

Results. Our synthesis protocol produced well-dispersed faced spherical MNPs with an average diameter of 21.6 nm a spinel composition. Except the predominant Fe-O band at 566 cm-1, characteristic of magnetite, the FT-IR spectrum primarily showcases bands associated with the dendron coating: the C-O-C band around 1100 cm-1 and phosphonate bands ranging from 1100 to 800 cm-1. The MNPs exhibited a slight widening of their hysteresis loops (coercivity of 8,75 kA/m) at room temperature, indicating a weak ferromagnetic-like behavior, with a high saturation magnetization of 72,6 emu/g. At an AFM amplitude (H) of 5 kA/m, the SAR measured 135 W/gFe; this value rapidly escalated to 310 and 500 W/gFe at H of 10 and 15 kA/m, respectively. The SAR values continued to rise, albeit at a slower rate, and as H is increased beyond 30 kA/m, the SAR reached saturation around 1100 W/gFe. Considering the viability threshold of 80% for nanomaterials to be safe for biomedical applications, the MNPs do not exhibit a toxic behavior over the tested dose range ( $12.5 - 200 \ \mu g/mL$ ). The internalized amount of MNPs is quite low reaching only 27,5 % for a doping dose of 200 µg/mL. Consequently, according to both AB and NR assays, the cellular viability is not affected by the MH exposure (30 min at 355 kHz and 27 kA/m). However, when the MNPs, at doping dose of 200  $\mu$ g/mL, are mixed with cancer cells, independently of the biochemical assay used, upon the MH exposure, the important heat released by the spherical MNPs induced overt cytotoxicity of cells, the observed cellular viability being close to 10%.

**Conclusion.** Dendronized spherical iron oxide MNPs, despite their low internalization profile, are promising candidates for *in vivo* destruction of cancer tumors though MH therapy.

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### Assessment of the vitamin B12 status in Romanian families: a pilot study

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Corresponding Author: Elena Cristina Crăciun e-mail: ecgagyi@yahoo.com **Introduction.** Vitamin B12 deficiency is widespread in many countries but little information is available about vitamin B12 status in the Romanian population.

**Material and methods.** This was an observational study carried out among 38 families of vegetarians and non-vegetarians from the city of Cluj-Napoca and the surrounding rural areas. In the study group were included only subjects who declared that did not take vitamin B12 supplements or vitamin B12 fortified-food.

The serum vitamin B12 levels were measured using a chemiluminescence assay on an ADVIA Centaur XPT Immunoassay System, and were classified as follows: under 200 pg/ml (vitamin B12 deficiency) and 200-350 pg/ml (borderline level).

**Results.** Vitamin B12 deficiency has been diagnosed in 24.32% of the total investigated subjects (5.4% non-vegetarians subjects vs. 18.9% vegetarians subjects). A high prevalence of marginal status was observed in both non-vegetarians and vegetarians subjects (48.83% versus 45.16%). The prevalence of marginal status in non-vegetarians subjects was greater for men (59%) in comparison with women (38%).

**Conclusion.** The results of our study highlights the importance of vitamin B12 status screening in order to identify subjects who present a high risk for the occurrence of vitamin B12 deficiency.

### A simple electrochemical sensor for the identification of biofilm formation

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Corresponding Author: Denisa Căpățînă e-mail: DENISA.ELEN.CAPATINA@elearn. umfcluj.ro **Introduction.** The biofilm consists of an organized bacterial community encased tightly in a complex architecture formed by self-produced extracellular polymeric substances, released by bacteria into the extracellular space. Bacteria can survive and develop through the biofilm in a variety of natural, clinical, and industrial environments, including medical indwelling devices, different surfaces in hospitals or food industry. The bacteria in the biofilm are up to 1000 times more protected than their planktonic counterparts from environmental stress, detergents, antibiotics, and the host's immune system. Thus, it is crucial to develop new methods to identify and monitor biofilm formation.

Cyclic diguanosine-monophosphate (c-di-GMP) is an intracellular signaling molecule with increased importance in biofilm formation. The detection of this molecule can provide important information regarding the presence of bacterial biofilm on different products.

Material and methods. A simple electrochemical sensor based on screenprinted electrodes modified with carbon nanotubes was developed for the sensitive and selective detection of c-di-GMP. To choose the best conditions for the study, the optimal conditions in terms of electrode surface, electrolyte, pH, and electrochemical technique were determined.

**Results.** The developed sensor showed a wide detection range, very low limit of detection, high specificity, and good results in detecting the molecules of interest in real samples.

**Conclusion.** This sensor represents an important starting point for the development of "Point-of-care" devices, which allow the monitoring of biofilm formation in real-case scenarios.

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#### The biological effects of an optimized Epilobium hirsutum extract in a murine model of Ehrlich ascites carcinoma

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Corresponding Author: Ana-Maria Vlase e-mail: gheldiu.ana@umfcluj.ro **Introduction.** Epilobium genus belongs to the Onagraceae family of flowering plants and consists of approximately 200 different species. Various Epilobium species are known for their therapeutic attributes and are commonly utilized for addressing a range of health issues, such as skin disorders and prostate problems. The present study aimed to investigate the anti-tumor potential of an optimized extract of Epilobium hirsutum in a murine model of Ehrlich ascites carcinoma.

**Material and methods.** Swiss albino mice with induced Ehrlich ascites carcinoma were divided into four groups: negative control, positive control treated with cyclophosphamide, a group treated with both cyclophosphamide and E. hirsutum, and a group treated with E. hirsutum alone. Various biochemical markers related to oxidative stress and inflammation, such as malondialdehyde, reduced glutathione, oxidized glutathione, glutathione peroxidase, and catalase activities, as well as IL-6 and TNF-alpha, were assessed. Additionally, Western Blot analysis on ascites fluid and histological staining on liver biopsies were performed.

**Results.** The optimized extract of E. hirsutum demonstrated a reduction in inflammation and oxidative stress markers comparable to the positive control group. Additionally, it displayed anti-tumor potential, as evidenced by biochemical and histological findings. Western Blot analysis revealed changes in key markers of apoptosis and cancer cell progression, such as caspase-3 and -9, p53, Bcl-2, and Bax.

**Conclusion.** The study underscores the potential of the optimized extract of E. hirsutum in mitigating oxidative stress and inflammation, as well as exhibiting antitumor efficacy in an animal model of Ehrlich ascites carcinoma. Further studies are needed to explore its mechanisms of action and potential for clinical application.

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### Unlocking new avenues: solid-state synthesis of molecularly imprinted polymers

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Corresponding Author: Bogdan-Cezar Iacob e-mail: iacob.cezar@umfcluj.ro **Introduction.** Molecular imprinting enables the fast, versatile, robust and costeffective synthesis of biomimetic polymeric receptors with tailored selectivity for a wide variety of target molecules. Nowadays, molecularly imprinted polymers (MIPs) are being widely used for separation, sensing, drug delivery and diagnostics. Solvents are a critical component in the synthesis of MIPs, both as a porogen and a reaction media, however their use comes with additional challenges. On a larger scale, especially the nonpolar ones, may imply environmental concerns. Some solvents can interfere with the binding of the target molecule to the polymer matrix, leading to reduced binding efficiency or selectivity. And last, but not least some polymerization methods, such as precipitation polymerization, require the use of specific solvents or solvent mixtures. To address some of the above-mentioned issues, but also to explore potential opportunities or further constraints, we report the first solvent-free mechanochemical synthesis of MIPs via liquid-assisted griding.

**Material and methods.** The successful synthesis of the imprinted polymer has been functionally demonstrated measuring its template rebinding capacity, as well as the selectivity of the molecular recognition process in comparison with the ones obtained by the conventional, non-covalent molecular imprinting process in liquid media.

**Results.** The proof-of-concept study demonstrated similar binding capacities towards the template molecule and superior chemoselectivity compared to the conventional MIP synthesis method.

**Conclusion.** The adoption of green chemistry principles with all its inherent advantages in the synthesis of MIPs, not only alleviates potential environmental and health concerns associated with their analytical (e.g. selective adsorbents) and drug delivery (e.g. drug carriers or reservoirs) applications, but might also offer a conceptual change in the molecular imprinting technology.

### Fast and cost-effective electrochemical fabrication of SERS substrates using screen-printed electrodes

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Corresponding Author: Petrică-Ionuț Leva e-mail: petreleva@gmail.com **Introduction and objectives.** Pollutants represent a serious issue for environmental health. Pharmaceutical compounds and Pesticides are two of the most studied pollutant classes.

Raman spectroscopy is a fast and high sensitivity analysis method, offering fingerprint-like information about the studied analytes which makes it ideal for detecting multiple compounds from various samples without the need of substrate specificity.

Metallic nanostructures generated on the analyzed substrate amplify the Raman signal significantly. Electrochemically roughening the surface of gold screen printed electrodes represent the purpose of this study, in order to obtain substrates suitable for EC assisted SERS determinations.

**Material and methods.** For this experiment DropSense 220BT gold screenprinted electrodes were used. A Metrohm Autolab PGSTAT204 potentiosta and a portable PalmSens SensitSmart were used for the electrochemical procedures. The SERS experiments were performed using an AvaSpec-ULS2048x64TEC-EVO detector with a 785 nm lightsource, conected to a Nikon Eclipse Ni-U microscope. For this purpouse three substances were taken into analysis: Thiabendazole (TBZ), Propranolole (PRNL) and 4-Aminothiophenole (4-ATP). The electrochemical methods used were Chronoamperometry (CA), Fast Chronoamperometry (CAF) and Cyclic voltammetry (CV).

**Results and discussion.** The maximum surface amplification of the Raman signal was obtained with CA using 0,1M KCl as working electrolyte: 36286 counts at 1081 cm-1 for 4-ATP (RSD=12,14%), 1863,77 counts at 1386 cm<sup>-1</sup> for PRNL (RSD=21,4%) and 301,93 for the 784 cm<sup>-1</sup> peak (RSD 20,32%%) and 441,72 for the 1012 cm<sup>-1</sup> peak (RSD 21,85%%) for TBZ.

**Conclusion.** The optimal electrochemical roughening technique for obtaining a SERS substrate from screen-printed gold electrodes is chronoamperommetry. The most suitable electrolyte used for the modification of the electrode surface using chronoamperommetry is 0,1M KCl.

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## *In vitro* selection of aptamers against glycopeptide antibiotics and their evaluation for therapeutic monitoring applications

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Corresponding Author: Magdolna Casian e-mail: magdolna.casian@elearn.umfcluj.ro **Introduction.** Glycopeptide antibiotics, such as vancomycin, are the first-line treatment for severe infections caused by antibiotic-resistant Gram-positive pathogens, particularly methicillin-resistant Staphylococcus aureus (MRSA). Vancomycin has a narrow therapeutic window, and it is rather difficult to ensure safe dose determination, reason why therapeutic drug monitoring is highly required. Aptamers are short, specific, single-stranded DNA or RNA sequences artificially selected through systematic evolution of ligands by exponential enrichment (SELEX). This poster presents the main strategy and results regarding the selection of aptamers for vancomycin through magnetic beads (MBs) SELEX technology.

Material and methods. Vancomycin was covalently immobilized on carboxylfunctionalized MBs and incubated with a randomized DNA oligonucleotide library. Sequences possessing affinity were separated, amplified by polymerase chain reaction, conditioned, and used for a new round of selection. Amplification yield and DNA purity were assessed using fluorimetry and gel electrophoresis. The evolution of the selection was monitored by enrichment assays. After cloning and sequencing, the affinity of the aptamers was evaluated using surface plasmon resonance (SPR).

**Results.** After 9 cycles of selection, round 7 showed the highest bound percentage towards vancomycin (47%) and was chosen for further cloning and sequencing experiments. Through SPR measurements, dissociation constant (Kd) values as low as 260 nM were obtained.

**Conclusions.** The most promising aptamer will be further incorporated into an electrochemical sensor for the quantification of vancomycin from clinical serum samples.

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#### Electrochemical aptasensor for cortisol detection in biological fluids based on a customized platform

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Corresponding Author: Maria-Bianca Irimeş e-mail: maria.bi.irimes@elearn.umfcluj.ro **Introduction.** Cortisol (COR) is an active endogenous compound involved in cellular and humoral immune response, glucose homeostasis, and other several physiological and pathological processes. It is secreted in numerous biological fluids and its levels change in various chronic diseases, for example in inflammatory-associated disorders. Sensitive and selective detection of COR is therefore of major importance in evaluating the diagnosis of the disorder and the response to therapy. Electrochemical methods represent an advantageous approach for analyzing biomarkers, such as COR, in biological samples due to the high sensitivity and specificity, suitability for miniaturization, and in situ analysis. The main objective of the study was to design a customized platform for COR specific electrochemical detection in biological samples with prospects for biomedical applications.

**Material and methods.** Flexible, customized carbon electrodes were in-lab printed by using conductive and insulating inks. Then, the surface of the working electrodes was functionalized/decorated using a nanocomposite based on Au and Pt to increase the sensitivity and an aptamer to increase the specificity for COR detection in complex matrix. The aptamer was bound via thyol-gold chemistry to the functionalized electrode using multipulse amperometry. A thiol with a linear chain was used to minimize the non-specific adsorption of species present in real complex matrices such as biological fluids. Lastly, the aptasensor was incubated with COR. All modification steps were confirmed using cyclic voltammetry and electrochemical impedance spectroscopy.

**Results.** The elaborated platforms were characterized via specific electrochemical methods, analyzed regarding the analytical performances (detection limit, limit of quantification, and sensitivity for COR) and will be used for real samples analysis.

**Conclusion.** The elaborated aptasensor allows COR specific detection and it can be further developed for medical applications.

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#### Fatty acid profiles of omega-3, 6, 9 enriched vegetable oils

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Corresponding Author: Katalin Nagy e-mail: Nagy.Katalin@umfcluj.ro **Introduction.** The omega-3 and omega-6 fatty acids (FAs) are important components of the human body, due to their multiple biological roles1. In the last few years, a wide variety of functional foods enriched with omega-3, 6 and 9 FAs have become commercially available2. Hence, this study aims to compare the traditional vegetable oils to their omega enriched counterparts, and to distinguish which are only marketing strategies and which are truly beneficial for the consumers' health.

Material and methods. The sample preparation involved a transesterification processes, followed by a derivatization with boron trifluoride-methanol solution and an extraction in hexane. Samples were analyzed by GC-MS, using a special column, Zebron<sup>™</sup> ZB-FAME.

**Results.** Comparing the traditional sunflower oil and the high oleic sunflower oil, there is a huge difference in their fatty acid composition. The traditional one has a larger amount of PUFA, mainly omega-6, which consumed in large quantities supports inflammation. On the other hand, the high oleic sunflower oil is more stable to heat and oxidation, having a higher percentage of MUFA and a lower amount of PUFA. The composition of the high oleic sunflower oil is similar to the olive oil, made up of about 75% oleic acid. However, the olive oil is richer in the omega-3 fatty acid. Vegetable oils marketed with omega 3, 6 label have a high omega-6/omega-3 FA ratio, as is found in today's Western diets, which promote the pathogenesis of many diseases. Not only the components of the vegetable oils can influence the percentage of the omega-3 FA, but also the method of extraction. Results demonstrate that the refining process can reduce the quantity of these type of fatty acids.

**Conclusions.** The present study shows that unrefined rapeseed oils and high oleic sunflower oils have a better fatty acid composition, although the omega-3 FA content is very low compared to the recommended daily dose.

#### Heterocyclic chalcones and their flavonoid cyclization products: synthesis, chemical behavior and biological properties

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Corresponding Author: Denisa Leonte e-mail: leonte.denisa@umfcluj.ro **Introduction.** Natural chalcones and their flavonoid cyclization products are recognized for their vast therapeutic potential and represent structural models for the creation of new synthetic analogs with improved pharmacological properties. Our aim is to provide an overview of the synthesis, chemical behavior and biological properties of some synthetic analogs of chalcones with heterocyclic structure. Attention is focused on the reactivity of the  $\alpha$ , $\beta$ -unsaturated carbonyl system in the chalcones structure, which provides access to new flavonoid analogs, as well as to other polyheterocyclic compounds: epoxides, azoles and azines.

Material and methods. Heterocyclic chalcones and ortho-hydroxychalcones were synthesized by Claisen-Schmidt condensation of heterocyclic aldehydes with substituted acetophenones. The oxidative cyclization of heterocyclic orthohydroxychalcones was investigated in different reaction conditions in order to establish the most efficient methods for the synthesis of flavones, flavanones, hydroxyflavones and aurones, considering that in practice it is difficult to predict the cyclization pathway in certain reaction conditions.

**Results.** A vast series of heterocyclic chalcones and ortho-hydroxychalcones have been synthesized, characterized and evaluated for their anticancer activity. The cyclization of ortho-hydroxychalcones occured differently depending on the reaction conditions, providing access to new flavonoid analogs with heterocyclic structure. Several chalcones and flavonoid cyclization products presented significant anticancer activity on multidrug-resistant cancer cell lines.

**Conclusions.** The most efficient methods for the synthesis of heterocyclic flavones, hydroxyflavones, flavanones and aurones by cyclization of orthohydroxychalcones have been established. The obtained heterocyclic chalcones and their flavonoid cyclization products with anticancer activity represent structural models for the design of new anticancer agents.

#### Impact of COVID-19 pandemic on diet and lifestyle

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Corresponding Author: Oana Mîrza e-mail: oana.stanciu@umfcluj.ro **Introduction.** The COVID-19 pandemic has had a notable impact on various aspects of life around the world. One area that has registered considerable changes is food consumption and lifestyle choices. The restrictions imposed to limit the spread of the virus, together with the uncertainty surrounding the pandemic, have led to substantial changes in people's consumption habits, food choices and lifestyle. The purpose of this research was to investigate the impact of the COVID-19 pandemic on food consumption habits and lifestyle behaviors on a group of subjects in Romania, with the objective of understanding the factors underlying these changes.

**Material and methods.** An original observational and retrospective study was conducted, distributing an anonymous online questionnaire via Google Forms between May and July 2023. Information related to diet and lifestyle during the COVID-19 pandemic was collected from 205 participants aged 18 years and older, from urban and rural environments in Romania, the data being processed statistically.

**Results.** The study revealed significant increases in the consumption of snacks between meals (48%), sweets (48%) and fast food (36%). At the same time, the frequency of preparing meals at home increased by 60%, and 54% of the subjects increased their consumption of dietary supplements for immunity. There was also a 40% decrease in regular physical activity and a 69% increase in stress and anxiety levels. However, to date most participants have maintained their weight relative to the period of restrictions caused by the COVID-19 pandemic, but 37% reported weight gain during the isolation restrictions.

**Conclusion.** Even if, in relation to the present moment, the subjects returned to their pre-pandemic weight, under the conditions caused by the stress of the restrictions, significant changes in nutrition were observed. These data can contribute to the development of more effective approaches promoting a healthy lifestyle.

## Dinner in the daily routine - habits of Romanian young adults (18-45 years)

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Corresponding Author: Oana Mîrza e-mail: oana.stanciu@umfcluj.ro **Introduction.** Dinner is one of the three main meals of the day and is the last meal of the day, before sleep. Although for some reasons, many people tend to skip dinner, it is very important because it is followed by the night fast during sleep. Skipping dinner is not a good choice because it comes with a series of dysfunctions of the body's metabolism, the disruption of the circadian clock and can lead to certain pathologies, including insomnia, obesity, cardiovascular diseases, diabetes. The purpose of this study was to evaluate dinner habits among young people in Romania.

**Material and methods.** To achieve the objective of the study, an anonymous questionnaire containing 23 questions was applied between May and July 2023, online, using the Google Forms platform. The target group was randomly selected, depending on the availability, interest and curiosity of each person. The only exclusion criterion from the study was not falling within the age range of 18-45 years. In total, a number of 256 completed questionnaires were obtained from both women and men, from rural or urban areas.

**Results.** To begin with, 83.6% of the subjects stated that they had eaten dinner the previous day, but only 60% indicated that they had a daily evening meal consumption. The time at which the participants stated that they usually serve dinner was generally between 18:00 and 20:00, followed by 20:00-22:00. Among the respondents' preferences, it was observed that fresh fruits, cheeses, dairy products and bakery products were declared as the most consumed, and chicken was the respondents' next favorite food during the evening meal (56.5%), being consumed with a frequency of 2 to 6 times a week, paticularly by those with increased BMI.

**Conclusion.** Considering the fact that it is the last meal before sleep, it is important to consider what food is eaten at dinner and in what quantity, but the most important is the time at which it is served.

#### Diet influence in the development and treatment of acne

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Corresponding Author: Denisia Paşca e-mail: denisia pasca@yahoo.com **Introduction.** Acne can occur when excess sebum clogs the pores in the skin at the base of hair follicles, causing small pustular eruptions, most often affecting teenagers and young adults, although it may also be present in some older people. Eating behavior plays a crucial role in this process, alleviating or aggravating the symptoms of this pathology. In this sense, the aim of this work was to establish the relationship between diet and acne, but also to observe how diet can influence acne prevention and management in order to complement medical treatment on Romanian population.

**Material and methods.** A cross-sectional, non-interventional study was conducted between June-July 2023. A questionnaire that included demographic data, description of pathology manifestations, dietary habits and food frequency was

administered. The inclusion criteria were the involvement of subjects from Romania, aged between 15 and 40 years.

**Results.** A total of 348 subjects participated in this study, with a majority of 93.4% female subjects. Regarding eating habits, it was observed that less than half (35.7%) of the participants consumed daily fruit, vegetables and leafy green vegetables. Considering the frequency of consumption of milk and dairy products, the differences were not significant between people with and without acne. Consumption of fish and seafood once or 3 times a week was higher among participants without acne. A percentage of 73.5% of the subjects experienced acne problems when they increased their consumption of junk food and fast food. It was observed a correlation between increased milk consumption and the development of acne lesions. In addition, participants observed an increase in acne lesions when they increased their consumption of carbonated beverages and pastries.

**Conclusion.** Nutrition had an important contribution in acne pathology, so unhealthy eating habits have aggravated the symptoms of this condition.

### Rydberg-type electronic excited states in sodium-doped water clusters

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Corresponding Author: Roxana-Diana Paşca e-mail: roxana diana pasca@yahoo.com **Introduction.** Electronic transitions in sodium-doped water clusters were investigated considering the CCSD-type coupled-cluster level of theory. The equation-of-motion coupled cluster method combined with the second similarity transformation expanded on the domain based local pair natural orbitals (DLPNO-STEOM-CCSD) provides an efficient way to calculate excitation energies of the Rydberg-type electronic transitions with high accuracy. The results for different electronic transitions show Rydberg-type orbitals with different special configuration, indicating large delocalization over the water molecules for the 3s1 electron of the sodium atom.

**Methods.** Back transformed equation-of-motion coupled cluster (bt-PNO-EOM-CCSD); DFT: double-hybrid wB2PLYP exchange-correlation functional; Software: Orca 4.2.1; Orca 5.0.1.

**Results.** Electronic excited state energies obtained at DFT level of theory, considering the wB2PLYP exchange-correlation functional match very well with results computed with accurate wavefunction method considering the back-transformation equation-of-motion coupled cluster with singlet and doublet excitation (bt-PNO-EOM-CCSD) expanded on the localized pair natural orbitals.

**Conclusions.** All of the electronic transitions found for different Na-(H2O)n cluster structures show Rydberg-type excitation character, where due to the excitation the 3s1 electron of the sodium moves on the water cluster. It was also found that the first ionization energy lies mainly between the fourth and fifth excited states.

### The use of surface microscopy and ultrasensitive vibrational spectroscopy techniques in life sciences

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Corresponding Author: Nicoleta-Simona Vedeanu e-mail: nicoletavedeanu@yahoo.com **Introduction.** Scientific and technological progress, manifested through high precision methods for investigating various types of biological samples, holds significant premise in modern medicine. The will of developing non-invasive, painless, fast, and safe analyses represents a true challenge. Techniques such as Atomic Force Microscopy (AFM), Raman spectroscopy, and Surface-Enhanced Raman Spectroscopy (SERS) can fulfill all these aforementioned criteria.

This study focused on two primary research pathways. Firstly, we have evaluated the properties of specific dental materials with the goal of quantifying their level of penetration into dental tissues. This parameter was determined via AFM and SERS. The second part of the study was based on identifying new biomarkers present in liquid biopsies (blood and saliva) using Raman/SERS, which offer notable diagnostic potential.

**Material and methods.** On the evaluated teeth, cavities were performed and treated with the investigated material dentin and enamel. AFM was used to identify the topographic characteristics of the material-to-tooth interface. Additionally, SERS was employed to determine the penetrating ability of the material.

Moreover, the SERS technique was applied to assess serum and saliva samples isolated from a number of patients and volunteers to highlight the distinctive characteristics of the two sample groups.

**Results.** Following AFM and SERS analyses, it was determined that the dental material exhibits a penetration of approximately hundreds of nanometer.

Regarding the SERS analysis of liquid biopsy samples, vibrational bands situated at 639, 1136, and 1657 cm-1 (in serum) were attributed to uric acid and hypoxanthine, amino acids, and phospholipids, amide I, and 732 and 2107 cm-1 (in saliva) were attributed to hypoxanthine and potassium thiocyanate. In addition to these bands, the spectrum was dominated by the characteristic molecular fingerprint of the protein spectrum.

**Conclusion.** AFM and Raman/SERS techniques can serve as a promising starting point for obtaining valuable insights in addressing the concerns of both clinicians and researchers. These methods offer a hopeful approach for evaluating dental material properties and identifying biomarkers in liquid biopsies, opening new avenues in modern medicine and non-invasive diagnostics.

#### Deep eutectic solvents and ultrasound-assisted extraction applied in the analysis of polyphenolic compounds from Ribes nigrum L. leaves

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1) Department of Toxicology, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The nutritional and nutraceutical benefits of blackcurrants are widely recognized. When it comes to bioactive compounds, blackcurrant leaves surpass the fruits, presenting significant potential for health improvement.

**Objective.** This study aimed to assess the efficiency of deep eutectic solvent (DES) extraction in obtaining polyphenolic-rich extracts from Ribes nigrum L. leaves

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Corresponding Author: Maria-Beatrice Solcan e-mail: beatricesolcan@yahoo.com collected in Obcinile Bucovinei, Romania, and to select the most efficient eutectic solvent.

**Material and methods.** The extraction process involved a combination of traditional solvents, specifically ethanol: water (1:1, v/v) (S1) and acetone: 1% acetic acid (1:1, v/v) (S2), as well as a variety of deep eutectic solvents, applying ultrasound-assisted extraction (UAE). The obtained extracts underwent LC-MS analysis for a detailed phytochemical profile assessment.

**Results.** Compared to UAE extracts in conventional solvents, the UAE-DES extracts displayed the same phytochemical profile but with lower concentrations of polyphenolic compounds (e.g.: isoquercitrin: 75.760 µg/mL in S1 and 75.298 µg/mL in S2 vs. 58.757 µg/mL in citric acid:choline chloride), except for kaempferol (0.888 µg/mL in S2 vs. 1.411 µg/mL in citric acid:choline chloride). The determined values are comparable to those reported in other similar studies that used UAE for the analysis of bioactive compounds from blackcurrant. Future work aims to optimize UAE-DES extraction by using rational design of experiments (DoE) for extraction's optimization.

**Conclusions.** UAE proves to be an environmentally friendly and highly effective technique for extracting bioactive elements from the leaves of Ribes nigrum L. Deep eutectic solvents, particularly the citric acid:choline chloride (1:1, w/w) mixture, are noteworthy for their low toxicity. The optimization of extraction parameters through DoE approaches is anticipated to increase the extraction's efficiency.

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#### **PHARMACY Pharmaceutical Specialties**

## **Development of a PAT platform for the prediction of granule tableting properties**

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Corresponding Author: Tibor Casian e-mail: casian.tibor@umfcluj.ro **Introduction.** This work proposed the development of a multi-instrument PAT platform for the prediction of granule downstream processability in terms of tabletability, detachment (DS), and ejection stress (ES). Predicting these attributes, by fusing data derived from NIR spectra and particle size distribution (PSD) is expected to provide a better control of the tableting process.

**Material and methods.** The calibration set formulations were prepared according to a full factorial experimental design with 3 factors (Granulation temperature, time, Binder content) and two levels of variation. Granule samples were characterized using laser diffraction method and ransmittance NIR spectra. Dynamic compaction analysis was performed using a single punch Gamlen GTP, series D tablet Press.

**Results.** The complementarity between NIR spectra and particle size distribution (PSD) data was highlighted, revealing that 69.7% of the variability in the NIR data was correlated with 50.5% of changes in PSD. Further, the decomposed sources of variability in the NIR data were regressed against the varied factors during sample preparation. As the binder percentage and granulation temperature had an impact on granule growth, the latent variables correlated with PSD data were significant. Also, multiple unique sources of variation (orthogonal components) from the NIR dataset were correlated with the binder content, demonstrating the complementary nature of the data sets. The use of Mid Level Data Fusion (MLDF) enabled the development of models with improved predictive performance compared to individual methods.

**Conclusions.** The results of this work demonstrate the advantages of fusing complementary sources of data for the control of complex quality attributes relevant for the tableting process.

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# **Optimized preparation of herbal extracts and evaluation of their biological properties for wound care**

Diana Antonia Safta (Drîmbărean)<sup>1</sup>, Cătălina Bogdan<sup>1</sup>, Ana Maria Vlase<sup>2</sup>, Laurian Vlase<sup>3</sup>, Anca Pop (Cherfan)<sup>4</sup>, Sonia Iurian<sup>3</sup>, Rahela Carpa<sup>5</sup>, Mirela L. Moldovan<sup>1</sup>

 Department of Dermopharmacy and Cosmetics, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The objective of the study was to obtain optimized plant extracts from three plants harvested from the spontaneous Romanian flora: Sambucus nigra, Epilobium hirsutum, Lythrum salicaria.

Material and methods. By applying the experimental plans, the extraction of the active principles was maximized. Thus, their biological effects were evaluated. Three



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Corresponding Author: Cătălina Bogdan e-mail: catalina.bogdan@umfcluj.ro D-optimal experimental plans with N=13 experiments were used to study the influences of the extraction method (ultra-turrax-assisted extraction, ultrasonic-assisted extraction), ethanol concentration in the extraction solvent (30%, 50%, 70%) and extraction time (3, 5, 10 minutes) on the total content of polyphenols and flavonoids The optimization of the extraction was achieved by maximizing the response variables, and the phytochemical profile of the optimized extracts was analyzed by LC-MS/MS and LC-UV-MS/MS. The antioxidant capacity was assessed by colorimetric tests: DPPH, TEAC, FRAP. The antimicrobial effect on Escherichia coli, Pseudomonas aeuginosa, Staphylococcus aureus (MSSA, MRSA) was also determined. Cell viability assay, antioxidant capacity and scatch assay were performed on HaCaT and BJ, and the anti-inflammatory effect on BJ was analyzed by measuring the levels of IL-6 and IL-8, using ELISA kits.

**Results.** The following optimal extraction conditions were obtained: ultra-turraxassisted extraction with 70% ethanol for 3 minutes for Epilobium hirsutum, Lythrum salicaria, respectively for 6 minutes for Sambucus nigra. The major compounds of the optimized extracts were rutin and chlorogenic acid. Sambucus nigra extract displayed high biocompatibility, while Lythrum salicaria and Epilobium hirsutum extracts showed increased antioxidant capacity. Sambucus nigra and Lythrum salicaria extracts showed anti-inflammatory effects, and Epilobium hirsutum extract exhibited the best in vitro wound healing effect.

**Conclusion.** The optimized herbal extracts showed promising in vitro biological activities and complementary effects, with wound healing potential.

## Pharmacokinetic drug-drug interaction study of aripiprazole with bupropion in rats

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Corresponding Author: Iulia-Maria Ciocotișan e-mail: iulia.ciocotisan@umfcluj.ro **Introduction.** Aripiprazole (APZ) is currently a first line atypical antipsychotic drug for schizophrenia. CYP2D6 and CYP3A4 are the primary metabolic pathways which form its active metabolite dehydro-aripiprazole (DHA). Bupropion is an antidepressant agent, known for inhibiting the CYP2D6 isoenzyme. The purpose of the experiment was to assess the pharmacokinetic (PK) drug interaction of bupropion on APZ and DHA using in vivo animal model.

**Material and methods.** The two-period study consisted of 12 Wistar albino rats. During the first period (reference), rats received a single, oral dose of 8 mg/kg body weight (b.w.) APZ. The second period (test) consisted of a 5 day pretreatment with 43 mg/ kg bupropion b.w. followed by another bupropion dose and the APZ single dose. Venous blood samples were collected. LC-MS was used to determine plasma concentrations of APZ and DHA. A non-compartmental analysis was conducted to determine APZ and DHA PK parameters for the two periods.

**Results.** Bupropion pretreatment led to a 2-fold increase in the mean peak plasma concentration (Cmax) and a greater than 4-fold increase in the time to reach Cmax for both unchanged APZ and metabolite, compared to the reference period. Areas under the curve increased by 570% for APZ and by 400% for DHA when bupropion was administered.

**Conclusion.** Aripiprazole and dehydro-aripiprazole's pharmacokinetics were significantly modified when bupropion was administered in animal model, increasing the drug exposure. The clinical significance of this pharmacokinetic interaction has to be further investigated.
# Expanding community pharmacists' roles in pharmacovigilance in Romania

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Corresponding Author: Alexandra Toma e-mail: toma.alexandra@umfcluj.ro **Introduction.** Community pharmacists are the health professionals that are the most accessible to ambulatory patients, being in the best position to assist them with the safe use of medicines. The aim of our paper was to analyze the legal and professional framework for the community pharmacists' activity in Romania, to identify ways of expanding their roles in pharmacovigilance.

**Material and methods.** To this end, we carried out documentary research and a thematic analysis in comparison with the Best Practice Paper on Pharmacovigilance and Risk Minimisation, which expresses the Pharmaceutical Group of the European Union (PGEU) policy regarding the European community pharmacists' roles in pharmacovigilance.

**Results.** The Romanian standards of pharmacy education and training do not include pharmacovigilance among mandatory disciplines, contrary to the development and complexity of this field. The Romanian legislation acknowledges the community pharmacists' competence, but it does not include all the roles they may play in pharmacovigilance. It only mentions informing patients about risks associated with dispensed medicines, monitoring flu vaccinated patients in community pharmacies and reporting adverse reactions to the competent authority. The ongoing regulatory process regarding pharmaceutical services may be beneficial for expanding the community pharmacists' roles in pharmacovigilance, by setting specific standards for training and monitoring patient treatments.

**Conclusion.** Building up a culture of pharmacovigilance, with expanded roles for community pharmacists, requires patient-centered education and training, legislation to include pharmaceutical services in the health insurance system and standards of professional ethics in pharmacovigilance.

# Study of the bioprotective capacity of bilberries against ochratoxin. A bioaccessibility and biological effects of gastrointestinal digests *in vitro*

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2) Laboratory of Food Chemistry and Toxicology, Faculty of Pharmacy, University of Valencia, Burjassot, València, Spain **Introduction.** The presence of mycotoxins in cereals and cereal products remains a significant issue. The use of natural ingredients such as bilberries (Vaccinium myrtillus L. species, VM), could be a strategy to reduce mycotoxin content and also to counteract their harmful effects. In this sense, the aim of this work was to evaluate the effects of bilberries on reducing ochratoxin A (OTA) bioaccessibility and cytotoxicity.

**Material and methods.** Contaminated barley flour was produced by incubating barley with Aspergillus steynii fungus for about 30 days to a concentration of  $149.05 \pm 7.89$  mg/kg. Four different bread typologies were prepared and subjected to an in vitro

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Corresponding Author: Denisia Paşca e-mail: denisia\_pasca@yahoo.com digestion model: Control (C), VM, OTA and OTA-VM. To evaluate the cytotoxicity of gastrointestinal digests and the possible influence of bilberries at the cellular level, the MTT assay was performed and cytofluorometric studies were carried out.

**Results.** The concentration of OTA in contaminated breads were:  $15.42 \pm 0.95$  mg/kg for OTA-bread and  $17.09 \pm 0.75$  mg/kg for OTA-VM-bread while in C and VM breads the presence of OTA was not detected. In the intestinal digestion experiments, the presence of VM decreased OTA bioaccessibility by 16-19%. Compared to OTA digest, OTA-VM digest had a beneficial effect on cell viability at every exposure time. Regarding the alterations in cell cycle phases and in apoptosis/necrosis pathway, a significant increase in cellular death was observed for the OTA digest, while the addition of VM demonstrated a protective effect. These positive results have also been confirmed by ROS analysis and mitochondrial ROS generation, with a significant decrease in ROS for OTA-VM digest comparing to OTA digest.

**Conclusion.** Overall, it is confirmed the use of bilberries as a potential functional ingredient, showing protective effect in mitigation of OTA.

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# Continuous versus intermittent linezolid administration in critically ill patients. A prospective pharmacokinetic study

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5) Department 2 of Anesthesiology and Intensive Care, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Linezolid is an antibiotic used in the treatment of infections with gram-positive bacteria, including in critically ill patients. They present important pathophysiological changes that cause changes in linezolid pharmacokinetics (PK) – pharmacodynamics (PD). Thus, fluctuating concentrations were identified with periods of subtherapeutic concentrations leading to a variable clinical response and implicitly with an increased risk of developing bacterial resistance. To overcome these shortcomings, the alternative variant of continuous administration of linezolid was proposed.

The study objective was to compare the pharmacokinetic parameters of linezolid administered to critical patients by intermittent (II) versus continuous (CI) infusion.

**Material and methods.** In the study were included 31 patients, divided into two groups. CI group received linezolid by continuous infusion (600 mg loading, followed by 600 mg every 12 hours administered over 12 hours), and II group by intermittent infusion (600 mg every 12 hours administered over 1-2 hours). The serum linezolid concentrations were measured using a validated method of liquid chromatography coupled to mass spectrometry (LC-MS). Pharmacokinetic parameters of linezolid were evaluated.

**Results.** Differences in serum linezolid concentration were observed between the two groups. In group II, important fluctuations were recorded during the treatment in most patients. More stable serum concentrations were recorded in the CI group, avoiding periods of subtherapeutic concentrations.  Intensive Care Unit, Clinical Municipal Hospital, Cluj-Napoca, Romania

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#### Effects of preanalytical factors on human saliva proteome

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Corresponding Author: Andreea-Maria Soporan e-mail: soporanandreea28@gmail.com **Introduction.** Salivary biomarkers are increasingly being used as an alternative to diagnose and monitor the progression of various diseases due to their ease of use and non-invasiveness. Regardless of the saliva collection method, efficiency and reproducibility in sample preparation key steps are pivotal in proteomic studies. The aim of this study was to assess different protein isolation techniques and investigate the impact of the solubilization agent on the salivary proteome.

**Material and methods.** In this study, unstimulated saliva was collected and pooled from 10 healthy adult volunteers. Given the matrix's low protein content compared to other biological fluids, both raw and concentrated saliva were used. Here, 3 different proteome isolation methods were tested: precipitation by methanol-chloroform (MeOH-Chl) procedure, incubation with trichloroacetic acid for 60 minutes (TCA60) and overnight. Impact of the solubilization buffer was considered by resuspending the protein pellet in 8M urea/ 2M thiourea (UT) buffer or 0.1% Rapigest® prepared in 50 mM ammonium bicarbonate. Protein concentration was determined by Bradford Assay prior to SDS-PAGE and in-gel digestion with trypsin. Samples were subjected to nanoLC-MS analysis and processed with Progenesis QI.

**Results.** The protein content relied on the isolation method rather than the buffer used, TCA60 isolation method being the most effective. Additionally, SDS-PAGE analysis revealed a significant reduction in the abundance of HMW proteins when MeOH-Chl method was used and an improved band separation with Rapigest®buffer. By LC-MS we were able to identify more matrix specific proteins when using the UT buffer and confirm a shared core of 123 proteins between all conditions tested.

**Conclusion.** By this study we were able to optimize two important proteome sample preparation steps for the saliva matrix, confirming TCA60 together with UT buffer for improved coverage of the saliva proteome.

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

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Corresponding Author: Maria-Georgia Ștefan e-mail: stefan.georgia@umfcluj.ro **Introduction.** Oxidative DNA damage can lead to mutations and influence gene expression. 8-oxo-2'-deoxyguanosine (8-oxo-dG) and 8-oxo-2'-deoxyadenosine (8-oxo-dA), oxidation products of 2'-deoxyguanosine (dG) and 2'-deoxyadenosine (dA), respectively, have been used as biomarkers of DNA oxidation, but raise analytical challenges, given their low concentrations in samples compared to non-oxidized nucleosides. The purpose of this study was to develop and validate a novel method for the quantitation of 8-oxo-dG and 8-oxo-dA that facilitates the evaluation of the pro-oxidant/ antioxidant potential of xenobiotics, including selective serotonin reuptake inhibitors (SSRIs).

**Material and methods.** LC-ESI(+)-MS/MS analysis was performed using a Waters Acquity UPLC system coupled with a TQD detector. Chromatographic separation of analytes was achieved with gradient elution on a C18 column, using a mixture of 0.1% acetic acid/methanol as mobile phase. 15N5-2-deoxyguanosine and 2'-fluoro-2'-deoxyadenosine were used as internal standards.

**Results.** Adequate peak shape and separation of analytes were achieved, which allowed their accurate quantitation. The method showed good linearity for all analytes (dG, dA, 8-oxo-dG, 8-oxo-dA). The intra- and inter-day assay precisions (<5% CV) and the inaccuracy for each of the analytes ( $\pm15\%$ ,  $\pm20\%$  at LLOQ) were satisfactory.

**Conclusions.** A UPLC-MS/MS method for the fast and sensitive analysis of dG, dA, 8-oxo-dG and 8-oxo-dA, was developed and validated as a tool for the assessment of DNA oxidation in biological matrices and, consequently, to evaluate the antioxidant/prooxidant effects of xenobiotics. Limited data has been reported regarding SSRI influence on DNA oxidation. Quantifying these DNA oxidation biomarkers after SSRI exposure could reveal new aspects regarding their redox modulating potential.

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### UPLC-MS/MS investigation of the redox pathways involved in the electrochemical degradation of selected synthetic cathinones

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 Department of Toxicology, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The development of fast and accurate detection methods for emerging substances of abuse, such as synthetic cathinones (SCs) is essential for limiting illicit drug production and trafficking. A promising option for on-site detection of SCs are electrochemical sensors, including screen-printed electrodes (SPEs). The development of such sensors requires knowledge of the redox pathways involved in the electrochemical degradation of SCs. The purposes of this study were to confirm 2) Department of Analytical Chemistry and Instrumental Analysis, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

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Corresponding Author: Maria-Georgia Ștefan e-mail: stefan.georgia@umfcluj.ro the electrochemical degradation of selected SCs and to identify the obtained oxidation products.

**Material and methods.** Aqueous solutions of alpha-pyrrolidinopentiophenone (PVP), N-ethylhexedrone (NEH), 3-chloromethcathinone (3CMC) and 4-chloroethcathinone (4CEC) were subjected to chronoamperometry and the electrolyzed (E) and non-electrolyzed (NE) samples were analyzed using a UPLC-PDA-MS/MS system. E and NE solutions were infused into the mass spectrometer to identify supplementary ions occurring in E solutions. In addition, to confirm the identity of the oxidation products, LC-PDA-MS (/MS) analysis (Scan mode) was performed and fragmentation patterns were proposed in accordance with the obtained mass spectra.

**Results.** The electrochemical degradation of all SCs was confirmed by the decrease of the chromatographic peaks corresponding to parent compounds. The presence of oxidation products was suggested by the occurrence of supplementary ions in the MS spectra of E solutions. PVPox (m/z = 246), NEHox (m/z = 192), 3CMCox (m/z = 184) and 4CECox (m/z = 184) could be observed as novel chromatographic peaks, during LC-PDA-MS/MS analysis.

**Conclusions.** UPLC-PDA-MS/MS analysis allowed the identification of the compounds formed during the electrochemical oxidation of PVP, NEH, 3CMC and 4CEC, which were in accordance with previously reported data for SCs.

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### LC-MS profiling, antioxidant, and antiproliferative assessment of a phytotherapeutic product

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Corresponding Author: Alina Uifălean e-mail: alina.uifalean@umfcluj.ro **Introduction.** Conventional chemotherapy's side effects and multidrug resistance drive the ongoing search for more well-tolerated and effective agents. Thus, natural compounds with antitumor activity hold an immense potential. This study aims to comprehensively characterize a commercially available herbal preparation, evaluating its composition, antioxidant properties, and antiproliferative effects.

**Material and methods.** Analysis encompassed the reconstituted herbal mixture (RHM) and the individual plant grinds. Extraction involved 50° ethanol refluxing followed by lyophilization. Phytochemical characterization employed a Waters I-Class instrument coupled with Synapt G2-Si high-resolution mass spectrometer. Antioxidant activity was assessed using Folin-Ciocalteu, aluminum trichloride, and DPPH free radical scavenging assays. Cytotoxicity investigations used the MTT assay against LX-2 normal hepatic cells and SK-HEP-1 hepatic adenocarcinoma cells. The antiproliferative mechanism was determined by measuring the lactate dehydrogenase (LDH) release and caspase-3 activity.

**Results.** LC-MS results revealed that the main bioactive compounds were phenolic acids and flavonoids. Of these, sixteen were quantified using 5-point calibration curves. The lyophilized RHM extract exhibited high levels of chlorogenic



acid, 3,5-di-caffeoyl quinic acid, and rosmarinic acid. The ethanolic RHM extract displayed a total phenolic content of 28.50±2.5 mg GAE/g, a total flavonoid content of 7.28±0.7 mg QUE/g, and 17.42±1.2 mg AAE/g. The IC50 value was 228.24±25.2  $\mu$ g/mL for the tumoral SK-HEP-1 cells, and more than double for LX-2 cells. LDH and caspase-3 assays indicated membrane permeabilization and LDH release, indicating necrosis as the primary cell inhibition mechanism.

**Conclusion.** The investigated phytochemical preparation contains various phenolic acids and flavonoids, exhibiting clear antioxidant and antitumoral properties.

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### Effects of exenatide versus sitagliptin on beta-cell function, insulin resistance and cardiovascular risk factors

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Corresponding Author: Anamaria Apan e-mail: anamaria.cristina@elearn.umfcluj.ro **Introduction.** In this study, we aimed to compare the effects of exenatide long-acting release (LAR) and sitagliptin on beta-cell function, insulin resistance, and cardiovascular risk factors.

**Material and methods.** A 12-week interventional, open-label, single-center study, including 30 patients (19 males and 11 females) with uncontrolled type 2 diabetes (HbA1C>7%), already treated with metformin and sulfonylureas, that needed therapy intensification with a GLP-1 receptor agonist (Exenatide LAR) or a DPP-4 inhibitor (Sitagliptin) was conducted. Patients received either exenatide LAR 2 mg (subcutaneous) once per week or sitagliptin 100 mg (oral) daily. Blood samples were collected at the inclusion visit and after 12 weeks of therapy to investigate the effects of the two drugs on glycemic parameters, HOMA-IR, C-Peptide, and C-reactive protein (CRP).

**Results.** After 12 weeks, both treatments showed a significant reduction from baseline of HbA1C (p<0.001). A significant treatment difference (p<0.008), favoring exenatide, was shown at endpoint for HOMA-IR (-19.3% decrease; p<0.005) and C-Peptide (-67.1% decrease p<0.001). CRP levels were slightly decreased by both treatments, without statistical significance. Exenatide LAR showed a significant decrease in BMI (from 34.9 kg/m<sup>2</sup> [28.6;41.2], to 33.6 kg/m<sup>2</sup> [27.4;39.8], p<0.001) and waist circumference (from 112.7 cm [103.1;122.3], to 109.8 cm [100.9;118.7], p<0.001) compared to baseline and to the sitagliptin group.

**Conclusion.** Exenatide LAR showed better effects compared to sitagliptin in terms of improving glycemic parameters, insulin resistance and slightly lowering cardiovascular risk factors.

### The evaluation of antipsychotics side effects using the GASS scale among hospitalized patients

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Corresponding Author: Maria Mădălina Andrei e-mail: madaandrei225@yahoo.com **Introduction.** The antipsychotic treatment requires side effects monitoring to assure treatment safety and patients adherence. The aim of this study was to apply the GASS (The Glasgow Antipsychotic Side-effect Scale) (1), consisting in 22 self-explanatory questions, to evaluate the adverse reactions occurred during the treatment with antipsychotic drugs for inpatients from a psychiatric hospital in Romania.

**Material and methods.** After translation and validation, the GASS scale was applied to 81 male patients hospitalized for at least 7 days in the psychiatry department of Emergency County Clinical Hospital in Cluj-Napoca. The frequency of the adverse effects and their association with other drug classes such as thymostabilizers, benzodiazepines, antidepressants and anticholinergics was evaluated.

**Results.** The SNC side effects were the most reported, 60.49% of patients accusing sleepiness during the day, while 38,27% admitted they felt "like a zombie". Also, a significant percent of 41.97% patients complained they gained weight. An equal number of patients mentioned their movements were slower than usual, which suggests the presence of extrapyramidal side effects. The most frequent anticholinergic side effect was found to be xerostomia (38.27%).

**Conclusion.** The GASS is a useful tool for the detection of antipsychotic adverse reactions and can also be applied by the clinical pharmacist. The identification and management of adverse reactions could reduce the patient's level of distress and therefore could increase the adherence to treatment.

### Elevated plasma levels of D-amino acids as biomarkers for chronic kidney disease

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3) Department of Nephrology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Chronic kidney disease (CKD) is a long-term condition in which kidneys gradually lose their function. Currently, serum creatinine is the most used marker in evaluating kidney function but has several shortcomings. The aim of this study was to investigate alterations of D-amino acids (D-AAs) plasma levels as a diagnostic tool.

**Material and methods.** Analysis of D-AAs in plasma samples was conducted using an enantioselective LC-IM-MS method. A straightforward sample preparation approach for plasma was implemented, involving the removal of proteins and phospholipids. The method was evaluated in compliance with the latest regulations in terms of matrix effect, calibration curve and range, accuracy and precision, carry-over and sample stability. Plasma samples collected from 30 CKD patients and 30 healthy controls were analyzed.

**Results.** Analysis of the two datasets (CKD and control) revealed significantly altered D-AAs plasma levels. In particular, PLS-DA highlighted six D-AAs, namely

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Corresponding Author: Luisa-Gabriela Bogoș e-mail: BOGOS.LUISA.GABRIELA@elearn. umfcluj.ro D-Gln, D-Asn, D-Ser, D-Met, D-Lys, and D-Ala, being elevated compared to the control group. Each of these D-AAs can differentiate among the two groups with a high degree of confidence (AUC>0.92).

**Conclusion.** This study revealed a subset of six D-AAs as potential biomarkers for CKD, with possible application in early diagnosis and monitoring. Further studies are required to validate these results on a larger cohort.

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### Potentially inappropriate medications in Romanian older adults - comparison of three widely used explicit (criteria-based) screening tools

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Corresponding Author: Corina Briciu e-mail: Briciu.Corina@umfcluj.ro **Introduction.** Polypharmacy and use of potentially inappropriate medications (PIMs) is common among older adults and can be associated with numerous adverse outcomes, including an increased risk of death, falls and hospitalization. This study aimed to identify PIMs in older adults using three sets of widely known explicit criteria, to compare the screening results and to evaluate their concordance.

**Material and methods.** In this observational study, medications prescribed to Romanian community-dwelling older adults ( $\geq$ 65 years) during October-December 2022 were retrospectively analyzed. PIMs were identified using three explicit criteria-based tools: AGS Beers Criteria (2023), Screening Tool of Older People's Prescriptions (STOPP)-version 3 criteria (2023), and The European Union (EU)(7)-PIM list (2015). Cohen's kappa coefficient and the prevalence adjusted biased adjusted kappa (PABAK) were used to measure the level of concordance between the three sets of screening results.

**Results.** Based on our preliminary analysis, a total of 534 medical prescriptions (86.14% electronic) were collected from 62 community pharmacies. They belonged to 511 patients (61.84% women), most of whom (88.45%) were aged between 65 and 84 years. Cardiovascular and rheumatologic indications were the most frequent. Of 2344 medications prescribed, 31.78%, 15.18%, and 27.94% were identified as PIMs according to Beers, STOPP and EU(7)-PIM criteria. The most common PIMs were diuretics (25.1%)-Beers criteria, Z-drugs (11.52%)-STOPP criteria, respectively nonsteroidal anti-inflammatory drugs (NSAIDs; 10.84%)-EU(7)-PIM list. A fair to moderate level of concordance was found among criteria.

**Conclusion.** The screening tools could be useful to community pharmacists for assessing PIM use in older adults, but access to more health care data is needed to optimize their interventions. Based on our analysis, we highlight the need to develop a country-specific tool better adapted to our local context.

### The formulation of orodispersible dosage forms containing natural compound-based nanocarriers for pediatric use

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Corresponding Author: Andreea Cornilă e-mail: cornila.andreea@yahoo.com **Introduction.** This study follows the development of orally disintegrating tablets (ODT) and oral lyophilisates (OL) containing zein-based nanocarriers loaded with loratadine. Due to its biocompatibility and structural particularities, zein is a protein that shows great potential as an excipient for paediatric oral dosage forms.

**Material and methods.** An optimal nanosuspension (oNS), obtained through the antisolvent precipitation of the zein-loratadine solution in an aqueous dispersion containing sodium alginate and caseinate, was defined with the aid of an experimental design. The oNS was subsequently formulated into OL and ODT. The OL were prepared by dispersing a matrix former and a bulking agent in the oNS and subsequent lyophilization. To prepare ODT, the oNS was turnedinto lyophilized powders with the aid of three cryoprotectants, these powders being further mixed with co-processed excipients for ODT and compressed. Both dosage forms were submitted to pharmaceutical testing.

**Results and discussion.** All the OL and most ODT exhibited disintegration times under 180 seconds, as required by the European Pharmacopoeia, while the tablets compressed under lower pressures tended to be friable beyond the acceptable limit.

**Conclusions.** Because of the controlled release properties of the main constituting protein in the nanocarriers and the added functionality brought on by the other polymers, this proof-of-concept could be used in the future for the development of innovative patient-friendly solid oral dosage forms.

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### Identification of clinically relevant genotypes – the experience of a Romanian medical testing laboratory

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2) Department of Morphologic Sciences II, Cellular and Molecular Biology and Histology, Faculty of Medicine, "Carol Davila" University of Medicine and Pharmacy, Bucharest; Synevo Romania **Introduction.** Pharmacogenetic testing aims to assess the existence of a genetic predisposition that could influence the efficacy or safety of pharmacotherapy.

The objective of the present study was to offer a descriptive analysis of the results of the pharmacogenetic tests carried out between 2017 and 2022 within the Synevo laboratories, a provider of medical testing with national expansion.

**Material and method.** To carry out this analysis, data on the following tests offered by the Synevo laboratories were evaluated: genotyping CYP2D6, CYP2C9, CYP2C19, TPMT (thiopurine S-methyltransferase) and factor V Leiden. For each type of test, information was collected on the demographics of the patients tested, as well as the test result. Data were statistically analyzed and interpreted.

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Corresponding Author: Cristina Pop e-mail: cristina.pop.farmacologie@gmail.com **Results.** In total, 27.788 pharmacogenetic tests were performed in the considered time interval. Most patients for whom pharmacogenetic testing was performed were women (83.47%), and as for the age range, patients between 31-40 years old (38.76%) and those between 19-30 years old (31.68%) predominated. In the evaluated sample, genetic variants associated with a potential risk of influencing pharmacotherapy could be identified in a proportion of 54% for the CYP2D6 gene, 43% for the CYP2C9 gene, 47% for the CYP2C19 gene, 5% for the TPMT gene and 11% for factor V Leiden.

**Conclusions.** Pharmacogenetic tests can provide useful information to clinicians in order to personalize pharmacotherapy. Although the interest of medical professionals in these tests is increased, there are currently several impediments to the prescription and routine clinical implementation of pharmacogenetic testing.

### Development of sustained release gastroretentive floating tablets with carvedilol fabricated via fused deposition modelling 3D printing

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Corresponding Author: Ioan Tomuță e-mail: tomutaioan@umfcluj.ro **Introduction.** Three-dimensional printing (3DP) enables the fabrication of complex pharmaceutical products that are readily customizable depending on the specific needs of each patient. **The aim** of this work was to fabricate 3D-printed sustained-release gastroretentive floating tablets. Specifically, we focused on the development of a dual-compartment tablet design consisting of an immediate-release compartment (IRC) that promotes the prompt onset of the desired pharmacological effect through the fast release of the active substance, and a slow-release compartment (SRC) that could maintain the effect over a prolonged timeframe. Carvedilol was selected as a model drug that could benefit from being included in dosage forms with prolonged gastric residence times.

**Material and methods.** Hot melt extrusion was employed for the preparation of polyvinyl alcohol-based API-loaded filaments used as feedstock material for the fabrication of the IRC, while hypromellose-based carvedilol-loaded filaments were prepared and used for the fabrication of the SRC. The filament drug loadings ranged between 5-25 % w/w. The tablets were manufactured via fused deposition modeling 3DP. Low infill percentages that created voids in the internal structure of the tablets were applied to support buoyancy.

**Results.** The evaluation of the carvedilol-loaded filaments revealed that proper printability is attainable through a comprehensive understanding of the effects

of formulation variables on the mechanical properties of the filaments. Our results highlighted that through an appropriate selection of formulation and tablet design strategies coupled with optimized process parameters, the fabrication of sustainedrelease gastroretentive floating tablets with tailored API doses and release profiles is achievable.

In **conclusion**, this work emphasizes the value of FDM-3DP as a fabrication platform that could readily deliver personalized medications.

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### Evaluation of disulfide bond poly(amido amine) nanoparticles as suitable nanocarriers for mRNA delivery

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Corresponding Author: Ioan Tomuță e-mail: tomutaioan@umfcluj.ro **Introduction.** Poly (amine amido) (PAA) (NP) disulfide bond nanoparticles are composed of cationic and bioreducible polymers and are promising nanocarriers for mRNA delivery. This study was an attempt to further improve the transfection efficiency of these PAA NPs, at lower concentrations of low cytotoxic mRNA.

**Material and methods.** The QbD approach was initiated with conducting a failure mode effects analysis (FMEA) to identify critical factors. It indicated that the type of polymer, polymer-genetic payload (P:G), and dose of mRNA(D) used were the critical factors for which a screening design of the experiments was performed. In this study, 3 different PAA polymers with different functional groups were compared in order to determine the best polymer for NP formulation.

**Results.** The result shows that the P:G ratio has less significance in cell transfection, compared to the type of polymer and mRNA dose which showed significant variations in transfection rates. Cell transfection was inversely proportional to P:G ratios and directly proportional to mRNA dose. The optimization design inferred that the P:G ratio to 10:1 to 18:1 and the dose of RNA administered from 408 to 480 ng, gave the best transfection rates. These design space results were then validated by performing transfection experiments under the conditions indicated by the optimal reference point (P:G:10:1 ratio and 432 ng RNA dose). Results on cell viability and transfection were shown to be accurately predicted by the model to provide the highest mean cell transfection and viability of HEK293 cells (CV-103.13% and CT - 3670.8  $\mu$  units/ug), Jurkat cells (CV - 76.9% and CT - 302.44  $\mu$  units/ug), and C28/I2 cells (CV - 100.54% and CT - 2126  $\mu$  units/ug).

**Conclusions.** The design space for higher cell transfection rates was successfully determined. PAA NPs that have been formulated from optimal runs could also transfect hard-to-transfect cells, such as Jurkat cells, with less toxicity.

### Improvement of simvastatin loaded filaments processability in order to prepare 3D printed tablets via fused deposition modeling

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Corresponding Author: Ioan Tomuță e-mail: tomutaioan@umfcluj.ro **Introduction.** Nowadays, 3D printing (3DP) is gaining momentum to prepare customized solid pharmaceutical forms, one of the most used and accessible techniques for this purpose is that of fused deposition modeling (FDM). This technique requires filaments loaded with active pharmaceutical ingredients (APIs), filaments that will be used to obtain printed tablets. The objective of the study was to improve the printability of filaments containing simvastatin obtained via hot melt extrusion (HME), where polyvinyl alcohol (PVA) was used as filament former.

**Material and methods.** Different extruders (single screw and twin-screws extruder) were used to prepare the filaments. Simvastatin filaments were prepared based on an experimental design with two variables (percentage of API and presence of a secondary polymer in the filament) and three levels of variation.

**Results.** The 11 filament formulations were tested regarding the elasticity and fracturability (texture analysis), fracturability during feeding through the printer's feeding system and preparation of imprints from the studied filaments. It was determined that the type of extruder significantly influences the ability to obtain suitable filaments for 3DP, usable filaments only being obtained in the case of the twin-screw extruder. Also, the presence of the secondary polymer (Soluplus) being essential in obtaining filaments that can be processed by FDM and the increase in the percentage of API determines the increase in the fracturability of the filament during feeding into the printer nozzle.

**Conclusion.** For simvastatin, the technique of filament preparation, the percentage of API and the secondary polymer significantly influences the quality of the filaments and implicitly of the obtained tablets.

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### **DENTAL MEDICINE**

### Salivary metabolomics: a source of biomarkers in oral health

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Corresponding Author: Ana-Maria Condor e-mail: ana.mari.condor@elearn.umfcluj.ro **Introduction.** Metabolomics is an emerging technology with biomarker discovery potential. Saliva contains many components found in blood and is easily obtainable and bioinformation-rich. Salivary metabolomics could provide biomarkers for oral diseases and become a diagnostic, prognosis and disease monitoring tool in oral health, thus motivating further research. Our purpose was to highlight the possibilities of salivary metabolomics in oral health.

**Material and methods.** A comprehensive search of electronic databases was performed to identify studies using salivary metabolomics in oral health. The inclusion criteria were clinical trials published in English over the past decade that used saliva samples and metabolomics analysis.

**Results.** In oral diseases, salivary metabolomics research has concentrated mainly on periodontitis and oral cancer. Children's carious lesions were also investigated. Salivary metabolomics can potentially discover biomarkers for these pathologies. This presentation emphasizes the importance of researching new analytic technologies in order to develop new methods of screening, diagnosis and prognosis of oral pathologies.

**Conclusions.** The salivary metabolome is complex and still not completly elucidated. Further research is required, on larger samples and using established protocols. Biomarker research and development is fundamental to screening strategies and oral health preventive protocols.

# AGEs biomarkers in periodontitis – emerging compounds of diagnosis

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3) Department of Pedodontics, Faculty of Dental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The objective of this study was to evaluate periodontal status in a population group, correlated with local and general parameters. Moreover, seven advanced glycation end products (AGEs) were investigated as potential salivary and plasmatic biomarkers of periodontitis.

**Materials and method.** The human cohort study was approved by ethics committee no. 93/8.03.2017 and included patients above 18 years old. Salivary and blood samples of the patients were collected for AGEs assessment. Saliva was harvested using a disposable Salivette®, whereas blood was collected from the upper arm in sterile vacutainers. The periodontal diagnostic was established clinically and radiologically, using the classification of periodontal diseases proposed in 2018.

**Results.** A total of 159 patients were enrolled into the present study, with 85% of patients (n=135) diagnosed with periodontitis. Out of the 135 patients diagnosed with periodontitis, 18% (n=25) presented stage I of periodontitis, 21% (n=28) presented stage



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Corresponding Author: Vlad Andrei e-mail: dr.andreivlad@gmail.com II, 35% (n=47) presented stage III, whereas 26% (n=35) were diagnosed with stage IV of periodontitis. Out of the evaluated AGEs, the plasmatic concentrations of Carboxymethyllysine (CML), Fructose-Lysine (FruLys), Pyralin (Pyr) increased with the severity of periodontal disease.

**Conclusions.** The present study reveals a high presence of periodontitis in the general population, with the more severe forms of periodontal disease (stages III and IV) more prevalent. Three plasmatic concentrations of AGEs (CML, FruLys and Pyr) were correlated with the severity of the periodontal disease and have the potential of being applied as biomarkers of periodontitis.

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### Immunological correlations between oral health and general health

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Corresponding Author: Ana Emilia Constantin (Oprița) e-mail: ae.constantin13@gmail.com **Introduction.** In the current context in Romania, most cases of gastric cancer are detected in advanced stages. Screening campaigns for gastric cancer such as screening tests (digestive endoscopy) are not implemented, and they are generally invasive and not very easily accepted by patients. P-53 protein increased levels are linked with gastric cancer. The aim of this review was to identify and highlight the correlations between blood and saliva concentrations of p-53 protein in gastric cancer correlated with oral health, in order to develop an easy and rapid screening test.

**Material and methods.** A literature search was conducted of 305 articles published at an interval of 5 years on the platforms PubMed, Science Direct, Web of Science, Scopus, using as keywords: "gastric cancer", "p-53 autoantibodies", and "oral health". The study was descriptive, with the aim of synthesizing the data published on this topic.

**Results.** Searching the scientific platforms with the keywords "oral health" and "gastric cancer" returned a total of 305 articles, and applying the inclusion and exclusion criteria, 18 articles were included.

**Conclusion.** The results of this study have opened the way for new research to clarify the subject in dispute, but which still does not have enough data from the literature to indicate a clear direction.

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### **Evaluation of condylar inclination by using artificial inteligence: Axiograph versus Modjaw**

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Corresponding Author: Cosmin Ifrim e-mail: cosminifrim95@gmail.com **Introduction.** As modern dentistry is constantly evolving, artificial intelligence is widely used to improve the diagnosis and treatment options for the complex pathology of the stomatognathic system. The electronic Cadiax Compact (Gamma Dental, Klosterneuburg, Austria) and Modjaw® (Modjaw, Villeurbanne, France) are used to track the functional movements of the temporomandibular joint and to assess the accurate values of the condylar inclinations. The aim of this study was to evaluate the repeatability and the reliability of the sagittal (SCI) and transversal (TCI) condylar inclination values recorded by using two different digital devices, the Axiograph and Modjaw.

**Material and methods.** The clinical study was carried out on 17 patients, aged between 20 and 30 years, 10 women and 7 men. The SCI and TCI values were measured at 3 and 5 mm of condylar displacement, in three different recording sessions for each patient, by using the Axiograph and Modjaw. For the statistical analysis, the left and right SCI and TCI values were used. The intraclass correlation coefficient (ICC) was used to assess the repeatability of the recordings. The comparative analysis between the right and left sides and between the two analysis devices was performed by using the Wilcoxon signed-sum test. The Bland-Altman diagram assessed the agreement between the two quantitatively measured methods.

**Results.** For both Modjow and Axiograph recordings, the ICC values were above 0.90, indicating an excellent repeatability of the measurements. The SCI measurements were statistically significantly higher (p<0.05), both at 3 mm and at 5 mm, for Modjaw registrations compared to those performed by using the Axiograph. Still, the TCI values were higher for Modjaw, but close to the level of statistical significance. For the average SCI and TCI values recorded on the left and right temporomandibular joints, for each device, at 3 mm or 5 mm, there were no statistically significant differences, except for the SCI recorded with Modjaw at 5 mm, for which the median had higher values on the right side (7.56 mm) compared to the left side (p=0.024). The Bland-Altman plot showed that the SCI values were higher for Modjaw compared to Axiograph by 5.9 (95% CI 3.9 - 8.2) and the differences were greater for 3 mm recordings compared to 5 mm ones.

**Conclusion.** The Modjow and Axiograph recorded showed excellent repeatability. No significant differences were found between the SCI and TCI values recorded on the left and right temporomandibular joints, for each device and for each type of movement, at 3 mm and 5 mm. For Modjaw measurements, SCI and TCI values were greater at 3 mm and 5 mm compared to those recorded by using the Axiograph.

### Orthodontic tooth movement acceleration via local administration of pharmacological agents: a comprehensive systematic review

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Corresponding Author: Cristina Dora Ciobotaru e-mail: cd.ciobotaru@gmail.com **Introduction.** Enhancement of orthodontic tooth movement (OTM) in order to decrease the total treatment time has gained an increased interest over the last decades, with local administration of pharmacological agents being a widespread approach, mostly trough local injections. The aim of this systematic review was to investigate the outcomes, action and efficiency of different substances that modulate the OTM.

**Material and methods.** A literature search was conducted trough eight electronic databases, of which two electronic registers, up to March 2023. Grey literature was also searched by hand trough the references of the included studies. The Prisma 2020 checklist was followed throughout the study. The PICOS format was used, evaluating experimental *in vivo* controlled studies in which healthy participants were undergoing OTM and local administration of pharmacological substances to accelerate the rate of OTM was performed. The researched outcome was quantitative, and where possible, qualitative data concerning the rate of OTM in comparison to control groups. A number of 28 (animal model) studies were included, as well as 8 human studies.

**Results.** Among the included studies – up to March 2023, only one animal study used a topical route of administration of the researched pharmacological substance, while administration trough local injection was chosen in the vast majority of the eligible studies. Among the agents with proposed potential of accelerating OTM, arachidonic acid metabolites (PGE1 and PGE2), hormones (PTH, Calcitriol) and cytokines were mostly investigated.

**Conclusion.** The vast majority of the experimental studies employs local (injectable) methods of drug administration for OTM acceleration, with non-invasive topical administrations in the form of mucoadhesive systems remaining insufficiently evaluated. Suitable pharmacological preparations could be developed to provide the appropriate release of the active agents, at the desired rate and amount in order to enhance OTM in difficult cases.

# A comparative evolution of the open bite treatment of monozygotic twins

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Department of Orthodontics, Faculty of Dental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Open bite malocclusion is a vertical discrepancy characterized by the lack of contact between the upper and lower teeth, with a genetical and functional etiology. This paper presents a comparative evolution of the open bite treatment of a pair of monozygotic twins. The etiology of the malocclusion was both hereditary and functional, with a tongue thrusting habit overlapped. In theory, similar treatment outcomes would be expected when following the same treatment protocol for twins with similar initial

Corresponding Author: Olimpia Bunta e-mail: olimpia.bunta@yahoo.com diagnosis, but different results make us question the proportion between the genetical and functional etiological factors, and the way they influence the malocclusion in the two reported cases.

**Material and methods.** A pair of monozygotic twins was selected from the database of the Orthodontics and Dentofacial Orthopedics Department at the University of Medicine and Pharmacy "Iuliu Hațieganu". The orthodontic morphological diagnosis was the same in both cases: skeletal open bite. Tongue thrusting was present in both cases. The treatment plan included fixed orthodontic appliances, high-pull Headgear and open bite elastics. A comparative analysis was carried out on the initial records (orthopantomography and cephalometric analysis), the records made during treatment and present-time records.

**Results.** At the time of the examination, one of the twins had normal vertical occlusion, as a result of the counter clockwise rotation of the mandible, whereas for the other one the anterior open bite was still present, no mandibular autorotation being observed during treatment.

**Conclusion.** Although the diagnosis, ethiology and treatment approach were similar for both twins, the treatment outcome was different due to distinct mandibular rotational response. In addition, it seems that functional factors also play an important role in treatment response.

### Influence of 2D vs 3D imaging on endodontic strategies in clinical decision making

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Corresponding Author: Daria Brădățan e-mail: dariabradatan@gmail.com **Introduction.** In recent years, the Cone Beam Computed Tomography (CBCT) has been used more and more in dentistry, including in endodontics. Therefore, relevant studies are necessary to evaluate the effectiveness of this paraclinical investigation. The aim of the present study was to identify if, in certain cases, the CBCT imaging can change the treatment plan and the perceived difficulty of a case in endodontics. A secondary objective of this study was to identify the differences in the treatment plan based on work environment, experience, postgraduate studies of endodontics and radiology and speciality in dentistry.

**Material and methods.** To achieve the purpose of this study, an online form was used. The form consists of three sections. One section that collects data for the statistics, one section with 2D imaging and another section with CBCT imaging of 5 cases. For each of the 5 cases in the two radiology sections, two questions are asked. The first question asks for a treatment plan from the options given and the second question asks for the perceived difficulty of the case.

**Results.** The examiners altered the treatment plan in 40.71% of the cases. After seeing the CBCT imaging, the non-invasive treatment plans were changed for the endodontic retreatment or extraction. The indication for extraction increased among experienced examiners. Also, the clinicians who did not attend postgraduate studies avoided the retreatment option. The perceived difficulty of the cases changed in 56.07% of the cases and, out of those, 69.10% perceived an increased difficulty after seeing the CBCT imaging. Also, the perceived difficulty decreased in the experienced category and for the clinicians who did not attend postgraduate studies.

**Conclusion.** CBCT imaging influences the decision-making process and the perceived difficulty of a case and it is a useful paraclinical examination in endodontics. Therefore, further studies are needed to offer scientific support for the indications and the development of this imaging method.



#### The predominant types of bacteria in peri-implantitis

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Corresponding Author: Ondine Patricia Lucaciu e-mail: ondineluc@yahoo.com **Introduction.** Nowadays, dental implants are widely used in the treatment of edentulous patient and the restoration of lost functions of the dento-maxillary apparatus. Although they offer an aesthetic and functional rehabilitation, being the most natural therapeutic solution, dental implants present certain susceptibilities, such as the deposition of bacterial plaque and the appearance of peri-implant conditions of infectious etiology, mucositis and peri-implantitis. These conditions lead to the destruction of soft and hard tissues and ultimately, the loss of the implant. Both mucositis and peri-implantitis are caused by bacteria from the oral biofilm on the surface of the dental implants, however, its exact composition is currently unknown. We have done this literature research in order to summarize the articles published on this topic and to find out which are the main bacteria species identified in peri-implantitis.

**Material and methods.** Articles published in three databases were searched: Pubmed, Embase and Web of Science using Prisma guides and combinations of MeSH terms and, by applying the inclusion and exclusion criteria we selected 25 items from the 980 found.

**Results.** The quantified results of the studies included in this review showed that the most commonly identified bacterial species in peri-implantitis were Gram-negative anaerobic species such as *Prevotella, Streptococcus, Fusobacterium* and *Treponema*.

**Conclusion.** The bacterial species most frequently identified in peri-implantitis were Gram-negative anaerobic species. The result of the study can be a good starting point for future research or for the development of new therapeutic protocols.

### Comparative study on the degree of marginal microinfiltration between two adhesive systems of different generations

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3) Department of Polymer Composites, "Raluca Ripan" Institute of Chemistry, "Babes-Bolyai" University, Cluj-Napoca, Romania **Introduction.** Today's minimally invasive dentistry is based on the effectiveness of dental adhesive systems, but marginal microinfiltration remains the main cause of secondary carious lesions. From this perspective, the present experimental study consists in the comparative analysis of two adhesive systems of different generations in achieving a stable interface between dental tissue and composite resins used as restorative materials.

**Material and methods.** To carry out the study, 20 wisdom teeth extracted for orthodontic purposes were used, which were divided in two groups. The ability to achieve a durable adhesive bond using a conventional adhesive system compared to a new generation one was identified by optical microscope evaluation of the degree of microinfiltration at the interface of a selected tracer. The hybrid layer obtained in both groupes was also analyzed, by assessing its continuity, thickness and structure.

Results. Marginal microinfiltration of the tracer was present in both groups, at

Corresponding Author: Monica Laura Rusu e-mail: rusu.monica.laura@gmail.com the level of the vertical walls of the cavities, while on the pulpal wall the presence of the tracer was not recorded for any specimen involved. The two adhesives compared, 4th generation OptiBond FL and 8th generation Futurabond DC have similar results regardind marginal sealing.

**Conclusion.** There is no statistically significant difference between the two adhesive systems studied regarding the degree of microinfiltration of the restorations. However, the group in which the new generation (8th) adhesive system was used had a lower frequency of marginal infiltration.

#### Full digital approach in a severe dental wear case using injection molding technique and glass ceramic restorations

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Corresponding Author: Manuela Tăut e-mail: tautmanuela@gmail.com **Introduction.** Tooth wear is a common and growing dental disorder in which tooth structure is lost by factors other than dental caries or trauma. Severe tooth wear accompanied by a large loss of tooth structure, exposed dentin, and a large loss (>1/3) of the clinical crown. Patients who have significant tooth wear may require complex restorative care, which entails complete rehabilitation at an increased vertical dimension of occlusion. In order to achieve a complex diagnosis and treatment protocol in specific severe dental wear, digital dentistry currently brings together all new digital technologies (intraoral scanners, digital smile design software, virtual facial bow, digital mandibular kinematics, and digital occlusal analysis).

**Material and methods.** This case study provides a comprehensive digital workflow for improving function and aesthetics in a patient with a severe and uneven dentition wear. The workflow focused on restoring the patient's occlusal function and stability. After using an intraoral scanning and a functional condylar analyser (MODJAW®), the virtual plan was created in a dedicated software. The aesthetic plan was created using a digital app (Smilecloud), which took into account all aesthetic criteria. A printed model of the proposed restorations was created using all the data and tested as a mock-up. After validation, twenty-two restorations were placed using the injection moulding technique and a flowable composite, together with six monolithic glass ceramic restorations for the upper frontal teeth.

**Results.** A good integration in terms of function and aesthetics were obtained with both composite and glass ceramic restorations. Marginal fit, insertion and interproximal contacts for the six glass ceramic restorations were achieved together with a pleasant chromatic transition and aesthetic integration of injected flow composite restorations. Both types of restorations were able to achieve both static and dynamic occlusion.

**Conclusion.** Severe dental wear can be treated using a full digital approach consisting of correct positioning of the maxilla and mandible using a virtual articulator in the proper hinge axis position, also the ability to replicate occlusal surfaces according to muscle and TMJ function.

#### Conventional versus digital analysis of dental occlusion

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**Material and methods.** Twenty-five patients met the criteria and were included in this study. The occlusal contacts were determined in maximum intercuspation position (MIP) by using the 8 and 40  $\mu$ m articulating paper (Dr. Jean Bausch GmbH & Co.). The same thicknesses of articulating papers were used to evaluate the anterior and lateral guidance, and intraoral photographs were taken. The MIP occlusal contacts and functional anterior and lateral movements were recorded by using the OccluSense (Dr. Jean Bausch GmbH & Co.) and the intraoral scanner (Medit i700). The Pearson's chi-squared test was used to assess any differences in contact point distribution between the three methods.

**Results.** Statistically analysis was performed and preliminary results were inconclusive regarding a significant correlation between the conventional articulating paper and the digital OccluSense device in recording occlusal contacts in MIP. The intraoral scanner, while effective in capturing the overall occlusal scheme, showed some discrepancies in the finer details of contact points when compared to the articulating paper and OccluSense. Pearson's chi-square test of the distribution of contact points regarding of the three methods used was statistically significant (p<0.05). The articulating paper of 8  $\mu$ m thickness showed the highest sensitivity in detecting both static and dynamic contacts, followed by the OccluSense device and intraoral scanner.

**Conclusion.** The study concludes that articulating paper remains the gold standard in terms of sensitivity and accuracy. The OccluSense device represents an alternative to articulating paper, especially for practices looking to integrate more digital devices. The intraoral scanner may require further refinement to match the precision of conventional methods. Future research should focus on improving the accuracy of digital devices and exploring their integration into routine clinical practice to enhance patient outcomes in complex oral rehabilitations.

### Evaluation of push-out bond strength of calcium silicate-based endodontic sealers compared to an epoxy resin-based sealer

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**Introduction.** The aim of this study was to investigate the dislodgement resistance of two different calcium silicate based-sealers (Total Fill Hi-Flow, AH Plus Bioceramic) compared with an epoxy resin-based sealer (AH Plus).

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Corresponding Author: Mihai Merfea e-mail: mmerfea@yahoo.com **Material and methods.** Root canals of 30 single-rooted human teeth were instrumented with Pro Taper Ultimate up to FX (size 35). All canals were irrigated with 2 ml NaOCl 5.25% and 1 ml EDTA 17% between each instrument. Final irrigation consisted of 5 ml EDTA 17% and 5 ml NaOCl 5.25%. Teeth were randomly divided into 3 groups (n=10) and obturated using the following sealers and filling techniques recommended for each sealer: Total Fill Hi-Flow (TFHF) with Continuous Wave Condensation (CWC), AH Plus Bioceramic (AHBio) with single cone technique and AH Plus with CWC. After 4 weeks of incubation at 37°C, teeth were embedded in resin, and roots were sectioned horizontally into 1 mm slices. Push-out test was performed using an Instron universal testing machine at a speed of 1 mm per minute and bond strength was calculated. Specimens were observed under stereomicroscope at 4x magnification to determine the mode of bond failure. Six slices of each group were analyzed using SEM EDX to analyze the dentin-sealer-core interface. Results were assessed using analysis of variance (ANOVA) and Tukey and Bonferroni test.

**Results.** Statistical analysis revealed that AH Plus had a higher resistance to dislodgement than both TFHF and AHBio (p<0.05), while TFHF had higher resistance than AHBio (p<0.05). AH Plus penetrated dentinal tubules from 10 to 55  $\mu$ m, while TFHF and AHBio penetrated 0.5 to 20  $\mu$ m.

**Conclusion.** Resin-based sealer AH Plus showed better bond strength compared to the two bioceramic sealers tested and better tubule penetration.

#### Effect of vitamin D on bone regeneration

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Corresponding Author: Ondine Patricia Lucaciu e-mail: ondineluc@yahoo.com **Introduction.** Vitamin D is an essential micronutrient for maintaining bone quality and healing. It is actively involved in bone formation, mineralization and maintenance of neuromuscular function. It also regulates bone metabolism by activating vitamin D receptors found in osteoblasts. Globally, vitamin D deficiency is a public health problem and affects more than a billion people. In developing countries, the magnitude of vitamin D deficiency ranges from 30 to 90 percent and is highest in old age and women. Vitamin D deficiency results from inadequate synthesis in the skin, decreased food intake, or impaired vitamin D activation in the liver and kidneys. Low serum levels of vitamin D (25[OH]D) in adults can precipitate or exacerbate osteopenia, osteoporosis, and cause osteomalacia and muscle weakness. Our article aimed to conduct a review of existing bibliographic data investigating the effect of vitamin D on bone regeneration.

Material and methods. To carry out this review, an electronic search was carried out in several databases, and the items found were selected and analyzed.

**Results.** The results of *in vitro* studies have demonstrated that vitamin D has high therapeutic potential by increasing stem cell differentiation in osteoblasts. Human and animal studies have been conducted using different methods, but most of them have shown that vitamin D has a positive influence on the bone regeneration process. The influence of vitamin D3 (VD3) on osteogenic differentiation and stimulating effects have been reported. Most of the studies were conducted with VD3 metabolites, while very little data on the impact of native VD3 are available. Recent investigations using various hybrid biomaterial scaffolding or VD3-loaded composites have demonstrated increased biocompatibility and/or osteoinductive



effects on mesenchymal stem cells (MSCs), implying the advantages of their use for the treatment of bone defects. Specifically, an osteoinductive effect was demonstrated for human bone marrow-derived MSCs (BM-MSCs) grown on VD3/vitamin K2/Mg-loaded biodegradable polymeric nanofibers, as well as on human dental pulp MSCs seeded on chitosan scaffolds constructed to deliver VD3 sustainably over 3–5 days. In addition, polycaprolactone/gelatin scaffolds loaded with VD3 in combination with nano-hydroxyapatite (nHAP) stimulated osteogenesis of MSCs in adipose tissue, increasing alkaline phosphatase (ALP) activity in early stages and mineralization in late stages of differentiation.

**Conclusion.** However, most studies suggest that more in-depth research is needed to find the most effective way of administration and the dose needed to achieve the desired effect.

#### The influence of selective etch and gingival retentive groove on marginal protection for Class II cavities

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Corresponding Author: Diana-Maria Plătică e-mail: dianaplati@gmail.com **Introduction.** This *in vitro* study investigated the microleakage attained with two resin-based materials used for the restorations of standard class II cavities, under artificial aging. The aim was to validate Cone-Beam Computer Tomography (CBCT) as a means to evaluate microleakage.

**Materials and methods.** Forty-eight freshly extracted human sound molars were cleaned, stored in chloramine water, and received standardized Class II mesial and distal cavities. Subsequently, they were assigned randomly into four groups: two control groups and two test groups. In addition to the control groups, the test groups received a 1 mm gingival retentive groove depth. After selective enamel etching and coating with a self-etching light cure universal adhesive system, a base of two different resin-based materials was applied on the vertical and horizontal walls of the cavities. All the groups were exposed to artificial aging for 30 days consisting of immersion in solutions with high citric acid concentration, three times daily. All the specimens were immersed in 25% volume/volume AgNO3 for 12 hours, in the absence of light. The teeth were evaluated by aligning the images on the CBCT using a 3D registration tool and a macroscopic view based on photographs of tooth sections.

**Results.** A multiple logistic regression model confirmed that the presence of selective etch had a statistically significant protective effect against microleakage (p = 0.014, OR microleakage=0.347). Neither the gingival retentive groove nor the material used had statistically significant protective effects. Importantly, CBCT renders similar results to the macroscopic view (Chi-square Test p<0.001; McNemar p>0.05).

**Conclusion.** Marginal sealing may be influenced by the selective etch, although the cavity preparation technique and the filling materials did not significantly impact microleakage. Importantly, CBCT can be considered a valid method for evaluating microleakage.

### Reducing morbidity of benign parotid tumors surgery based on the comparative evaluation of superficial parotidectomy vs. extracapsular dissection

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Corresponding Author: Rareş Mocan e-mail: mocanrares@gmail.com **Introduction.** Salivary gland tumors represent 2-6.5% of all the tumors in the head and neck region and the most frequent ones are found in the parotid glands. According to the World Health Organization there are 21 forms of malignant and 15 forms of benign tumors of the salivary glands. Regarding the surgical approach, today's gold standard is represented by superficial parotidectomy, while less invasive techniques like the extracapsular dissection have been successfully practiced in the last 25 years. Dealing with such a frequent pathology and having two techniques used for the same operation, evaluation of the effect on the quality of life from the point of view of the cured patient seemed worth undertaking.

**Material and methods.** The current research included patients from the Cranio-Maxillo-Facial Surgery Department in Cluj-Napoca who were treated surgically for benign parotid gland tumors through one of the two techniques from September 2019 to January 2023. The healed patients received a questionnaire regarding the most important morbidity features.

**Results**. This study included 51 patients, median age 55 ( $\pm$  11), 27 underwent surgery by extracapsular dissection and 24 through superficial parotidectomy for pleomorphic adenoma (n=20 patients), Warthin tumor (n=19) and papillary cystadenoma. Of all the features analyzed between the two groups (size of the tumor, pain and discomfort, scaring and deformities, esthetic outcome, the degree of comfort within society, changes of facial symmetry, deformities noticed by relatives, tingling and numbness and changes of quality and quantity of saliva) only esthetic outcome has brought a statistically significant result. Although both groups brought similar results regarding numbness in the ear area, these results described an increased degree of discomfort.

**Conclusion.** The group of patients operated through extracapsular dissection were more satisfied with the esthetic appearance compared to the superficial parotidectomy group. Although the anterior branch of the great auricular nerve is regarded as a less important anatomical element that can be sacrificed with the aim of obtaining improved surgical access, it came up as one of the main complaints regarding postoperative morbidity in both groups.

#### Identification of new biomarkers in human saliva by means of ultrasensitive vibrational spectroscopy

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Corresponding Author: Mihaela-Felicia Băciuț e-mail: mbaciut@yahoo.com **Introduction.** The increasing incidence of malignant oro-maxillo-facial pathologies represents a dire reality in our days. Conventional diagnostic methods, although they have gained notoriety over years, are laborious, leading to the loss of valuable time until a definitive diagnosis is obtained. This additional perilous factor affecting the survival rate of patients is a challenge to which the analysis of liquid biopsies using ultrasensitive vibrational spectroscopic techniques can provide a relevant answer.

Material and methods. In our study, a total of 35 filtered salivary samples were subjected to the aforementioned analysis, originating from both patients with oral cancer and the control group. The samples obtained could be grouped into two complementary categories.

**Results.** Firstly, the filtration process of the salivary samples allowed the elimination of disturbing spectra characteristic of proteins, making it possible to enhance the spectra of molecules of interest. Secondly, through the process of comparative analysis of the spectra of the two groups, the major difference was identified around the vibrational band ~1000 cm<sup>-1</sup>, attributing it for the first time to opiorphin. In the same manner, vibrational bands located at 729 cm<sup>-1</sup> (hypoxanthine), 635 cm<sup>-1</sup>, and 1135 cm<sup>-1</sup> (uric acid) were also noted.

**Conclusion.** Liquid biopsy using ultrasensitive vibrational spectroscopy can provide important orientation towards early diagnosis, nevertheless further exploration of the study is desirable in order to patent an innovative method for early detection of malignant oro-maxillo-facial tumors.

#### Comparative microleakage of different techniques of occlusal anatomy restoration using the dental operating microscope

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2) Department of Dental Propedeutics and Esthetics, Faculty of Dental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Microleakage in direct dental restorations is a primary causal factor in the restoration's failure. The aim of this study was to evaluate whether the technique for occlusal layering of the composite resin (the use of brush adaptation, the use of magnification, cusp build-up, stamp technique) has any effect on microleakage of direct restorations in occlusal cavities.

**Material and methods.** One hundred extracted human molars were randomly divided into 5 groups (A-E) (n=20) and restored using different restoration techniques: Group A - Packable Bulk technique; Group B - Occlusal Stamp technique; Group C - Successive Cusp Build-up technique; Group D - Successive Cusp Build-up technique and

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Corresponding Author: Răzvan Pop e-mail: poprazvan1905@gmail.com Brush adaptation; Group E - Successive Cusp Build-up technique with brush adaptation using The Dental Operative Microscope. The teeth were subjected to thermal ageing for 800 cycles at 5°C and 55°C, infiltrated with basic fuchsin dye for 24 h, and then sectioned buccolingually in the middle of the crown. Infiltration was measured in four areas of the tooth section by five different observers and then given a score of 1 to 3, proportional to infiltration depth.

**Results.** The lowest mean scores for infiltration (meaning less infiltration observed) were present in Group A ( $1.41 \pm 0.878$ ) and Group C ( $1.46 \pm 0.679$ ), while Group D showed the highest infiltration scores ( $1.75 \pm 0.853$ ). When comparing the groups for differences, no statistically significant difference in infiltration was found between any technique p < .586.

**Conclusion.** The techniques examined for placing the occlusal layer of composite indirect restorations do not differ significantly in terms of marginal infiltration, although a slight improvement was found when using the bulk technique and the successive cusp build-up.

#### Dental trauma in children and adolescents

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Corresponding Author: Meda-Romana Simu e-mail: romana.simu@elearn.umfcluj.ro **Introduction.** During childhood and adolescence, trauma can occur in the area of the frontal teeth, especially the upper incisors. Accidents mostly take place during recreational activities. Untreated dental caries, dental protrusion which may frequently interest the anterior sector of the dental arch are predisposing factors for this pathology.

**Material and methods.** In this work, are briefly presented five cases with trauma to the upper incisors of patients aged between 9 and 13 years. The patients were taken to the pediatric dentistry clinic. There were cases with fractures, avulsions and intrusions of permanent teeth. The treatments were performed according to the current guidelines. Patients generally arrived at our service the day after the trauma and were very cooperative and eager to restore their lost aesthetic appearance as quickly as possible. Sometimes the approach was multidisciplinary, the patient first addressing the surgery service and then, after the surgical stage, redirected to the pediatric dentistry service.

**Results.** All patients were very satisfied with the final result. Post-traumatic monitoring, regular check-ups and communication with parents in the first post-intervention days are particularly important. Oral hygiene and adequate nutrition are adjunctive elements of the treatment.

**Conclusion.** Traumas in the frontal area are events that can occur in childhood and adolescence and presenting to the doctor as quickly as possible increases the chances of a favorable prognosis. In the case of the avulsion, most of the parents were not concerned with the recuperation of the tooth, not knowing that it can be reimplanted. This shows the need to inform parents and staff from school and preschool units about some basic elements regarding the behavior in the case of the most frequent types of traumas in the oro-dental region.

### Results of non-surgical periodontal therapy in patients with systemic sclerosis

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Corresponding Author: Alina Stanomir e-mail: alina.stanomir@yahoo.com **Introduction.** Periodontitis is a chronic immune-mediated inflammatory disease characterized by the progressive and irreversible destruction of the periodontal supporting apparatus. This condition has been linked to various autoimmune diseases, including systemic sclerosis (SSc). Studies indicate an increased frequency of periodontitis in patients with SSc. Thus, close periodontal surveillance is mandatory for these patients, followed by suitable treatment if needed.

**Material and methods.** A 44-year-old patient diagnosed with diffuse systemic sclerosis was examined at the Department of Periodontology. The patient received an extraoral and a complete full-mouth examination, baseline, and at two months after the first two periodontal treatment steps following the EFP S3 level clinical practice guideline. Periodontal parameters such as periodontal probing depth (PD), clinical attachment loss (CAL), gingival recession (RG), hygiene score index (IHI), and gingival bleeding index (GBI) were recorded. The primary treatment outcome was the difference in the PD. In contrast, the secondary outcome was the difference in the total/interproximal PD, total/interproximal CAL, count of total/interproximal PD  $\geq$  5 mm, and count of total/interproximal PD  $\geq$  6 mm, as well as changes in the IHI and GBI index. The qualitative data derived from periodontal and SSc parameters were assessed using statistical indices of variability and central tendency in Microsoft Office Excel.

**Results.** The extraoral examination revealed loss of expression lines on the face and severe mouth opening limitation, giving a mask-like appearance. Following a fullmouth periodontal examination, the patient was diagnosed with periodontitis stage III, grade B. The baseline clinical periodontal examination showed a GBI index of 24%, an IHI index of 35%, 11 periodontal pockets  $\geq$  5 mm, two pockets  $\geq$  6 mm, and a mean CAL of 2.48. After periodontal therapy, the results showed a GBI index of 9%, an IHI index of 20%, and a full pocket closure.

**Conclusion.** The therapeutic approach resulted in significant improvement in the monitored periodontal parameters.

### The effect of bruxism and orthodontic treatment with clear aligners on the color of resin composite restorations

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2) Department of Dental Materials and Ergonomics, Faculty of Dental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The purpose of this pilot study was to investigate the effect of bruxism and clear aligners on the color of class 2 resin composite restorations.

**Material and methods.** Standardized Class II cavities were prepared on 8 human molars and restored using a resin composite (ENA HRi® Bio Function Dentin & Enamel-Micerium). The teeth were divided equally into a control group and a test group (n=4). The control group was stored in artificial saliva and did not undergo mechanical loading. For the test group, a clear aligner was fabricated on each restored tooth and the teeth with the aligners were subjected to parafunctional mechanical

Corresponding Author: Cristina Gasparik e-mail: cristina\_gasparik@yahoo.com loads using a dual-axis chewing simulator. The CIELAB color coordinates were recorded using a dental spectrophotometer (SpectroShade Micro- MHT) at baseline (T0) and after mechanical loading (T1). Four measurement locations were set (2 mm diameter each): P1 and P2 on the restoration at 3 mm and respectively 1mm away from the border of resin composite restoration, and P3 and P4 on the tooth at 1 mm and respectively 3 mm away from the border of the resin composite restoration. Mean values and standard deviations of color coordinates were calculcated for each measurement location and time point. In addition, color differences  $\Delta E_{ab}$  between T0 and T1 for each of the four measurement areas as well as between P2-P3, P1-P4 were calculated and compared to the perceptibility and acceptability thresholds (PT=1.2, AT=2.7). The data were analyzed statistically using a paired samples t test, and multiple comparisons were adjusted using the Bonferroni method ( $\alpha$ =0.002).

**Results.** There were no significant differences in color coordinates between T0 and T1 for the control group (p>0.05). However, in the test group, statistically significant differences were found between T0 and T1 for all color coordinates (p<0.001), except for b\* in P1 and P4 (p>0.05). For the control group, the color differences between T0 and T1 were below the AT and varied between 1.32-2.22  $\Delta E_{ab}$  units. For the test group the color differences were above the AT and ranged between 4.22-5.79  $\Delta E_{ab}$  units.

**Conclusion.** The mechanical loading affected the color of the tooth and the resin composite restoration. The color differences were mainly due to the changes in lighntess which increased after mechanical loading for both the resin composite and the tooth. The color changes were smaller in the areas closer to the border of the restoration (P2 and P3) than in the areas located at 4 mm away (P1 and P4).

#### Salivary biomarkers of anti-epileptic drugs

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4) Department of Dental Propedeutics and Esthetics, Faculty of Dental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Saliva biomarker analysis represents an emerging field with applicability in the evaluation of various pathologies and treatments. It is noninvasive, fast and easy to perform, with great potential especially in long-term treatments that require monitorization and adaptation. Anti-epileptic drugs (AEDs) are prescribed in numerous pathologies, such as epilepsy, neuropathic pain, mania, anxiety or spasticity. Measuring AED concentrations is important in order to assess the patient's initial response to the medication and to identify any need for an adjustment, since interindividual differences make it impossible to accurately pinpoint an optimum AED dose.

**Material and methods.** A thorough electronic literature search was conducted in MEDLINE through PubMed, Web of Science, the Cochrane Library and Google Scholar. The inclusion criteria were as follows: any study that described the determination of any of the aforementioned AEDs through sampled or enhanced oral fluid. Based on the studies that fit the criteria, individual levels of different AEDs were analyzed on their physico-chemical properties, their drug-drug interactions, their plasma binding and, consequently, their penetration into oral fluid. Taking into account the determination and the sampling methods, the correlation coefficients between the each AED's saliva level and another biofluid level were recorded. 5) Department of Mechanical Engineering, Faculty of Automotive, Mechatronics and Mechanical Engineering, Technical University of Cluj-Napoca, Romania

Corresponding Author: Ioana-Andreea Chiş e-mail: ioanaandreeachis@yahoo.com **Results.** Several AEDs showed great potential to be routinely determined through saliva sampling, such as: Clobazam, Clonazepam, Diazepam, Midazolam, Carbamazepine, Gabapentin, Lacosamide, Lamotrigine, Levetiracetam, Oxcarbazepine, Phenobarbital, Phenytoin, Primidone, Rufinamide, Topiramate and Valproic acid.

**Conclusion.** Assessing AED concentrations from saliva samples is an aid not just to avoid toxicity, but also in pharmacoresistant patients, in children or in patients with comorbidities. This presentation emphasizes the advantages of oral fluid drug monitoring and highlights the AEDs that show promise in salivary biomarker detection.

### Dental shade, oral health-related quality of life and dental aesthetic self-perception modification as result of prophylactic dental procedures in pediatric patients

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Corresponding Author: Alexandru Grațian Grecu e-mail: ag.grecu@yahoo.com **Introduction.** Dentofacial aesthetics is essential among children and adolescents, with important influences on self-perception and social integration. Recently, oral health-related quality of life (OHRQoL) has been directed toward pediatric dentistry. The current study aims to highlight how children of different ages and backgrounds perceive the changes of dental shade resulting from professional prophylactic procedures and how these changes influence their OHRQoL.

Material and methods. Two dental professionals examined in three sessions (before - T0, immediately after the prophylactic procedures - T1, and at one month recall - T2) 25 paediatric patients from urban (n=17) and rural areas (n=8), with unaltered cognitive and communication functions. The following data have been recorded: (i) Dental status (clinical examination and SOPRO intraoral camera in "Cario mode"), (ii) The oral hygiene index (OHI-S) (clinical examination and SOPRO intraoral camera in "Perio mode"), and (iii) Dental shade (visually - Vita Classical shade guide and instrumentally -Vita Easyshade V Spectrophotometer - VITA ZAHNFABRIK). Additionally, the patients provided data on self-perceived dental color and dental aesthetic aspects at the same three sessions (T0, T1, and T2) by completing an oral health-related quality of life assessment questionnaire, COHIP-19 (Children Oral Health Impact Profile-19) and a self-reported dental aesthetics assessment questionnaire (PIDAQ) both translated into Romanian. The prophylactic procedures involved: ultrasonic scaling, airflow with Cleaning powder and professional brushing using a soft brush and Depural Neo (SpofaDental) cleaning paste. A one-way repeated measures analysis of variance (ANOVA) was conducted. The variations were calculated separately for data recorded by clinical observations and instrumentally.

**Results.** The prophylactic procedures mainly led to changes in dental color, recorded classically for 68% of the participants (two shades 20%, one shade 48%,) and instrumentally for 84% of the participants (two shades 16%, one shade 52%, no shade modification 32%). OHI-S varied from 1.04 (T0) to 0 (T1) and to 0.55 (T2). A statistically significant effect of the prophylactic treatment upon the patients' objective dental health

status has been recorded: Wilk's Lambda = 0.21, F (2, 23) = 41.08, p = 0.001. The Mean COHIP-19Ro scores varied from 56.04 (T0) to 65.88(T1) and 69.20 (T2). The mean PIDAQ scores were 22.20 (T0), 22.92 (T1) and 23.88 (T2). A statistically significant prophylactic treatment effect upon the patients' self-reported OHRQoL: Wilk's Lambda = 0.27, F (2, 23) = 29.27, p = 0.001 has been found, as well as a statistically significant difference between the patients' OHRQoL self-perception at T0 vs. T1(p = 0.001) and at T1 vs T2 (p = 0.048). A statistically significant prophylactic treatment effect upon the patients self-perceived dental aesthetics have been found: Wilk's Lambda = 5.73, F (2, 23) = 0.66, p = 0.01.

**Conclusion.** The prophylactic dental procedures improved dental color and generated responsible behavior regarding oral hygiene. However, at one month's distance, the hygiene status decreased in comparison with the situation immediately after the treatment, remaining, still better, compared to the pre-therapeutical situation. In addition, the patients declared an improved self-reported OHRQoL after the prophylactic treatment session.



### **RESEARCH CENTERS**

# **Understanding nanoparticles - DNA interactions for reproducible SERS analysis**

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Corresponding Author: Rareș Ionuț Știufiuc e-mail: rares.stiufiuc@umfcluj.ro **Introduction.** Silver plasmonic colloidal nanoparticles (NPs) have gained prominence in recent years due to their unique plasmonic properties and high sensitivity to changes in their local environment. This sensitivity makes them a promising tool for the detection of DNA structural variations by means of Surface Enhanced Raman Spectroscopy (SERS) analysis. In our study, we have investigated different types of interaction between colloidal NPs (acting as plasmonic substrates for SERS analysis) with DNA samples collected from normal and malignant cells.

**Material and methods.** DNA samples were obtained from 2 normal and 2 cancer cell lines. Two different methods for DNA samples preparation were implemented: deposition and incubation. Moreover, distinct volume ratios between silver plasmonic nanoparticles and DNA samples (1:1, 1:2, 1:3, 2:1, 3:1) were tested. Their interactions have also been evaluated at two different temperatures: room temperature and 94°C.

**Results and discussion.** The deposition of DNA samples on silver solid plasmonic substrates has produced a SERS spectrum dominated by the vibrational bands of silver nanoparticles with little evidence of the presence of DNA bases. On the other hand, in the case of DNA incubation with silver nanoparticles, the SERS spectrum presented the molecular fingerprint of DNA molecules.

**Conclusion.** By increasing the silver nanoparticles concentration and heating the mixtures at 94°C for 4 minutes we were able to record highly specific and reproducible SERS spectra of DNA analytes. We explain this improvement by considering temperature induced DNA denaturation yielding to the occurrence of single stranded DNA (ssDNA) molecules and modifying their interactions with plasmonic nanoparticles. We believe that our method could be used as a powerful tool for demonstrating epigenetic changes in cancer, by means of vibrational spectroscopy.

### ROR1 as a therapeutic target: what about CAR T cell therapy?

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2) Department of Hematology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** First identified in 1992, ROR 1 has similar structure to other characterized RTKs with an additional C-terminal domain rich in proline, serine and threonine residues which represent a docking site for intracellular signaling molecules. ROR1 is a receptor for Wnt5a and other Wnt proteins and regulates cell migration, differentiation, and growth during embryonic development. ROR1 is expressed at very low levels in adult tissues like gastrointestinal, lung and parathyroid gland tissues, pancreatic islets, and adipose tissues, while high and variable levels of ROR1 have been reported in multiple tumor tissues. The development of ROR1 targeted therapies is continuously growing leading to remarkable novel therapeutical approaches using



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Corresponding Author: Adrian Bogdan Țigu e-mail: adrianbogdantigu@gmail.com mAbs, antibody-drug conjugates, several small molecules, or CAR-T cells.

**Material and methods.** Plasmid information – the CAR Construct was synthesized and subcloned into lentivirus vector by Creative biolabs. Cell culturing: the screening for ROR1 positive cell lines included solid and hematological malignancies models with various culture conditions. Flow cytometry: The samples were analyzed by FACS CANTO II using anti ROR1-APC conjugated antibodies and eGFP signal for establishing cell population ratios. LDH activity was determined using LDH PicoProbe assay.

**Results.** Several cell lines, both solid and hematological tumor models displayed ROR1 positive cell populations, with Z138 cell lines as more than 99% positive cells. The testing on Z138 – Mantle cell lymphoma showed a time-dependent inhibitory effect of our anti ROR1 CAR T cells, with an increased LDH activity in all groups.

**Conclusions.** With limited efficacy, the novel anti ROR1 CAR T cells need further evaluation and optimization of their activity.

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### New method of DNA analysis by means of ultrasensitive vibrational spectroscopy for cancer detection

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**Introduction.** Cancer is a complex and heterogeneous disease that often involves genetic alterations at the DNA level. In the case of multiple myeloma, understanding the molecular changes in DNA is of paramount importance for diagnosis and therapeutic intervention. In this study, we present a novel method of DNA analysis based on Surface Enhanced Raman (SERS) spectroscopy.

**Material and methods.** DNA samples were isolated from 2 normal and 2 multiple myeloma cell lines. In order to get spectral information related to DNA bases modifications, we have employed various strategies. For performing SERS measurements, silver plasmonic nanoparticles and DNA samples were mixed together for 1h. Then the mixtures were poured on a CaF<sub>2</sub> glass and heated to 94°C for 4 minutes. We have also investigated the molecular fingerprint of the four DNA bases: adenine, guanine, cytosine and thymine in order to guide us for a correct assignment of the vibrational bands of DNA samples. At the same time the DNA methylation pattern was evaluated based on 5-methyl-cytosine concentrations.

**Results and discussion.** SERS/Raman results emphasized important differences between normal and cancer DNA based on their aggregation behavior induced by the distinct methylation landscape present in the DNA samples. Both Raman and SER spectra collected on the same DNA samples showed a very intense vibrational band located at 1008 cm<sup>-1</sup> assigned to a rocking vibration of 5-methyl-cytosine. The intensity of this band strongly increases in cancer DNA due to the aberrant pattern of the methylation landscape occurring in multiple myeloma which can take place at a specific locus but also at CpG islands.
Corresponding Author: Rareş Ionuţ Ştiufiuc e-mail: rares.stiufiuc@umfcluj.ro **Conclusion.** Our results revealed distinct spectral profiles for normal and multiple myeloma cell lines, demonstrating the potential of this method for discriminating between healthy and cancerous DNA. This approach holds great potential for advancing our understanding of cancer genetics and improving early detection and treatment strategies.

### Bone marrow microenvironment-induced resistance to Venetoclax in acute myeloid leukemia

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Corresponding Author: Dávid Kegyes e-mail: kegyesdavid70@gmail.com **Introduction.** Apoptosis is a complex form of programmed cell death. Resistance to apoptosis is caused by dysregulation of the balance between pro-apoptotic (BH3-only) and pro-survival molecules. One of the main antiapoptotic proteins overexpressed in AML is B-cell lymphoma-2 (BCL-2). BCL-2 is targeted by venetoclax (VEN), a BCL-2 specific BH3-only mimetic drug. VEN was approved by for the treatment of elderly, newly-diagnosed AML patients ineligible for intensive induction chemotherapy. One of the drawbacks, however, even when combined with hypomethylating agents (azacytidine or decitabine) or low-dose chemotherapy (cytarabine), is that most patients experience an early disease relapse. Since these patients are unfit for bone marrow transplantation, managing relapse is challenging and leads to early mortality. As a result, VEN resistance has become a growing clinical concern, and translational researchers focus on the development of novel strategies to address this issue.

**Material and methods.** Several cell lines have been cultured together with the HS-5 cell line and primary mesenchymal stromal cells (MSCs). MSCs were derived from bone marrow mononuclear cells of healthy donors. To determine drug effect (DE) of VEN, the MV4-11 cell line was treated with increasing concentrations of VEN in the presence or absence of stromal cells. After 10-14 days, the recovery of CFUs was determined by colony counting under bright-field microscopy. To determine VEN concentrations in cell supernatants, a Vanquish ultra-high performance liquid chromatographer was coupled with a Quantiva triple quadruple mass spectrometer.

**Results.** To choose the best in vitro model for subsequent investigations, we assessed the sensitivity of 10 distinct AML cell lines to VEN in the presence or absence of human stroma-5 (HS-5) or primary human MSCs. Without stroma, the MV4-11 cell line exhibited robust sensitivity to VEN with a IC<sub>50</sub> of 67 nM. DE, however, significantly decreased when cocultured with HS-5 (DE= 48.26% vs 24.94%, P<0.001). Similar results have been obtained when primary human MSCs were used instead of the HS-5 cell line (DE= 48.26% vs 26%, P<0.001). VEN resistance was maintained in MV4-11 cells when cocultured with HS5 and MSCs (DE= 46.52% vs 24.33%, P<0.001 for HS5 and DE= 46,52% vs 26,87%, P<0.001 for MSCs). We were able to validate the results by CFU assays. Using HPLC coupled with MS to quantify VEN levels in the presence or absence of MSCs with or without clarithromycin.

**Conclusion.** Our results demonstrated that stroma-induced acquired VEN resistance is present in multiple AML cell lines. The resistance is not caused by stromal metabolism of the drug and it is maintained without direct cell-contact. All these findings suggest that a stroma-mediated soluble factor is responsible, at least partially, for development of VEN resistance in AML.

### Retinoid differenciating agents induce maturation of MDS cells *in vitro*

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Corresponding Author: Diana Cenariu e-mail: diacenariu@gmail.com **Introduction.** Myelodysplastic syndromes (MDS) are considered heterogeneous hematopoietic stem cell (HSC) disorders characterized by bone marrow (BM) dysplasia and peripheral cytopenias. CyP26 activity in the BME protects normal and malignant HSCs from ATRA-induced differentiation and contributes to drug resistance.

**Material and methods.** In vitro cultivation of MDSL cells and OP9 cells, treated with different ATRA concentrations (10e-8M, 10e-8M + R115866) and AM80 10-9M to induce differentiation. Talarozol (R115866), an inhibitor that blocks CyP26 was added to the ATRA treatment in the experimental design, at 1nM cc-tion. The experiment was set up, in EPO/G-CSF media, MDS-L cells were cultured with or without stroma OP9, in 3 successive days. Flow cytometry evaluation. The processed experimental samples are labelled with 5 antibodies: CD45PerCP-Cy5.5: CD36 FITC, CD38 APC H7, CD71 APC, GlyA PE and the mean fluorescence intensity is calculated. Colony forming units are performed to evaluate and validate the maturation of MDS cells following retinoic treatment, by counting the number of colonies formed in each plate.

**Results.** CD45 staining isolates the leucocyte population out of the analyzed cells; from here, specific antibodies that prove maturation of MDSL cells are used: CD36 FITC, CD38 APC H7, CD71 APC, GlyA PE. There is a shift in the positive population of mature cells dependent of the ATRA treatment concentration. Best results are observed at 10e-8M ATRA. The number of colonies formed decreases, once the differentiation of MDSL cells is induced due to the retinoic acid treatment, in the presence/absence of stroma.

**Conclusions.** Since myelodysplastic cells mature slower in the presence of stroma than those grown without stroma by the addition of Talarozol to the experimental design we could prove *ex vivo* that R115866 blocks CyP26, thus therapy resistance can be eliminated *in vitro*. The ATRA inactivation is stronger on MDSL in the presence of stroma OP9, which proves that Cyp26 is involved in limiting the production of the active ATRA, in vitro.

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# Elucidating the estrogen-dependent modulation of extracellular vesicle production and miRNA cargo in ER+ Breast Cancer

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Corresponding Author: Rareș Drula e-mail: drula.rares@gmail.com **Introduction.** Estrogen has been recognized as a critical modulator in the progression of estrogen receptor-positive (ER+) breast cancer (BC), influencing various cellular processes including extracellular vesicle (EV) secretion and miRNA profiles. This study aims to unravel the intricate relationship between  $17\beta$ -estradiol exposure, EV production, and miRNA cargo composition in ER+ BC cell lines.

**Methods.** Utilizing a dose-dependent approach, we analyzed the effects of 17 $\beta$ -estradiol on EV secretion and miRNA content in ER+ BC cells. Functional assays including luciferase, Chip-qPCR, and RNA-protein pull-down were employed to validate the involvement of specific miRNAs and their regulatory targets. Circulating EVs from ER+ and TNBC BC patients were also examined to translate our findings from cell lines to clinical scenarios.

**Results.** Our results demonstrated a significant increase in EV production and a distinct enrichment of let-7 family miRNAs in ER+ BC cells upon  $17\beta$ -estradiol exposure. We established that this response was mediated through the downregulation of miR-149-5p, a direct transcriptional target of ER. Further investigations revealed that the upregulation of SP1, a known target of miR-149-5p, was responsible for the increased EV production. Concurrently, the alterations in EV miRNA cargo were attributed to the hormone-induced modulation of hnRNPA1, a protein involved in miRNA sorting into EVs. Clinically, elevated levels of let-7 family miRNAs were detected in circulating EVs from pre-menopausal ER+ BC patients, establishing a link between hormonal status and EV miRNA profiles.

**Conclusions.** This study provides comprehensive insights into the estrogendependent mechanisms governing EV production and miRNA cargo selection in ER+ BC. By elucidating the molecular underpinnings of this process, we highlight the potential of exploiting EVs and their miRNA content for therapeutic advancements in hormone-sensitive breast cancer. Additionally, our findings underscore the potential of circulating EV miRNA profiles as biomarkers for hormonal status and disease progression in ER+ BC patients.

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#### Establishing a murine model for pre-clinical evaluation of Azacytidine combined with Olaparib in acute myeloid leukaemia (AML) treatment

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Corresponding Author: Ciprian Tomuleasa e-mail: ciprian.tomuleasa@gmail.com **Introduction.** Acute Myeloid Leukemia (AML) is a lethal hematological malignancy with a high mortality rate, necessitating the exploration of novel therapeutic strategies. Combination therapy has emerged as a promising avenue, and this study aims to evaluate the therapeutic potential of 5-Azacytidine (AZA) and Olaparib, a PARP inhibitor, in the treatment of AML, using a pre-clinical mouse model.

**Materials and methods.** Male athymic nude mice, eight weeks of age were injected intra-articularly in the femoral region with  $5 \times 106$  AML luciferase-positive (AML-Luc) cells. The tumors were let to develop for 20 days after which mice were divided into three treatment groups: control (PBS), AZA, and AZA combined with Olaparib. Doses were determined following FDA guidelines for human to animal dose conversion. Therapeutic efficacy was evaluated after 5 days of treatment through bioluminescent imaging.

**Results.** Our femoral injection technique successfully established the murine model, as evidenced by tumor development. The study further demonstrated a significant reduction in tumor formation, particularly when treated with the combination of 5-azacytidine and Olaparib compared to the monotherapeutic approach.

**Conclusion.** Our investigation into novel treatment options for AML demonstrates that the combination of 5-Azacytidine (AZA) with the PARP inhibitor, Olaparib, holds potential therapeutic benefits in a pre-clinical setting. This synergy might offer an alternative avenue for AML treatment, underscoring the importance of further studies to validate these preliminary findings.

### Distinct proteomic signatures in complicated Crohn's disease towards disease course prediction

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2) Department of 3<sup>rd</sup> Medical Clinic, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Crohn's disease (CD) is characterized by a chronic, progressive inflammation of the gastrointestinal tract often leading to complications, such as strictures and fistulae. Currently, there are no validated tools anticipating short and long-term outcomes at an early stage. This investigation aims to elucidate variations in protein abundance across distinct CD phenotypes with the objective of uncovering potential biomarkers implicated in disease advancement.

**Material and methods.** Serum samples collected from 30 CD patients and 15 healthy age-matched controls (HC) were subjected to depletion of 6 highly abundant proteins and to label-free mass spectrometry analysis.

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**Conclusion.** In this study, a unique serum biomarker panel for aggressive CD was identified, which could aid in predicting disease course.

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# Carbon quantum dots as fluorescent probes for indirect *in vitro* evaluation of apoptosis through cytochrome c detection

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Corresponding Author: Rareș Ionuț Știufiuc e-mail: rstiufiuc@gmail.com **Introduction.** Cytochrome c serves as a crucial biomarker during the initial phases of apoptosis, and many approaches have been developed to track the release from the mitochondria. Fluorescent nanoparticles, widely known for their excellent optical properties, have emerged as viable candidates in improving our knowledge of programmed cell death pathways. Carbon-based quantum dots have become more popular within the field of nanoparticles due to their biocompatibility and little cytotoxicity.

**Material and methods.** This study involved the synthesis of carbon quantum dots with a diameter smaller than 5 nm using sodium citrate and polyethylene imine through carbonization. The nanoparticles were characterized, using UV-Vis, TEM, FTIR, Raman and fluorescence microscopy, and their ability to detect apoptotic events was evaluated in A549 cells treated with staurosporine and etoposide. In order to assess the release of Cyt c, a process that is closely associated with apoptosis, a semiquantitative analysis was performed using confocal laser scanning microscopy.

**Results.** The results of this study highlight the effective application of carbon quantum dots as a valuable method for the detection of Cyt c through the use of fluorescence microscopy. A significant decrease in fluorescence intensity was seen in cells that were subjected to apoptosis-inducing compounds in comparison to control cells, thereby quantifying the release of Cyt c from mitochondria into the cytoplasm. The outcomes of this investigation provide evidence that this method has the capacity to be utilized as an indirect means of evaluating apoptosis in vitro.

**Conclusions.** This study demonstrates the potential of carbon quantum dots as fluorescent probes for the evaluation of apoptosis, providing a novel method for understanding the kinetics of programmed cell death.

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#### Comparative proteomic evaluation of prostate biopsies from paraffin embedded tissue samples

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Corresponding Author: Cristina-Adela Iuga e-mail: iugac@umfcluj.ro **Introduction.** Formalin-fixed paraffin embedded (FFPE) tissue archives represent an abundant resource of clinically relevant material for understanding molecular mechanisms that underpin certain pathologies and for the discovery of biomarkers that could enable non-invasive, early-stage diagnosis.

**Material and methods.** A label-free data-independent LC-MS/MS approach was used to compare the proteome profiles of both malignant and adjacent benign formalin-fixed paraffin-embedded (FFPE) prostate tissues using a within subject study design from 23 paired FFPE prostate tissue samples.

**Results and discussion.** Of the total of 1218 proteins identified, 176 were statistically significant different (p-value FDR: 0.05, FC>1.5) having the power to discriminate between the tumoral and non-tumoral tissue. These proteins were mapped to several pathways: gluconeogenesis, fructose metabolism, translocation of GLUT4 to the plasma membrane, signaling by GTPases, semaphorin interactions and others.. Based on the data obtained and HPA database we were able to propose a biomarker panel consisting of 12 significant proteins, highest expressed in the tumoral tissues but also found in plasma, classified as cancer biomarkers, with medium and high expression in prostate tissue by IHC. ROC analysis confirmed a 4 - protein panel consisting of GDF15, MIF, AZGP1 and KLK3 (AUC=0.94).

**Conclusion.** A comparative proteomics approach was applied to differentiate between tumoral and normal adjacent tissue in FFPE prostate tissue samples being able to propose a 4-protein biomarker panel. Future studies will focus on confirming the proposed protein panel both in FFPE tissue samples and in plasma.

Acknolwledgements. The study was funded by CNFIS-FDI-2022-0714 and CNFIS-FDI-2023-F-0193 projects.

## The impact of PHGDH inhibitors on HS578t triple negative breast cancer cell line: a proteomics approach

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2) Department of Drug Analysis, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The *de novo* serine synthesis pathway (SSP) represents an important source for sustaining malignant cells metabolic needs by powering cell growth and redox homeostasis pathways. The role of SSP as potential target for therapy reemerged following the discovery of two potent PHGDH inhibitors, namely NCT-503 and CBR-5884. Here, we used an in vitro TNBC model to characterize the metabolic changes that occur upon treatment with two PHGDH inhibitors.

Material and methods. A label-free shotgun proteomics approach was used to investigate alterations in the proteome profile of HS578t after treatment with PHGDH

Corresponding Author: Cristina-Adela Iuga e-mail: iugac@umfcluj.ro inhibitors. The cell pellet was used to retrieve the intracellular proteins. After digestion with trypsin, resulting peptides were analyzed by Acquity M-Class® nano-LC coupled with Synapt®G2-Si HDMS. Raw HDMSe data was processed by Progenesis®QIp, while differential pathway analysis was conducted using ReactomeGSA®.

**Results.** Through proteome profiling, a total number of 1702 proteins were identified. Both multivariate and univariate statistical analysis were conducted in a control vs treatment study design emphasizing different proteins implicated in the response of HS578t to the PHGDH inhibitors. Additionally, we used differential pathway analysis to better describe the response of HS578t to PHGDH inhibition. The lipid, protein and amino acid metabolism were found to be differently affected by treatments: NCT-503 had a more pronounced downregulating effect upon the lipid metabolism, while in the CBR5884 treated cells, an increase of the lipid metabolism was observed. As response to the NCT-503 treatment, the cell line significantly downregulated its catabolism of glycine, lysine and branched amino acids, carnitine synthesis and TCA cycle.

**Conclusion.** Using this proteomics approach we were able describe the metabolic impact of two SSP inhibitors upon TNBC cell line, emphasizing different impact of the two inhibitors on the lipid metabolism. Also, different potencies were attributed to the inhibitors tested regarding their effect upon protein and amino acids metabolism pathways.

Acknolwledgements. The study was funded by the Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, through the Doctoral Grant no. 1300/54/13.01.2017 and CNFIS-FDI-2022-0714 project.

# Molecular profiling of NSCLC tissues using spatial transcriptomics

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**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 deaths in both men and women (18%). Moreover, the majority of tumors are characterized by dynamic molecular and phenotypic changes that occur in tumor cells which influence therapy resistance and result in poor clinical outcomes.

**Material and methods.** FFPE lung tumor tissue from two lung adenocarcinoma (LUAD) and two lung squamous cell carcinoma (LUSC) patients were evaluated using the 10XGenomics Visium platform. The protocl included sample preparation, preparation of slides, fixing the slides on the capture areas, HE staining, deparaffinization and imagining, decrosslinking and probe hybridization, probe extension and library preparation. Sequencing was done using the Illumina platform, FastQC and SpaceRanger were used for primary analysis. Seurat and LoupeBrowser were used for the secondary analysis.

**Results.** Unsupervised clustering revealed six and three clusters in LUAD samples, and six and seven clusters in LUSC samples, based on the transcriptomic profile of the cells in the spots of the capture area. The top 10 upregulated genes in each



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Corresponding Author: Cecilia Bica e-mail: cecilia.bica@umfcluj.ro cluster were identified for each sample. It was noted that differentially expressed genes in clusters include genes encoding haemoglobin, cytokines, histones, and collagens. The inquiry revealed that T cells and B cells markers appear to be more present in LUAD tissue samples than in LUSC tissue samples. Moreover, LUSC tissue samples appear to have cancer associated fibroblasts markers whose expression is spatially variable.

**Conclusion.** Given the complex tumor heterogeneity in LUAD and LUSC tissue samples, we were able to observe gene expression in the context of spatial organization lung cancer tumor tissue.

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#### Lead-induced cell toxicity and important transcriptomic alteration in human normal intestinal fibroblasts and epithelial cells

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Corresponding Author: Cornelia Braicu e-mail: braicucornelia@yahoo.com **Introduction.** Lead (Pb) is a crucial contaminant in both industrial and environmental settings, capable of inducing pathophysiological alterations in various cellular and organ systems. These changes impact processes key biological processes. The intestinal tract is affected by Pb exposure, but the mechanisms through which Pb exerts its effects are not fully understood. Intestinal fibroblast and epithelial cells have an important role in intestinal homeostasis. The normal epithelial cells form a protective lining, aiding in nutrient absorption, while fibroblast cells provide structural support and contribute to tissue repair in the gastrointestinal tract, collectively ensuring its proper function and health.

**Material and methods.** We examined the cellular and molecular effect of Pb in normal intestinal fibroblast (CCD-18Co) and epithelial cells (HCoEpiC) after exposure to a dose of 100ng/ml for three serial passages. cell proliferation, apoptosis and cell cycle were analyzed using Celigo System, transcriptomic alteration was analyzed using Agilent microarray technology.

**Results.** The treatment with lead revealed cytotoxic effects and alteration of cell cycle, no important alteration on apoptotic related mechanism; this treatment also induces significant alterations in the transcriptome as shows microarray data, influencing the expression patterns of genes involved in various cellular processes related to inflammatory and cell adhesion mechanism in both cell lines.

**Conclusions.** These findings suggest that the exposure to Pb results in a molecular cascade that affect even at a low dose. This cascade disrupts various subcellular compartments, affecting normal cellular functions, cell cycle progression, the differentiation process, and ultimately leading to cell death as observed by microarray data.

# Investigation of L1 retrotransposon as a diagnostic and prognostic marker for glioblastoma

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Corresponding Author: Sergiu Chira e-mail: sergiu.chira@umfcluj.ro **Introduction.** Retrotransposons account for approximately 42% of the human genome and have been highlighted in human genome evolution. However, the cell tightly regulates its expression and mobilization through epigenetic mechanisms, and p53 is one of the key factors regulating this process. An increase in mobilization of the L1 family of retrotransposons has been observed in premalignant lesions and aggressive cancers. Therefore, studies suggest that L1 expression could represent a novel biomarker of diagnostic and prognostic value. This study aims to investigate the L1 expression in cancer cell lines and glioblastoma clinical samples, and to establish a potential correlation between L1 mobilization and TP53 mutation status.

**Material and methods.** Total RNA from glioblastoma cell lines A172 (TP53 wild-type) and U251 (TP53 mutant), and from cerebrospinal fluid from 5 glioblastoma patients was extracted using. The RNA samples were reverse-transcribed to cDNA, and L1 expression was detected using PCR and agarose gel electrophoresis. The expression level of L1 based on TP53 mutation status was determined by RT-qPCR on total RNA from U251 vs A172.

**Results.** Amplification data shows that L1 expression was present in A172 and U251 cells and cell culture supernatant, indicating that L1 RNA is secreted in the extracellular environment. Furthermore, L1 amplification was also detected in the cerebrospinal fluid of the glioblastoma patients at different intensities depending on the patient sample. The quantitative PCR data suggests that TP53 mutated U251 cell line displays a lower degree of expression than A172, which harbors a wild-type TP53 gene.

**Conclusion.** These results point that p53 might be regulate L1 expression in glioblastoma, and an increase in L1 mobilization could constitute a minimal invasive novel biomarker for diagnosis of TP53 mutated aggressive glioblastoma subtypes, and prognosis of clinical outcome.

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# Differential mutational landscape in early and late stages of ccRCC

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1) Research Center for Functional Genomics, Biomedicine and Translational Medicine, Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** RCC accounts for 85% of all renal cancers, with ccRCC as the main and most deadly histological subtype. Little is known about the mutational profile of ccRCC and how it changes from the early to late stages. Here we provide a preliminary look upon this matter.

Material and methods. We collected fresh-frozen pairs of tumoral and adjacent non-tumoral tissues from early-stage (I-II, n=8) and late-stage (III-IV, n=8) ccRCC

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Corresponding Author: Paul Chiroi e-mail: chiroipaul@gmail.com patients, performed DNA extraction and QC. Ion Ampliseq Cancer Panel was used for NGS on the Ion Torrent platform. We used Ion Reporter 5.6 software for primary and secondary analysis. For the clinical assessment of the mutations, we used COSMIC and ClinVar databases.

**Results.** Somatic mutations were found in 10 genes (FLT3, IDH1, KIT, NOTCH1, PIK3CA, PTEN, RB1, SMAD4, TP53, VHL) out of which 9 were pathogenic, while germline mutations were found in 15 genes (ATM, CSF1R, ERBB4, FGFR3, FLT3, KDR, KIT, MET, PIK3CA, RET, SMAD4, SMARCB1, STK11, TP53, VHL), out of which 6 were pathogenic. In patients with early-stage ccRCC, somatic mutations were found in NOTCH, PIK3CA, and VHL, while the germline mutations were found in ATM, GFR3, MET and RET. In patients with late-stage ccRCC, somatic mutations were found in FLT3, IDH1, PTEN, RB1, SMAD4, TP53, and VHL, and germline mutations in ATM, KIT, PIK3CA, STK11, VHL.

**Conclusions.** We observed an overlap between the mutational signature of early and late stages of ccRCC. However, some distinct patterns were also noticed: somatic c.3196G>A of PIK3CA was found more prone in the early-stages of ccRCC, while the somatic c.1621A>C of KIT, c.1173A>G of PIK3CA, and the germline c.381delG of VHL was more prevalent in the late-stages. Thus, a distinct mutational landscape between the early and late stages of ccRCC might exist.

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### The role of multi miRNAs panels in identifying common features in lung adenocarcinoma and lung squamous cell carcinoma patients

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Corresponding Author: Livia Budisan e-mail: liviuta.petrisor@umfcluj.ro **Introduction.** Lung cancer has limited therapeutic options despite some progress made for targeted therapies and actionable genes. Considering this context, our growing interest in the last decade is focused on investigating noncoding RNAs and their target/ targeted genes in many cancers and cancer subtypes.

**Material and methods.** This study included a cohort of 48 patients diagnosed with NSCLC (non-small cell lung cancer), of which 19 patients were diagnosed with lung adenocarcinoma (LUAD) and 29 with lung squamous cell carcinoma (LUSC). We evaluated the expression level of miR-96-5p, miR-144-3p and miR-210-5p was performed by qRT-PCR. All statistical analysis was performed using GraphPad Prism v.6 software. The identification of interactions between miR-96-5p, miR-144-3p and miR-210-5p and their related target genes was performed using the miRNet online tool and DIANA-miRPath v3.

**Results.** Two miRNAs show statistical significance in both histological subtypes, making them optimal candidates to accompany the pathological diagnosis, improving the active pathways involved in tumor evolution. Our data have shown a p-value of 0.0001 for miR-96-5p, 0.0026 for miR-210-5p and 0.0371 for miR-144-3p in LUSC. In

LUAD, values were 0.0251 for miR-96-5p, and 0.0425 for miR-210-5p. MiR-144-3p was not statistically significant, potentially due to the number of patients investigated. The present study has demonstrated the potentially critical roles of miR-96-5p, miR-144-3p and miR-210-5p in regulation of several key pathways (ECM-receptor interaction, and Adherents junctions) in the progression of NSCLC.

**Conclusions.** The present study has demonstrated the potentially critical roles of miR-96-5p, miR-144-3p and miR-210-5p in regulation of several key pathways (ECM-receptor interaction, and Adherents junctions) in the progression of NSCLC. The miRNAs and their related target genes can be used as biomarkers or therapeutic targets for future studies.

# The potential role of miR-155 expression level in Ceritinib resistance in an *in vivo* PDX model of ALK-rearranged NSCLC

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Corresponding Author: Ioana Berindan-Neagoe e-mail: ioananeagoe29@gmail.com **Background.** MiR-155 is an oncomiRNA whose expression is associated with a high risk of recurrence, an aggressive disease course and resistance to classic chemotherapy. ALK translocation is a recurring event in lung adenocarcinoma, which occurs in about 3-5% of NSCLC cases, being one of the few targetable mutations. Patients with NSCLC harboring ALK translocation benefit from targeted therapy with Crizotinib and Ceritinib, having good response rates with median survival rates of more than 6 years. In this study, we analysed the impact of miR-155 in the context of ALK-rearranged NSCLC.

**Material and methods.** Fresh tissue was collected from a patient with ALK rearrangement who progressed under first-line Crizotinib and second-line Ceritinib and had a high level of miR-155. We evaluated the impact of Ceritinib treatment on these PDXs to verify whether the resistance observed in the patient was preserved in the xenograft. Two experiments have been conducted. The first experiment evaluated the impact of Ceritinib administration on tumor progression. A second experiment investigated the impact of Ceritinib administration on tumor development upon engraftment in mice.

**Results.** Our data shows that Crizotinib and Ceritinib had no impact on tumor engraftment and minimal effect on tumor progression. Therefore, this miR-155 high ALK-rearranged NSCLC can be de novo resistant to this treatment.

**Conclusion.** We present an interesting case of an ALK-rearranged NSCLC model with an aggressive clinical course due to resistance to both lines of ALK-tyrosine kinase inhibitors. This resistance seems modulated by the expression level of miR-155, an oncomiRNA with important roles in chemotherapy resistance and cancer progression. Our results suggest that the expression of miR-155 should be tested in addition to classical known resistance mutations in ALK-rearranged NSCLC.

### A novel approach for improving hematopoietic recovery and survival from peripheral blood stem cell transplantation. Results of the preclinical study "TROFOSTEM"

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Corresponding Author: Andrei Cismaru e-mail: cosmin.cismaru@umfcluj.ro **Introduction.** An important limitation of the current standard approach of mobilizing hematopoietic stem cells (HSCs) in the peripheral blood (PB) using granulocyte-colony stimulating factor (G-CSF) for the prophylaxis of chemotherapy induced febrile neutropenia or in donors for PB stem cell transplantation (PBSCT) is insufficient mobilization. Based on our preliminary results on the effect of human chorionic gonadotropin (HCG) on stimulating the peripheral mobilization of HSCs in vivo, the aim of the current study was to assess the effect of the addition of HCG to mobilization with G-CSF on the overall survival (OS) as the primary endpoint in a mouse model of PBSCT.

**Material and methods.** Male donor mice (n=20) were pretreated with a single dose of either peg-G-CSF alone (group A, n=10) or HCG + peg-G-CSF (group B, n=10), 5 days prior to PBMC harvest. PBMCs were immediately transplanted to the equivalent number of Busulfan mieloablated female mice by intravenous tail injection and OS was assessed in both recipient groups.

**Results.** The median OS in the group of recipients transplanted with peg-G-CSF mobilized PBMCs (group A) was 81 days. In the recipients transplanted with HCG+ peg-G-CSF mobilized PBMCs (group B) the median OS is not reached at 204 days with 80% of the recipients still being alive at the time of the analysis.

**Conclusions.** Addition of HCG to the current standard mobilization approach with G- CSF in donors has almost doubled the survival rate in the recipients of a murine model of PBSCT with the median OS not yet reached after 204 days. This prompts for the translation of the preclinical study's approach in a human proof-of-principle/ feasibility clinical trial.

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# MicroRNAs profiling and their interconnected transcription factors regulators in NSCLC

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**Introduction.** In recent years, lung cancer has become widely recognized as one of the leading causes of cancer-related deaths worldwide. In this context, analysis of transcriptomic profile contributes to enlightening the differential mechanisms between

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4) Department of Experimental, Diagnostic and Specialty Medicine (DIMES), University of Bologna, Bologna, Italy

Corresponding Author: Ekaterina Isachesku e-mail: ekaterina.isachesku@umfcluj.ro specific molecular and histological cancer subtypes. The short sequences of the microRNAs (miRNAs) exhibit high investigational and therapeutic potential, as they are involved in multiple networks by regulation of the transcription factors (TFs) inclusively. As such, our main objective was to characterize the role of microRNAs (miRNAs) in the transcription processes in non-small cell lung cancer (NSCLC) and to correlate them with the modulation of TFs.

**Material and methods.** The expression level of three representative miRNAs was studied in cohorts of patients with NSCLC and healthy subjects in their tumors, adjacent normal tissues, plasma and exosomes using qRT-PCR. Subsequent bioinformatics analysis using GeneMania and Cytoscape was performed to highlight the TFs-miRNAs regulatory networks. Levels of representative TFs were quantified.

**Results.** A significant differential expression of miR-21, miR-181, and miR-155 was attested in all three types of samples. Bioinformatics analysis of the TFs network showed tightly connected functional modules related to the cell cycle and associated processes. Differential expression of the TFs MYC, SMAD3 and YAP1 was specifically correlated with the miRNAs of interest.

**Conclusion.** There is a strong correlation between microRNAs and the TFs they modulate, suggesting that microRNAs play a double role within the cellular network. Further analyses are required to establish whether combinatorial quantification of miR-21, miR-181, and miR-155 and MYC, SMAD3 and YAP1 can have prognostic roles in NSCLC patients.

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#### MicroRNAs as possible biomarkers for melanoma

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Corresponding Author: Lajos Raduly e-mail: lajos.raduly@umfcluj.ro **Introduction.** Melanoma represents the most fatal type of skin neoplasm. Molecular changes during the pathogenic processes of initiation and progression of melanoma are diverse and include genes and miRNA expression alteration. Several miRNAs like miR-137, miR-182 and miR-506 have been identified to be implicated in the biology of melanoma through modulation of expression of genes like MITF being involved in these pathways.

**Material and methods.** miRNA and gene expression profile analysis was performed in two melanoma cell lines SKMEL and MEWO and a normal skin cell line HACAT using qRT-PCR. The evaluation of miRNAs and MITF gene has been done in cells before and after treatment with miRNA inhibitor/mimic and siRNA-MITF.

**Results and discussion.** From the TGCA dataset analysis we identified overexpressed and underexpressed miRNAs for melanoma. QRT-PCR for miR-137, miR-182 and miR-506 in the two melanoma cell lines revealed an altered expression versus the normal skin cell line. Also, the MITF gene expression shows an altered expression in the cell lines. The same miRNA profiling and gene expression evaluation was performed in the treated cells versus untreated cells. 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 including melanoma development.

**Conclusions.** By integrating and interpreting the results obtained in our study with the ones presented in the literature, we concluded that microRNAs like miR-137, miR-182 and miR-506 and MITF gene could represent potential biomarker roles for early diagnosis and characterization of melanoma.

## The correlation of As3Mt polymorphisms with pregnancy loss in women from Timisoara County

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Corresponding Author: Laura Ancuța Pop e-mail: laura.pop@umfcluj.ro **Introduction.** Pregnancy loss (PL) affects approximately 15% of pregnant women, and recurrent pregnancy loss (RPL) affects 1-5% of women. RPL is associated with factors like chromosomal aneuploidy, genetic factors, anatomical abnormalities, immunological and endocrine disorders, infections and environmental factors. Approximately 50% of RPLs are attributed to genetic factors. Arsenic (As) is a toxic metal that is transform in a less toxic form like, monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA), by the arsenic methyltransferase (AS3MT). Studies have shown that MMAIII and DMAIII can also cause genotoxic and cytotoxic effects, and their urine percentage can be related to the efficiency of the AS3MT. In this study, we aimed to evaluate the correlation of several polymorphisms in As3MT with pregnancy loss.

**Material and methods.** The seven As3MT polymorphisms, were tested using the QiAcuity Digital PCR system on blood samples from 50 women with pregnancy loss and 50 women controls.

**Results.** Most cases and controls presented at least one of the tested polymorphisms. The tested polymorphisms were identified in a higher number of cases than controls. Polymorphisms rs7085104, rs3740390 and rs1046778 presented only heterozygote genotypes. We analyzed the haplotype observed for the controls and sample and identified 31 haplotypes for the As3Mt tested SNPs, with 4 haplotypes being the predominant ones. Linkage disequilibrium analysis identifies moderated LD between the tested polymorphisms in our cohort of patients. The predominant haplotypes were observed to be correlated to cotinine, MMA, DMA and smoking status in cases and only with DMA and MMA in controls.

**Conclusion.** We identified specific haplotypes already correlated to pregnancy loss in other populations. Our results present a correlation between the activity of AS3MT and the ability of women to transform arsenic and its negative effect on pregnancy outcomes in women from Timisoara County.

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# Cancer derived exosomes profiling following genistein and resveratrol treatment in colon cancer

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Corresponding Author: Oana Zănoagă e-mail: oana.zanoaga@umfcluj.ro **Introduction.** Despite significant advance in therapeutic options, colorectal cancer (CRC) continues to be the third most common cancer worldwide and the second leading cause of cancer-related deaths worldwide. Exosomes are extracellular vesicles that play an important role in development and progression of cancer. The aim of the present study was to establish the potential of some phytochemical compounds as adjuvants in the therapy of this type of malignancy, and to investigate the roles of cancer-cell-derived exosomes in colon cancer.

**Material and methods.** Four colon cancer cell lines (HCT-116, RKO, HT-29 and CCL-229) were treated with genistein and resveratrol (simple and combined treatment) with IC50 concentrations (60  $\mu$ M for HCT-116 and RKO, 50  $\mu$ M for HT-29 and CCL-229 of resveratrol, and 80  $\mu$ M for HCT-116 and RKO and 50  $\mu$ M for HT29 and CLL-29 of genistein). Further, exosomes were isolated from treated cells by ultracentrifugation and used to treat the four cell lines. The gene expression levels were determined by microarray, and detection of mutations through NGS. The treatment's biological effects were evaluated at cellular and molecular level at 24 hours after treatment.

**Results.** Treatment with genistein and resveratrol, and with exosomes isolated from treated cells inhibited cell proliferation, migration, invasion, and colony formation. Evaluation at molecular level confirmed the presence of some alterations in the treated cells.

**Conclusion.** The present study demonstrated a specific genomic profiling of cancer cells and their exosomes following the genistein and resveratrol treatment inhibitory effects on CRC, both as single and combined treatment. Moreover, our study supports the role of exosomes as promising biological carriers in CRC treatment.

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**DOCTORAL SCHOOL** 

### Label-free electrochemical aptasensors for the detection of grampositive and gram-negative bacteria

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Corresponding Author: Alexandra Canciu e-mail: alexandra.canciu@elearn.umfcluj.ro **Introduction.** The detection of pathogens (such as *Campylobacter jejuni* and *Staphylococcus aureus*) is a priority in the biomedical field for an early and accurate diagnostic. We aimed to develop two electrochemical sensors based on aptamers (APTs), ssDNA oligonucleotides that bind with high affinity to their target: the ONS-23 APT for *C. jejuni* cells and the PA#2/8 [S1-58] APT for *S. aureus* protein A (PrA).

**Material and methods.** Carbon-based screen-printed electrodes (SPEs) decorated with Au nanoparticles and commercial Au SPEs were employed for the functionalization with the thiolated APTs. The APTs were immobilized onto the surface by multi-pulsed amperometry, followed by the blocking of unbound sites with 6-mercaptohexanol to avoid the non-specific interactions. Optimization was conducted to determine the optimal electrode surface, electrolyte composition, and technique. Each step modification was monitored by differential pulse voltammetry and electrochemical impedance spectroscopy using a redox probe. Scanning electron microscopy was performed to confirm the morphology changes and capture of the target.

**Results.** The performance of the aptasensors was tested using *C. jejuni* NCTC 11322 and *S. aureus* ATCC 25923 strains. The quantitative determination was done by measuring the signal difference of the redox probe before and after incubation with the bacteria and correlating with the microbiological count method. The resistance to charge transfer in impedance increased proportionally with the tested concentrations, while the intensity of the current decreased. The performance of the aptasensors was also assessed with good recoveries in human serum.

**Conclusion.** Both aptasensors showed promising results for the detection of *C. jejuni* cells and protein A (as a target of *S. aureus*) in standard and biological samples.

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### Synthesis, *in vitro* antiproliferative activity and *in silico* studies on some new quinazolinyl-4-oxi-phenyl derivatives

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1) Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** The quinazoline core is a versatile scaffold used for the development of several significant anticancer compounds. The purpose of this study was to synthesize a series of novel 6,7-dimethoxy-4-phenoxy-quinazoline derivatives as potential VEGFR2 inhibitors with significant anticancer effect.

**Material and methods.** The molecular design of the novel compounds was achieved by combining already-established principals with new structural features (p-substitution of the phenyl group with various substituted thiazoles). Structural



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Corresponding Author: Alexandru Şandor e-mail: sandoralexandru32@yahoo.com confirmation of the molecules was realized through MS, IR, 1H RMN, and 13C RMN. The biological effect was evaluated *in vitro* by MTT assay on HepG2 and BJ cells and *in silico*.

**Results.** Spectral data confirm the identity of the compounds. *In silico* screening of the novel compounds (molecular docking, molecular dynamics, and quantum studies) supports the initial hypothesis. *In vitro* testing confirmed the hypothesis through the cytotoxicity evaluation of the compounds on HepG2 cells. Four out of the 7 compounds displayed superior  $IC_{50}$  on HepG2 compared to sorafenib and an interesting in silico profile with increased affinity for VEGFR2.

**Conclusion.** SA05 was identified as the most active compound, 4 times more active than sorafenib.

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### **Quercetin - a novel cardioprotective agent in chronic doxorubicin induced cardiotoxicity**

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Corresponding Author: Patricia-Lorena Dulf e-mail: pcimpan@gmail.com **Introduction.** Doxorubicin (DOX) is an effective anticancer drug, but its use is limited by dose-dependent heart toxicity, leading to acute and chronic cardiac issues. This toxicity is linked to DOX accumulation, causing mitochondrial dysfunction, reactive oxygen species generation, apoptosis, and cardiac remodeling. To date, dexrazoxane is the only approved cardioprotective agent, although not providing complete protection. Thus, this study aimed to explore the potential cardiovascular protective effects of quercetin (Q), a natural antioxidant, in chronic DOX treatment.

**Material and methods.** We conducted an *in vivo* study using 32 Wistar rats randomly divided into four groups: (1) Control group, receiving six i.p. injections of 0.9% saline solution; (2) DOX group, receiving six i.p. injections with 2.5 mg/kg body-weight DOX; (3) DOX/Q-50 group, receiving six i.p. injections with 2.5 mg/ kg body-weight DOX and 50 mg/kg/day Q orally; (4) DOX/Q-100, receiving six i.p. injections with 2.5 mg/kg body-weight DOX and 100 mg/kg/day Q orally. Animals were monitored using cardiac ultrasound (US) and serum markers for cardiotoxicity. Apoptosis, oxidative damage were measured. Electronic microscopy assessment of the hearts was also performed.

**Results.** Chronic DOX treatment led to a decline in cardiac function as shown by the reduced ejection fraction and alterations in the heart walls dimensions. These changes were accompanied with elevated values of serum NT pro-BNP, troponin and CK-MB, all indicating of cardiac stress. Q treatment slightly improved certain US parameters suggesting a potential positive influence on heart function. Notably, the treatment normalized serum NT pro-BNP levels indicating its effectiveness in mitigating cardiac stress. Furthermore, DOX induced DNA damage as showed by an increase in γH2AX, likely leading to the activation of apoptosis. Q treatment alleviated

**S165** 

these alterations albeit without achieving statistical significance.

**Conclusion.** Oral administration of Q demonstrated a promising alleviation of serum markers associated with DOX-induced cardiotoxicity. Furthermore, it exhibited a favorable impact on the cardiac US parameters. This suggests that Q may have a potential role in mitigating the adverse effects of DOX on the heart, providing valuable insights into its cardioprotective properties.

#### Novel thiazolyl-methyl-thio-quinazolin-4(3H)-one compounds. Chemical design and *in silico* studies to predict the anticonvulsant potential and druggability

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Corresponding Author: Gabriel Marc e-mail: marc.gabriel@umfcluj.ro **Introduction.** A series of deficiencies of the anticonvulsant compounds, especially the adverse effects and clinically relevant drug interactions, but also the lack of an active agent against all types of convulsions, represent important arguments for the computational exploration and drug design of novel therapeutic agents, to assign a better control of this condition. The purpose of this study was to develop novel anticonvulsant agents through computer-aided drug design (CADD) and assay their druggability properties.

Material and methods. SwissADME and AdmetSAR 2.0 online applications were used for ADMET prediction. The 3D structures of the corresponding thiazolyl-methyl-thio-quinazolin-4(3H)-ones were prepared as ligands for the molecular docking study, using the macromolecular structure of  $\alpha 1\beta 2\gamma 2$  subunit of GABAA receptor as target in AutoDock 4.2. The binding energies were expressed as variation of Gibbs free energy ( $\Delta G$ ). The series was synthesized through nucleophilic substitution of 2-phenyl-4-chlormethyl-thiazole with various 2-mercapto-quinazolin-4(3H)-ones, with with substituted in the third position. The structures were confirmed through IR, MS, 1H NMR, and 13C NMR spectral analysis.

**Results.** The ADMET prediction showed that the proposed molecules have good druggability properties, with no more than one violation of Lipinski rule in any case. Molecular docking studies showed that the compounds can interact, theoretically, through hydrogen, hydrophobic, and  $\pi$ - $\pi$  bonds. Compounds substituted with cyclohexyl, phenyl, or 4-fluorophenyl on the quinazolone ring showed the highest affinity. Based on the chemical design, 15 new compounds were obtained with excellent yields (60-89%).

**Conclusions.** Based on the results, the selected HIT/Leader molecules will be further tested *in vivo* for the anticonvulsant effect, to establish a correlation between *in vivo* activity and *in silico* prediction, as well as describing qualitative and quantitative structure-activity relationships.

#### Electrochemical sensors for the detection of two molecules involved in quorum sensing in *Pseudomonas aeruginosa*

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Corresponding Author: Denisa Căpățînă e-mail: DENISA.ELEN.CAPATINA@elearn. umfcluj.ro **Introduction.** *Pseudomonas aeruginosa* infections are associated with high mortality due to multidrug resistance and biofilm formation, necessitating early diagnosis. 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 key roles in virulence and biofilm formation. *P. aeruginosa* produces various QS molecules, including N-3-oxo-dodecanoyl L-homoserine lactone (3-O-C12-HSL), and 2-heptyl-3-hydroxy-4-quinolone (PQS).

**Material and methods.** Two electrochemical sensors based on screen-printed electrodes (SPE) were developed for 3-O-C12-HSL and PQS detection. For 3-O-C12-HSL, the electrode was modified with gold nanoparticles to facilitate specific aptamer binding, followed by 2-mercaptoethanol treatment to reduce nonspecific interactions. The last step consisted in incubating the sensor with a solution containing the molecule of interest and monitoring the difference in the electrochemical signal. The sensor for PQS detection used nanomaterial-modified SPEs and the detection of PQS occurred in an acidic medium, using differential pulse voltammetry.

**Results.** All steps in sensors development were optimized to achieve a very low limit of detection, high specificity, and good results in detecting the molecules in real samples.

**Conclusion.** These sensors provide a crucial foundation for "Point-of-care" devices, enabling the detection of *P. aeruginosa* in real samples.

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### IL-6 and neutrophil/lymphocyte ratio predict the severity of SARS-COV2 infection in patients with diabetes

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Corresponding Author: Iulia Făgărășan e-mail: fagarasan\_iulia@elearn.umfcluj.ro **Introduction.** Inflammation has a pivotal role in the evolution and prognosis of patients with SARS-CoV-2. Severe inflammatory response during coronavirus infection leads to impaired adaptive immune function, with unbalancing the immune system. Taking into account the variable clinical symptomatology and potential evolution, identifying the hyper-inflammatory state should be up front in the defining the disease stage. This study aimed to evaluate inflammatory biomarkers that could predict disease severity for patients with diabetes mellitus (DM).

**Material and methods.** The present study was conducted on a consecutive series of patients admitted to the "Leon Daniello" Pulmonology Hospital from Cluj-Napoca, Romania. After applying the inclusion and exclusion criteria, 366 participants were

included, of which 90 required transfers to intensive care unit (ICU). From the total number of ICU patients, 44 had DM as a comorbidity. To predict which marker is a predictor of severity, univariate and multivariate analysis were applied.

**Results.** The results of this study demonstrated that interleukin 6 and the neutrophil/lymphocyte ratio (NLR) collected on the day of admission could predict a severe form of infection, requiring ICU care.

**Conclusion.** The present study demonstrated for the first time that interleukin 6 and NLR on the day of admission could predict disease severity for patients with DM. The present results could help the clinicians to a better management of the disease severity and in reducing the mortality in patients who also associate diabetes.

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#### Pulmonary evaluation of patients with long COVID or post-COVID syndrome: an one year longitudinal study

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Corresponding Author: Ruxandra Puiu e-mail: puiu.ruxandra@elearn.umfcluj.ro **Introduction.** Coronavirus disease 2019 (COVID-19) is a rapidly progressive and sometimes fatal infectious disease caused by severe acute respiratory syndrome coronavirus. Severe acute respiratory syndrome coronavirus SARS-CoV-2, described for the first time in China (Wuhan city, Hubei province) at the end of 2019, was declared, in March 2020, a pandemic by the World Health Organization. For a subset of individuals with COVID-19 disease, symptoms may persist beyond 1 month, with some patients reporting symptoms at least 6 months later, termed 'long COVID'. The World Health Organization defined long COVID as generally occurring 3 months from the onset of COVID-19 with symptoms that last for at least 2 months. The aim of our study was to evaluate and describe the long COVID syndrome of the patients of our clinic.

**Material and methods.** In this study, we evaluated prospectively clinical and demographic data from 210 patients who were monitored at 3 months for clinical long COVID symptoms, by imaging (HRCT) and functional test in our pneumological hospital. Out of 210 patients with severe infection, 197 underwent chest HRCT scan at 3 months follow-up. The patients with evidence of pulmonary fibrotic like lesions in the first 3 months of follow-up, underwent a new HRCT again at 6 months. Monitoring of persistent symptoms and sequelae was performed through interviews conducted in person for each patient at 3 months after diagnosis, and at 6 months and at 12 months from November 2021 to November 2022. Individual patient information was collected by the questionnaire and included demographic aspects (age, sex), smoking status, ICM, comorbidities, COVID confirmation, severity of acute infection, initial HRCT severity score, number of the hospitalization days, treatment. We also evaluated risk factors for long COVID syndrome and correlated the symptoms and variables with the presence of pulmonary lesions.

**Results.** We evaluated 210 patients. We report that the median age of patients at post COVID-19 evaluation follow up was 60.39 years. Slightly most of the patients

were men and the majority had a non-smoker status). 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 metabolic and cardiovascular disease. 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. Half (50.5%) of the hospitalized patients needed supplemental oxygen. At 1-3 months after the infection during the follow-up visit, 95.1% of patients report symptoms. The most prevalent ones were dyspnea, fatigability and exercise intolerance. Severe pulmonary lesions have been correlated significantly with older age, ICU admittance and the presence of symptoms at 1-3 months.

**Conclusions.** COVID-19 is a multisystemic disease that affects different and various organs, with significant long-term effect on patients'respiratory health. The development of fibrotic-like abnormality is associated with older age and with the presence of ICU admission. Following COVID-19 infection, especial severe, pulmonary fibrotic-like involvement should be monitories for up to 3 months, and it should be highlight that there is a chance of regression with treatment. Future studies are required to investigate the risk factors for pulmonary fibrosis.

# VCAM-1 is associated with higher cardiovascular risk in obstructive sleep apnea patients

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Corresponding Author: Ioana-Maria Chețan e-mail: Ioana.Chetan@umfcluj.ro **Introduction.** The link between obstructive sleep apnea (OSA) and cardiovascular disease (CVD) is still not fully elucidated, despite the associated high cardiovascular morbidity. It is well known that atherosclerosis is a chronic inflammatory pathology, and that OSA-induced hypoxia accelerates the atherogenic process. Adhesion molecules (VCAM-1, ICAM-1) have been shown to be associated with atherosclerotic disease and increased cardiovascular risk. Thus, the aim of our study was to evaluate whether the levels of VCAM-1 and ICAM-1 correlate with the cardiovascular risk associated with OSA.

**Material and methods.** We enrolled 80 patients diagnosed with OSA and 37 healthy volunteers. SCORE 2 and SCORE 2OP regional charts were used to quantify cardiovascular risk. Serum levels of VCAM-1 and ICAM-1 were also assessed in all participants.

**Results.** Subjects with OSA were all assigned to the high cardiovascular risk class. VCAM-1 levels were higher in the OSA group compared to the control group. There was a statistically significant association between the cardiovascular risk categories and VCAM-1. No significant correlations were identified with respect to ICAM-1 levels.

**Conclusion.** VCAM-1 is directly associated with increased cardiovascular risk in OSA patients. The addition of novel biomarkers such as VCAM-1 to conventional risk stratification scores may improve risk stratification and also guide treatment eligibility in CVD prevention in the OSA population.

## Single channel multiple fluorophore imaging of *Staphylococcus* and *Pseudomonas* biofilm matrix

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Corresponding Author: Pavel Șchiopu e-mail: schiopu.pavel@elearn.umfcluj.ro **Introduction.** Microorganisms can form complex, multi-layered colonies named biofilms, through attachment to surfaces (e.g. implanted devices, mucous membranes). These multicellular structures protect the bacteria from antimicrobials and the immune system. Biofilms consist of bacteria enclosed in an extracellular matrix (polysaccharides, proteins and extracellular DNA). In this paper, we describe a method for the microscopic visualization of *Staphylococcus aureus* and *Pseudomonas aeruginosa* biofilms using fluorophores that bind to matrix components.

Material and methods. Biofilms were cultured directly on glass slides halfway immersed in nutrient broth (Oxoid), incubated at 37°C for three days in aerobic conditions. Standard bacterial strains were used, namely *S. aureus* ATCC 25923 and *P. aeruginosa* ATCC 27853. Slides were wiped with 99% isopropyl alcohol on one side and heat-fixed at 70°C for 10 minutes (except for Live/Dead staining). Staining was performed with Concanavalin A, Alexa Fluor 488 conjugate (1 mg/mL (w/v)) for matrix polysaccharides, and SYPROTM Ruby stain for matrix proteins. A second staining protocol involved SYTO 9 and Propidium Iodide from a Live/Dead<sup>™</sup> BacLight<sup>™</sup> viability stain kit according to manufacturers' manuals. All dyes were obtained from Thermo Fisher Scientific. Microscopic imaging was conducted on a Zeiss Axio Lab A2 microscope using a 100×/1.25 oil objective using a 470nm LED for excitation, a 515nm long pass emission filter and an Erc 5s camera for image acquisition.

**Results.** The staining patterns demonstrated compositionally distinct regions within the biofilms. In the case of *P. aeruginosa* biofilms, the periphery was more intensely stained by SYPRO Ruby, and the center was more intensely stained by ConA. Planktonic *P. aeruginosa* cells were still stained with SYPRO Ruby, but they were dispersed rather than aggregated around a ConA core. Both *S. aureus* biofilms and planktonic cells were stained by SYPRO Ruby, but biofilm cells appeared in aggregation. Neither stained with ConA.

**Conclusion.** Concanavalin A conjugates can be used together with SYPRO Ruby stain for the visualization of in vitro grown *S. aureus* and *P. aeruginosa* biofilms. However, only *Pseudomonas* matrix polysaccharides can be reliably visualized.

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# Innovative strategies for glypican-3 biomarker targeting: aptamer selection for assisted treatment of hepatocellular carcinoma

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Corresponding Author: Magdolna Casian e-mail: magdolna.casian@elearn.umfcluj.ro **Introduction.** Hepatocellular carcinoma (HCC) is one of the leading causes of cancer-related mortality worldwide and is characterized by a constantly increasing incidence, low-sensitivity screening methods, and resistance to conventional therapy. The use of DNA aptamers as biorecognition elements has numerous advantages over antibodies, such as improved stability, smaller size, low immunogenicity, and the possibility of being obtained *in vitro*. This poster presents the selection of a novel aptamer through magnetic-beads (MBs) SELEX technology for glypican–3 (GPC–3), an HCC expressed biomarker.

**Material and methods.** The hexahistidine-tagged protein was immobilized on tosyl-activated MBs, after which multiple selection rounds were performed using different counter molecules to make the selection more stringent. The progress of aptamer selection was monitored by quantitative real-time PCR, melting curve and enrichment assays. After selection, the resulting oligonucleotides were cloned, sequenced for primary structure determination, and analyzed using different bioinformatics tools.

**Results.** The results indicated that round 4 yielded the highest bound percentage towards GPC–3. Upon cloning and sequencing experiments, a total of 50 sequences were selected, out of which five most promising were analysed by surface plasmon resonance technique for affinity evaluation.

**Conclusions.** The aptamer with the highest affinity will be used for the development of a targeted delivery system based on MBs functionalized with an antiangiogenic tyrosine kinase inhibitor drug, which can be guided to the tumor site using a magnetic field for both imaging and drug delivery.

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# Electrochemical direct detection of inflammation-associated biomarkers

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Department of Analytical Chemistry and Instrumental Analysis, Faculty of Pharmacy, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Kynurenic acid (KA) and cortisol (COR) are endogenous compounds characterized by vital biological functions whose concentration provides information about the existence of inflammation-associated processes. Thus, their rapid and sensitive detection in biological samples can be successfully applied in clinical diagnosis, monitoring, and evaluation of medical interventions in inflammatory conditions. In this regard, the development of electrochemical sensors represents a

Corresponding Author: Maria-Bianca Irimeş e-mail: maria.bi.irimes@elearn.umfcluj.ro suitable approach for the determination of these biomarkers considering that they present the properties mentioned above and, in addition, they present suitability for miniaturization with prospects for wearable devices and in situ analysis. The main objective of the study was to design customized platforms for KA and COR direct electrochemical detection in biological samples with prospects for biomedical applications.

**Material and methods.** Flexible, customized carbon electrochemical cells were in-lab printed. The surface of the working electrodes was modified using a nanocomposite based on reduced graphene oxide for KA and based on Ni nanocomposite for COR detection, respectively.

**Results.** The obtained platforms were fully characterized using both electrochemical (cyclic voltammetry, electrochemical impedance spectroscopy) and morphological techniques (AFM and SEM) and further applied for the detection of KA through differential pulse voltammetry and of COR through cyclic voltammetry. The analytical performances (detection limit, limit of quantification, and sensitivity for KA and COR respectively) were evaluated and the platforms were used for real sample analysis.

**Conclusion.** The elaborated sensors allow KA and COR direct electrochemical detection and can be applied for medical applications.

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# The importance of cerebrospinal fluid analysis in first-episode psychosis

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 Department of Neurology and Pediatric Neurology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** First-episode psychosis (FEP) refers to a heterogeneous disorder characterized by the emergence of new psychotic features i.e., delusions, hallucinations, accompanied by bizarre behavior. While >85% of FEPs are eventually diagnosed as primary psychiatric disorders (pFEP, including first-episode schizophrenia, FES), approximately 10% have an underlying organic cause. Yet, evaluation methods such as cerebrospinal fluid (CSF) analysis are often overlooked in FEP, despite generating first-hand valuable data on neuronal pathology.

**Material and methods.** We conducted a non-systematic review of the current literature in order to provide an updated perspective on the potential value of CSF analysis in FEP.

**Results.** In clinical practice, CSF analysis remains essential when suspecting anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis as >85% of patients present with a clinical picture indistinguishable from pFEP. Regarding the use of CSF analysis to build characteristic profiles in pFEP, we reviewed 29 studies that reported on 10 different classes of potential biomarkers: inflammatory, immunological, blood-brain barrier impairment, neurodegenerative, synaptic, neuroprotective, metabolomic, proteomic, lipidomic, and glycomic biomarkers. Despite providing a valuable data pool, no single parameter emerged



Corresponding Author: Denis Pavăl e-mail: paval.denis@yahoo.com as a reliable biomarker given that studies were underpowered and provided conflicting data that was difficult to integrate.

**Conclusion.** Lumbar punctures remain an exception during psychiatric evaluation making CSF analysis an often-overlooked evaluation method in FEP. While neural antibody testing became available in most centers, characteristic biomarker profiles in pFEP will probably not experience the same large-scale development and will remain limited to specialized research centers.

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### The dopamine hypothesis of autism spectrum disorder: from molecule to behavior

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Corresponding Author: Denis Pavăl e-mail: paval.denis@yahoo.com **Introduction.** Despite intensive research into the etiopathogenesis of autism spectrum disorder (ASD), limited progress has been achieved so far. Among the plethora of models seeking to clarify how ASD arises, a coherent dopaminergic model was lacking until recently. In 2017, we provided a theoretical framework that we designated "the dopamine hypothesis of ASD". In the meantime, numerous studies yielded empirical evidence for this model. Four years later, we provided a second version encompassing a refined and reconceptualized framework that accounted for these novel findings.

**Material and methods.** We conducted a non-systematic review in which we highlight the evidence backing the previous versions of our model and add the most recent developments to the picture.

**Results.** Our model is supported by numerous evidence encompassing human (neuroimaging, pharmacological interventions, genetic) and animal model studies.

**Conclusion.** Along these lines, we lay out a comprehensive analysis of the supporting evidence for the dopamine hypothesis of ASD.

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### Analyzing antibiotic removal efficiency, seasonal variations, environmental risk assessment, and isolated bacterial strains in conventional wastewater treatment plants

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Introduction. Wastewater treatment plants (WWTPs) play a crucial role in removing antibiotics and other pollutants from wastewater before its discharge into the

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Corresponding Author: Svetlana Iuliana Polianciuc e-mail: svetlanaiuliana@gmail.com environment. Our study aims to show a seasonal pattern of the following antibiotics amoxicillin, piperacillin, ciprofloxacin, norfloxacin, azithromycin, clarithromycin, doxycycline, detected in the influent and effluent wastewaters, to determine the efficiency of antibiotic removal of wastewater treatment processes, to estimate the risk on the environment and, to determine the antibiotic resistance profile of isolated bacteria.

**Material and methods.** The sampling was organized in autumn 2021, winter, spring, and summer 2022 from three WWTPs. Solid phase extraction was used for the pre-concentration of the samples followed by an HPLC-MS analysis. Bacteria strains isolated were characterized morphologically through Gramm staining and the resistance to the chosen antibiotics was assessed through the classic antibiogram method.

**Results.** The concentration of antibiotic residues varies across seasons. The antibiotic removal rate in all three WWTPs varied between 100% and -315%. All the targeted antibiotics at some point showed a high level of risk based on the ecological risk assessment (RQ > 1). We identified resistant or intermediate-resistant strains in WWTP C effluents from the Q2 spring season to all monitored antibiotics and high RQs for amoxicillin and norfloxacin.

**Conclusion.** The detected antibiotics showed discrepant seasonal variation. A negative and low antibiotic removal efficiency demonstrates that the WWTP cannot remove the antibiotics efficiently. Most of the antibiotics targeted showed a high RQ level. A possible correlation was observed between the high RQ of antibiotics and the identification of resistant or intermediate-resistant strains in the same harvest season.

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# Socio-demographic characteristics of patients with schizophrenia: a single center retrospective study

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Corresponding Author: Răzvan Pop e-mail: razvan9116@gmail.com **Introduction.** Schizophrenia is a severe, chronic, and enfeebling psychiatric disease that causes functioning impairment (e.g. professional, interpersonal relationships or self-care). Our study aimed to evaluate the socio-demographic characteristics of patients with schizophrenia and full clinical evaluation (severity of symptoms and brief psychiatric rating scale).

**Material and methods.** A retrospective cohort study of adults (18-65 years) with schizophrenia (ICD-10), hospitalised from 2018 to 2022 at the first and second psychiatric clinics of the County Emergency Hospital of Cluj-Napoca, Romania was conducted. Socio-demographic factors (sex, living accommodation, season of birth, occupation, marital status), clinical family history of schizophrenia, cardiac and metabolic comorbidity, and drug use were analysed. Incomplete clinical data in medical records led to exclusion. We split the cohort into groups according to age (18-30, 31-40, and 41-65) to investigate if patterns exist.

**Results.** There were more men than women patients (207/350), especially in the youngest group (p=0.079). Most patients live with the family (234/301), with a decrease of percentage with the increase of age group (90%, 79%, 69%; p=0.004). Most patients were born in spring (100/350), with 56% born in winter or spring. The unemployment status decreases with age; 72% of the youngest are unemployed, and 73% of the oldest are



retired (p<0.0001). Most participants had no family history of schizophrenia (193/260). As expected, cardiovascular (22% oldest, p<0.0001) and metabolic co-morbidities (40% oldest, p=0.0021) are associated with age class, while drug use is more prevalent in youngsters (27%, p<0.0001).

**Conclusion.** Patients with schizophrenia are more likely to be male, born in winter or spring, without a family history of schizophrenia, unemployed if they are young, retired if they are older than 40 years, with metabolic and/or cardiovascular comorbidity as the age is higher and a drug used for young patients.

#### General anesthesia improves procedural efficiency of high-power short-duration ablation for paroxysmal atrial fibrillation: a comparison with mild conscious sedation

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Corresponding Author: Ioan-Alexandru Minciună e-mail: iaminciuna@gmail.com **Introduction.** Atrial fibrillation (AF) represents the most common cardiac arrhythmia in adults worldwide. Catheter ablation (CA) of paroxysmal AF (PAF) provides higher efficacy with comparable safety as antiarrhythmic drug therapy. Recently, high-power short-duration (HPSD) approach has emerged as an alternative to standard-power standard-duration settings, showing reduction in ablation times and increasing patient tolerability, with similar outcomes in terms of safety and efficacy. Although the advantages of general anesthesia (GA) are well established for standard-power standard-duration settings, there is currently limited data comparing GA to mild conscious sedation (MCS) for HPSD approach.

**Material and methods.** We included patients with PAF who underwent HPSD CA using a contact-force sensing catheter (50W, ablation index 450 on the anterior wall and 320 on the posterior wall) either under GA or MCS. Procedural characteristics and success rates were compared between the two groups, as well as mid-term outcomes. Procedural safety was evaluated by intra- and post-procedural complications. Procedural efficiency was evaluated by total procedural time, number of radiofrequency applications, fluoroscopy time and dose. Acute success was defined as confirmation of entrance block in all pulmonary veins and mid-term success as freedom of AF at 6-months follow-up visits.

**Results.** A total number of 102 patients were included in the study, 34 which underwent HPSD CA for PAF under GA (group 1, mean age 60.1±10.6), and 68 under MCS (group 2, mean age 58.6±10.6). We found lower mean total procedure time in the GA group (101.6±24.0 vs. 165.7±42.5 min, p<0.0001), as well as lower radiation exposure (1156.6±1032.3 vs. 3049.2± 2303.5  $\mu$ Gy, p<0.0001 and 4.4± 2.5 vs 9.3± 7.5 min, p<0.0004) and lower number of radiofrequency applications (68.9± 19.2 vs. 104.2± 27.6, p<0.001). At the 6-months follow-up AF recurrence rate was lower in GA group (11.7% vs. 26.4%), however without reaching statistical significance (p=0.09). There was one moderate pericardial effusion in the MCS group which remitted with pharmacological treatment.

**Conclusion.** Our data suggest that GA improves procedural outcomes during HPSD CA for PAF and may be associated with lower mid-term recurrence rate.

#### Fetal bilateral diaphragmatic agenesis – a case report

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Corresponding Author: Viorela-Elena Suciu e-mail: suciuviorela@yahoo.com **Introduction.** Congenital diaphragmatic agenesis is a rare type of diaphragmatic defect with an incidence of 1:250,000 births, reported to be 6% of all congenital diphragmatic hernias. It can be unilateral or bilateral and also it can be associated or not with other malformations. The etiology is not well defined. An autosomal recessive mode of inheritance has been proposed, but is not agreed universally.

**Material and methods.** We report the case of a 3100 gram male infant born by Cesarian section at 41 weeks of gestation to a 25-year-old IG IP mother. Pregnancy was uncomplicated and maternal medications consisted of prenatal vitamins only. No family or past medical history of note. There was no history of smoking, alcohol, illicit drug use and all prenatal labs were normal. There was no parental consanguinity.

**Results.** The infant's APGAR score was 6/6 at 1 and 5 minutes respectively. Immediately postpartum, severe respiratory distress occurred requiring intubation, mechanical ventilatory assistance and pharmacological support. Chest radiography reveled massive left pneumothorax and right lung atelectasis. Despite the evacuation of the pneumothorax, a cardio-pulmonary arrest occurred and the death occurred. The autopsy revealed bilateral diaphragmatic agenesis, bilateral pulmonary hypoplasia, bilateral pneumothorax, pulmonary hypertension and ostium primum-type atrial septum defect. No chromosomal study was performed.

**Conclusion.** Bilateral agenesis of the diaphragm is a very rare condition with few cases reported in the literature. Regarding the fact that congenital diaphragmatic defects are sporadic or as a component in various syndromes, some of them with chromosomal anomalies, is essential to do a detailed antenatal scan to determine the need for early intervention and for genetic counselling for possible hereditary syndromes and future pregnancy planning for the parents.

## Development of molecularly imprinted polymer-based electrochemical sensor for thiabendazole detection

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Corresponding Author: Szabolcs I. Győrfi e-mail: szabolcsjanos.gyorfi@gmail.com **Introduction.** Pesticides are widely used in agricultural practices to protect crops from pests and diseases. However, their excessive and indiscriminate use can pose serious threats to human health and the environment. Thus, the development of sensitive and selective detection methods for pesticide residues is of utmost importance. Employing direct electrochemical techniques can be difficult for the trace analysis. However, a thin electrochemically synthesized molecularly imprinted polymer (MIP) layer able to selectively preconcentrate the target molecule in the vicinity of the electrochemical transducer may represent a viable option. This study presents the design and fabrication of an electrochemical sensor modified with indole-3-acetic acid (3IAA) MIP for the detection of thiabendazole (TBZ), a commonly used fungicide and pesticide.



**Material and methods.** The thin 3IAA-based molecularly imprinted polymer film was electrodeposited onto the surface of a gold electrode (GE) using cyclic voltammetry, providing selective recognition sites for the target molecule, thiabendazole. The electrochemical behavior of the modified sensor was investigated using differential pulse voltammetry (DPV) and impedance spectroscopy (EIS). The sensor exhibited enhanced electrocatalytic activity and increased sensitivity towards thiabendazole compared to the bare electrode. Moreover, the fabricated sensor demonstrated excellent selectivity, runto-run stability, and reproducibility.

**Results.** To determine the detection performance, calibration curves were constructed by measuring the electrochemical response of the sensor at different concentrations of thiabendazole in synthetic and real sample matrices. The sensor exhibited a linear response within the concentration range of interest, with a low detection limit, indicating its suitability for thiabendazole detection in real samples.

**Conclusion.** The proposed electrochemical sensor holds great promise for rapid, on-site detection of thiabendazole residues in different water samples. Its high selectivity, sensitivity, and simplicity make it a valuable tool for monitoring and ensuring food safety, environmental protection, and public health. Further research could focus on optimizing the sensor's performance parameters and investigating its applicability in other real-world scenarios.

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## Myelodysplastic syndrome: less frequent cause of cognitive impairment in the elderly – a case report

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The myelodysplastic syndrome can damage the frontal-subcortical pathway causing cognitive impairment. An 82 years old female patient, known with mild cognitive impairment, hypertension, atrial fibrillation, presented at the outpatient clinic accusing aggravation of the short-term memory loss, tension-type headache and dizziness. In the previous two years, the patient underwent repeated neurophysiological examination, the latest 4 months prior to the current presentation, which showed a stable mild cognitive impairment. Neurologic examination done at this time revealed central vestibular syndrome, visuospatial dysfunction, motor perseveration, anomia and dyscalculia. The new neurophysiological test revealed a rapid deterioration of the cognitive function. Brain computer tomography without contrast showed bilateral thalamic, bilateral periventricular lacunar ischemic lesions and frontal, temporal, and parietal lobe atrophy. Because the routine laboratory work up revealed megaloblastic anemia and leucopenia, we referred the patient to the hematology clinic, where the patient was diagnosed with myelodysplastic syndrome. The rapid deterioration of cognitive function in elderly patients can also lead to less common conditions, which is why careful multidisciplinary evaluation is required.

## Delta/Alpha ratio in traumatic brain injury - a biomarker for treatment evaluation

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Corresponding Author: Olivia Verişezan-Roşu e-mail: olivia.rosu@brainscience.ro **Introduction.** Quantitative electroencephalography (qEEG) is a non-invasive diagnostic technique, which provides objective measures of cerebral activity, offering insights about brain dysfunction. One of its most reliable indices, DAR (delta/alpha ratio), was selected for analysis in a subset of patients with moderate-severe traumatic brain injury (TBI) from the CAPTAIN-rTMS clinical trial.

**Material and methods.** Fifty patients underwent two qEEG recordings, at 30 and 180 days post-initial traumatic brain injury. They were randomly assigned to one of three groups: Cerebrolysin + repetitive transcranial magnetic stimulation (CRB+rTMS), Cerebrolysin + sham (CRB+sham), and Placebo + sham (PLC+sham). Brainstorm processed qEEG signals, while R Matlab analyzed data, calculating the DAR as the delta-to-alpha power ratio. We assessed DAR for both frontal and all scalp electrodes.

**Results.** We observed a statistically significant increase of DAR between visits (p=0.023-global DAR and p=0.026-frontal DAR), without a meaningful therapeutic influence - for treatment-visit interaction the p-values were 0.2 and 0.3. The biggest effect size was recorded for the patients treated with Cerebrolysin and sham, with a p-value of 0.01 and a  $\delta$  of 0.46 for global DAR and a  $\delta$  of 0.33 for frontal DAR, without a significant difference. No other differences were observed between groups or visits.

**Conclusions.** This study explored the utility of qEEG, focusing on DAR, as a tool to assess cerebral activity in patients with moderate-severe TBI. Despite the observed temporal shift, no therapeutic influence on DAR was found, as indicated by the non-significant treatment-visit interaction results. These findings suggest that DAR dynamics may be inherent to the recovery process following TBI, regardless the therapeutic interventions. Further research is necessary, focusing on a deeper understanding of the clinical implications of DAR changes and the potential benefits of these therapies for TBI patients.

### Solid pseudopapillary neoplasms of the pancreas - a case report and literature review

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1) Department of Surgery 3, Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, Romania

2) Regional Institute of Gastroenterology and Hepatology Cluj-Napoca, Romania **Introduction.** Solid pseudopapillary neoplasms (SPNs) represent a rare type of pancreatic tumors (between 0.9 and 2.7% of all exocrine pancreatic neoplasms), with an uncertain pathogenesis and risk of malignancy. This type of tumor generally affects young women (median age of 28) and is asymptomatic, its discovery being mostly incidental. Men are less frequently affected by this pathology and are usually older than women at diagnosis. Given the possibility of malignancy, surgical resection is considered the gold standard of treatment.



Corresponding Author: Iulia Vlad e-mail: iulia.vlad94@yahoo.com **Case presentation.** We present the case of a 40-year-old male patient with an atypical pancreatic mass incidentally found at a routine abdominal ultrasound. In order to obtain a conclusive diagnosis an endoscopic ultrasound was performed, which described a poorly demarcated, echo-poor, inhomogeneous mass in the pancreatic tail, of 25/30mm, with intimate contact with the splenic artery. EUS-FNA was also carried out, with a histopathological report suggestive for a solid pseudopapillary neoplasm. Exploratory laparoscopy was performed and a 4/3 cm tumor involving the pancreatic body and tail was discovered, in close contact with the splenic vessels. Due to a very difficult dissection of the splenic hilum we converted to classic surgery and performed a corporal-caudal pancreatectomy associated with splenectomy. The postoperative evolution was favorable, with no notable complications. The patient was discharged on the seventh postoperative day. The final histopathological report confirmed the diagnosis of solid pseudopapillary neoplasm (pT2N0MxL0V0Pn1R0). The five-month follow-up ultrasound and routine blood work did not reveal any pathological findings.

**Conclusion.** Even though data is still unclear regarding the pathogenesis of the solid pseudopapillary neoplasms, the fact that they can present malignant characteristics makes surgical resection the standard of care for this pathology. As demonstrated in multiple studies, the prognosis and quality of life after surgery are both favorable, even in metastatic forms of the disease.

### The degree of recommendation of DPYD testing among oncologists in Romania

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7) Department of Oncology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania **Introduction.** Fluoropyrimidines remain the cornerstone of many chemotherapy protocols despite the progress of anti-cancer treatments. Fluoropyrimidines-related mechanism of toxicity is a well-known subject, and one of the method to asses toxicity is the DPYD gene testing. In the present study, the goal is to evaluate the conditions and limitations regarding DPYD mutation testing recommendations among medical oncologist from Romania.

**Material and methods.** An online survey was sent through electronic platforms to the prescribing medical oncologists from Romania who are members of the Romanian Society of Medical Oncology (SNOMR).

**Results.** 28.2% of the prescribing Romanian oncologist filled out our survey. 25% of the responders report using fluoropyrimidines based chemotherapy daily, and gastrointestinal tract cancers followed by head and neck cancers represent the most frequent tumour locations in which there are used. Grade 2 adverse event (AE) were the most common AE in clinical practice reported with a frequency of 90%. Only 3% of the oncologists declared that they recommended DPYD testing. The lack of reimbursement from the authorities is the main reason why Romanian oncologists do not recommend testing.

**Conclusion.** The degree of recommendations of DPYD testing among Romanian medical oncologists is low due to lack of reimbursement. The frequency of AE in

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Corresponding Author: Andrada Larisa Deac e-mail: andrada.deac@gmail.com clinical practice is much higher than clinical studies, therefore the lack of testing can burden the medical system and the cost of complications treatment.

# Polyphenolic profile and antioxidant activity of some Betula sp. extracts

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Corresponding Author: Timea Bab e-mail: bab\_timi@yahoo.com **Introduction.** Betula genus includes about 60 species, spread in the Northern Hemisphere, of which 4-5 are better known in the Romanian spontaneous Flora. The leaves of Betula species are recognized for their diuretic properties. The study aims to compare the polyphenolic profile of two indigenous species of Betula: B. pendula Roth. respectively B. pubescens Erhr.

**Material and methods.** The comparative study was carried out on various parts of the plant: buds, leaves, bark, seeds and sap, harvested from Cluj Country, Mărişel and Baciu area. Specific phytoterapeutic or gemmotherapic extracts were prepared from the plant materials. The extracts were chemically evaluated by spectral and chromatographic methods.

**Results.** The result of LC/MS analysis indicated the presence of polyphenolic compounds in all extracts. The extracts obtained from B. pubescens were richer in gallic acid, chlorogenic acid, trans-p-coumaric acid, luteolin-7-O-glucoside, hyperoside, isoquercitrin, quercetin, naringenin and those from buds and leaves of B. pendula were richer in gallic acid, chlorogenic acid, hyperoside, quercetin and naringenin. The polyphenol contents were higher in B. pendula extracts.

**Conclusion.** The results are in accordance with the antioxidant properties of the extracts evaluated by in vitro methods (DPPH and FRAP).

### Facial reanimation after peripheral facial nerve paralysis: a singlecentre surgical experience

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Introduction. Patients with facial asymmetry and no facial muscle contractions have long experienced social difficulties and psychological distress, so they seek



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Corresponding Author: Georgeta Magdalena Balaci e-mail: balacimagdalena@yahoo.com treatment to restore facial symmetry and improve quality of life and self-image. Researchers have evaluated numerous surgical techniques, but achieving results without side effects remains a significant hurdle. Specifically, anastomosis between the ansa cervicalis (AC) and facial nerve (FN) can impair the patients' physical appearance. This study examined the efficiency of AC and FN anastomosis for facial motor function recovery and assessed its usefulness for treating patients with chemotherapy or hypothyroidism-induced peripheral neuropathy.

**Material and methods.** Four patients diagnosed with grade VI facial palsy on the House & Brackmann Scale (HB) after vestibular schwannoma (VS) resection (Koos grade IV) via the retrosigmoid approach underwent AC and FN anastomosis. Two female patients had histories of malignancies: the first underwent surgery for breast cancer, and the second underwent surgery for uterine cancer and melanoma. Both patients developed chemotherapy-induced peripheral neuropathy (CIPN). A third patient (male) did not have CIPN and did not meet the study criteria but was included to provide evidence of anastomosis efficacy. A fourth patient (female) developed peripheral neuropathy as a consequence of persistent hypothyroidism. The outcomes were related to tumor grade, previous therapy, and time between postoperative facial palsy and anastomosis. Images and neurophysiological results were evaluated.

**Results.** After VS resection, all four patients exhibited grade VI facial palsy for an average of 17 months. During follow-up (6-36 months), two patients were diagnosed with HB grade III facial palsy, and two were diagnosed with HB grade IV facial palsy. No patient developed tongue atrophy, speech disorder, or masticatory dysfunction.

**Conclusions.** AC and FN anastomosis is safe and effective for treating complete facial paralysis after cerebellopontine tumor resection. Nerve reanimation is feasible even for patients with chemotherapy- or posthypothyroidism-related peripheral polyneuropathy. This study also offers a new therapy for patients with progression-free status.

### **Burnout among OMF surgery interns – another side of the story of the pandemic**

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Corresponding Author: Anamaria Beşleagă e-mail: anabesleaga@gmail.com **Introduction.** Oral and maxillofacial (OMF) surgery interns are a particular type of surgical interns because of their academic requirements and on the other hand they often also work in private dental practices. The ICD-11 defines burnout as a syndrome which derives from chronic workplace stress that has not been successfully managed. From an occupational point of view, it is comprised of three dimensions: feelings of energy depletion or exhaustion, increased mental distance from one's job, or feelings of negativism or cynicism related to one's job and reduced professional efficacy. The aim of this study was to identify the main characteristics of the OMF surgical interns and highlight the need for emotional support and for diminishing the mental load of the average surgical intern in the context of the Covid-19 period.

**Material and methods.** The study was conducted online via Google forms through an anonymous mixt questionnaire, comprised of both multiple choice and open questions. The target population were Oral and maxillofacial surgery interns working in University Hospitals in Romania. The questions they were asked concerned aspects of their professional, personal and psychological status.
**Results.** There were thirty-eight oral and maxillofacial surgery interns who completed the questionnaire - most of them under 30 years old, males, in their third year of internship. 34.2% had four or more on call shifts per month and 78.9% worked normal day shifts after being on call. 57.9% reported insomnia. Most of them denied having any medical conditions (78.94%), but only 18.4% denied experiencing symptoms related to stress. Half experienced disturbances in their social life and most of them in their personal life. Many of them reported a sense of being overwhelmed by the workload and not having full control over their daily issues.

**Conclusions.** Practicing surgery has additional stress factors as opposed to other specialties and professions. The patients' perception of their doctor, fear of failure, long hours, mental load and poor coping mechanisms may lead to early burnout amongst young doctors. Acknowledging the professional and psycho-social aspects of medical trainees' lives can improve daily medical practice and the educational process of future medical professionals.

## Lavender oil enhances the effect of nadroparin calcium in experimental thrombosis

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Corresponding Author: Sorana D. Bolboacă e-mail: sbolboaca@umfcluj.ro **Introduction.** Previous studies have demonstrated the therapeutic effects of lavender oil (LO), which include antinociceptive, sedative, anxiolytic, antimicrobial, antifungal, anti-inflammatory, and antioxidant activities. This study aimed to evaluate the additional effects of LO to nadroparin calcium (NP), on carrageenan-induced thrombosis in rats.

**Material and methods.** We conducted an experimental study on rats. The Wistar Bratislava male rats were randomly divided into four groups of ten rats as follows: Group 1 (C), referred to as the control group, was administered intraperitoneal saline (i.p.) and vehicle (DMSO). Group 2 (T), referred to as the thrombosis group, received saline along with vehicle pretreatment and subsequently underwent thrombosis. The third group (TNC) received subcutaneous (s.c.) treatment with NP and also underwent thrombosis. The fourth group (TNCLO) was pretreated with LO at a dose of 200 mg/ kg body weight i.p. and NC s.c. The study evaluated several indicators of oxidative stress, including malondialdehyde, nitric oxide, and total oxidative stress, as well as antioxidant measures such as total antioxidant capacity and thiols. In addition, levels of TNF- $\alpha$ , MCP-1, and RANTES were measured.

**Results.** The study outcomes indicate that the rats receiving pre-treatment with LO showed improvements in oxidative stress, antioxidant status, and pro-inflammatory levels, compared to rats that were treated only with NC (p-values<0.0001).

**Conclusion.** Our results demonstrated that active compounds of lavender oil significantly improve the effect of Nadroparin calcium, suggesting potential benefits in decreasing the inflammatory component of thrombosis.

## IL-31—Pruritus Interleukin: serum values and clinical impact in chronic spontaneous urticaria

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Corresponding Author: Carmen-Teodora Dobrican-Băruța e-mail: dobrican.carmen@umfcluj.ro **Introduction.** This research was conducted to evaluate the role of interleukin-31 (IL-31) in chronic spontaneous urticaria (CSU) by comparing its serum levels in CSU patients to those in healthy controls. The study also aimed to correlate IL-31 levels with other clinical and paraclinical parameters to assess its immunological significance and explore its potential as a therapeutic target in CSU.

**Material and methods.** We measured the serum IL-31 levels in 50 CSU patients diagnosed according to internationally recognized guidelines, alongside a control group of 38 individuals without a history of urticaria.

**Results.** The data indicated a significant elevation in serum IL-31 levels in CSU patients compared to the control group (p < 0.0001). Despite the lack of direct correlation with inflammatory markers such as the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), eosinophil counts, or total IgE levels, there were notable associations of IL-31 levels with the severity of CSU, the impact on quality of life, the intensity of itching, and the response to H1 antihistamine treatments (all with p-values < 0.05).

**Conclusion.** The study underscores the non-associative nature of IL-31 with general inflammation, eosinophilia, or atopy in CSU. However, its levels are significantly influenced by the disease's severity, pruritus severity, and treatment response to H1 antihistamines. These findings contribute valuable insights into the pathogenesis of CSU, highlighting the potential for IL-31 to be a focal point for new treatment strategies, given the current treatment limitations in managing the full spectrum of CSU symptoms.

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## Differential mRNA and miRNA expression and interaction patterns in lung and thyroid cancers

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**Introduction.** Lung and thyroid cancers are a serious, worldwide, health burden. When it comes to their genomic architecture, a better understanding is required. This *in silico* analysis aimed to identify novel biomarkers and gene-interaction networks in these cancers.

**Material and methods.** TCGA datasets were obtained from the University of California Santa Cruz via the Xena browser. With GeneSpring GX we analyzed the differential expression levels of mRNAs and miRNAs associated with these cancers, while a gene set enrichment analysis was performed using enrichR. The Kaplan-Meier

Corresponding Author: Paul Chiroi e-mail: chiroipaul@gmail.com survival was evaluated using the Graph Pad Prism. The miRNA-mRNA interaction networks were analyzed using miRNET, TargetScan, and miRTarBase online tools, as well as through a weighted gene co-expression network analysis. Network visualization and analysis was performed using Cytoscape.

**Results.** In the lung cancer datasets, CD300LG, LOC149620, C13orf36, MYOC, SLC6A4 were the most downregulated genes, ABCA12, CST1, PRAME, PITX2, CA9 the most upregulated ones, while miR-184, miR-133a-3p, miR-144-3p, miR-133b, miR-1-3p were the most downregulated miRNAs, and miR-196a-5p, miR-1269a, miR-31-5p, miR-105-5p, miR-767-5p the most upregulated ones. In the thyroid cancer datasets, KCNA1, ODAM, STAB2, SLC6A15, SLC5A5 were the most downregulated genes, LOC400794, GRHL3, MUC21, FIBCD1, HAPLN1 the most upregulated ones, while miR-7-5p, miR-1179, miR-7-2-3p, miR-1247-3p, miR-1247-5p were the most downregulated miRNAs, and miR-196a-5p, miR-187-3p, miR-146b-3p the most upregulated.

**Conclusions.** Based on these mRNAs and miRNAs differential expression patterns we are able to further analyze the miRNA-mRNA interaction networks and provide more insights into the biological process and molecular pathways underlying these cancers.

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## Evaluation of the response to resynchronization therapy in patients with heart failure: study protocol

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Corresponding Author: Sorana D. Bolboacă e-mail: sbolboaca@umfcluj.ro **Introduction.** Cardiac resynchronization therapy (CRT) may improve quality of life (QOL), survival and raise ventricular ejection fraction. The interventricular resynchronization and reverse remodeling are assessed with echocardiography parameters (strain and myocardial work). We aimed to provide long-term outcomes, with regard to the quality of life improvement, survival and the occurrence of sudden cardiac death (SCD), in CRT patients with (CRT-D) and without defibrillator (CRT-P).

**Material and methods.** Patients with ischemic or non-ischemic dilated cardiomyopathy that had a CRT at "Nicolae Stăncioiu" Heart Institute Cluj -Napoca between January 2010 and December 2022 were eligible for the enrollement. We assessed QOL at baseline, after six-month and one year post-implant using Minnesota Living with Heart Failure (MLHF) questionnaires. Standard 2D and speckle tracking echocardiography were performed before CRT and at six-month and one year follow-ups, with the calculation of global and regional myocardial constructive work and wasted work. Overall mortality rates and specific causes of death were assessed.

**Results.** We expect comparable QOL score after six months after device implantation, with potential QOL differences after one year, especially between CRT-P and CRT-D recipients. Also, we expect that pre-specified characteristics, including ventricular disfunction and QRS duration, to significantly influence all-cause mortality after one year.

**Conclusion.** Cardiac resynchronization therapy is expected to reduce mortality and improve quality of life in the long term after implantation. Beyond implantation, these patients and devices required specialized follow-up with continued medical therapy and echocardiography guided adjustments of device programming.

### Identification of sentinel lymph nodes in colon cancer using nearinfrared indocyanine green (NIR-ICG) guided fluorescence

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Corresponding Author: Vlad Făgărăşan e-mail: fagarasan.vlad@yahoo.com **Introduction.** The use of lymphatic mapping using near infrared (NIR) fluorescence with indo-cyanine green (ICG) has recently been introduced as an ancillary technique in the surgical management of colon cancer. Although the concept of sentinel lymph node biopsy (SLNB) has become widely accepted for certain types of tumors (breast cancer, melanoma), the particularities of colorectal lymphatic drainage has prevented the widespread implementation of this concept. We aimed to present our early experience with using real-time fluorescence lymphatic navigation in both laparoscopic and open surgery for colon cancer.

**Material and methods.** Indocyanine green was administered intraoperatively through subserosal injection in 4 points at the edges of the tumor in both laparoscopic and open procedures for colon cancer. A NIR fluorescence camera was used to visualize the lymphatic drainage pathways, as well as identify the sentinel lymph nodes which were marked with sutures and harvested ex-vivo.

**Results.** ICG-guided lymphatic navigation allowed the identification of sentinel lymph nodes, as well as more centrally located periaortic lymph nodes which might have otherwise been missed intraoperatively.

**Conclusions.** Real-time fluorescence lymphatic navigation using ICG may be a useful adjuvant in radical colon cancer surgery due to improved intraoperative visualization of distant lymph nodes. Despite its limitations, SLNB may also have an impact in the oncological management of colon cancer.

Acknowledgements. The presented research is part of the doctoral thesis of Vlad Fagarasan and has been granted approval by the Ethics Committee of UMF Cluj Napoca 4626/01.10.2021.

### **Doxorubicin as a potential treatment option in canine mammary tumors**

Mădălina Luciana Gherman<sup>1,2</sup>, Oana Zanoaga<sup>2</sup>, Livia Budişan<sup>2</sup>, Lajos Raduly<sup>2</sup>, Ioana Berindan-Neagoe<sup>2</sup>

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2) Research Center for Functional Genomics, Biomedicine and Translational Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Mammary tumors represent the most frequent neoplasia in female dogs. The high number of dogs with mammary cancer show lymphatic or vascular invasion and high rates of recurrence and metastasis. One of the most used therapeutic agents in human cancer is the anthracycline Doxorubicin (DOXO). Doxorubicin induces the production of free radicals, causing DNA damage and activating caspases, ultimately leading to apoptosis. Studies performed in humans, identified EMT to be involved in DOX-resistance to therapy, stimulating migration of tumor cells and metastasis; furthermore, EMT mediates resistance of cancer cells to DOX-mediated apoptosis.

Corresponding Author: Mădălina Luciana Gherman e-mail: luciana.gherman@umfcluj.ro **Material and methods.** The study was conducted in two canine mammary carcinoma cell lines (P114 and CMT-U27). The aim of the present study was to comparatively analyze the inhibitory effect of Doxorubicin in vitro models of canine mammary cancer to evaluate the efficiency of this therapeutic agent, and also to evaluate the expression levels of key genes involved in the EMT process.

**Results.** Fluorescence microscopy assay revealed that DOXO treatment after 48h induced in P114 and CMT-U27 cell lines a decreased mitochondrial membrane potential activity and morphological changes, including nuclear DNA condensation, nuclear shrinkage, and fragmentation. A significantly suppressed invasion ability was observed in both canine mammary cancer cell lines treated with DOXO. Based on PCR analysis a total of 41 for the P114 cell line and 38 for the CMT-U27 cell line significantly differentially expressed EMT-related genes were identified.

**Conclusions.** Our study demonstrates that Doxorubicin effectively impairs mitochondrial function and invasion capabilities in canine mammary carcinoma cell lines, while significantly altering the expression of EMT-related genes.

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## Dynamic vs. rigid spine stabilization in reducing degenerative spine disease progression

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Corresponding Author: Sergiu Maior-Rosca e-mail: sergiu.maior@icloud.com **Introduction.** Back pain is the most common musculoskeletal condition. Degenerative spinal disease is currently not curable, the only option being to slow its progression. One of the manifestations of degenerative spinal disease is vertebral instability, which is surgically treated using dynamic or rigid stabilization techniques with different outcomes for spinal biomechanics. While there are advantages to vertebral fusion, such as reducing instability and improving local pain, any segmental instrumentation will lead to an additional increase of the mechanical stress on the adjacent levels of the spine, making them prone to exacerbations of degenerative spinal disease. We aim to evaluate the outcomes of dynamic procedures compared to rigid ones in a group of patients with spondylolisthesis who are undergoing surgical treatment.

**Material and methods.** This retrospective study analyzed 100 patients who underwent surgical treatment for vertebral instability, with 56 patients receiving rigid instrumentation and 44 patients receiving dynamic instrumentation. Clinical outcomes were assessed using the Oswestry Disability Index and the Visual Analog Scale for back and leg pain on the first day post-op, at one month, six months, and two years.

**Results.** Regarding the Oswestry Disability Index and the Visual Analog Scale, we found no significant differences at the two-year follow-up between the dynamic

and rigid instrumentation groups. Statistically significant results were observed in the short term, at the first two follow-ups, where patients with dynamic fixations exhibited better scores on both scales. There was no difference in complication rates between the two groups.

**Conclusions.** Pain and recovery immediately post-op are reduced in patients with dynamic instrumentations compared to those with rigid ones. However, no long-term differences were observed between the two techniques.

### Investigating pathogenic variants in Romanian Noonan syndrome patients using Sanger sequencing - inaugural phases of the study

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Corresponding Author: Florina-Victoria Nazarie e-mail: nazarie.florina.victoria@elearn. umfcluj.ro **Introduction.** Noonan syndrome (NS) is a common autosomal dominant condition characterized by short stature and congenital heart disease (CHD), most often pulmonic stenosis. The prevalence of NS is widely quoted as 1 in 1000 to 1 in 2500. Based on our knowledge, there is no study of pathogenic variants causing NS in the Romanian population. The aim of this study was to identify pathogenic variants in Romanian patients selected in 1st Department of Pediatrics, Clinical Emergency Hospital for Children Cluj-Napoca, with high clinical suspicion of NS, using Sanger sequencing.

**Material and methods.** Based on literature, we decided to start with Sanger sequencing of the PTPN11 gene, exon 3, 7, 8, 13. We selected 3 patients with short stature, facial dysmorphism, congenital heart anomalies (2 of them presenting pulmonary valve dysplasia). These patients were previously tested for NS with another method, but only for the PTPN11 922A>G variant, and they had negative results. For the first run we added one positive control – a patient positive for PTPN11 922A>G.

**Results.** The protocol was successfully adapted, was identified the known pathogenic variant in the control patient, and we identified a variant of unknown significance (VUS) in these patients, PTPN11 907 G>A - a missense variant.

**Conclusion.** Our findings indicate that performing targeted Sanger sequencing of exons with the highest reported pathogenic variants may be beneficial, although further comprehensive investigations are warranted for establishing the molecular defects and for genotype-phenotype correlations in a larger group.

Acknowledgement. This study is founded through the Iuliu Hatieganu University of Medicine and Pharmacy Doctoral Research Program PCD 771/48/ January 2023.

# Chemical composition evaluation and investigation of the *in vitro* antiproliferative effect of *Agastache foeniculum* "Aromat de Buzău" variety and *Agastache rugosa* essential oils (Lamiaceae)

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Corresponding Author: Mihaela-Ancuța Nechita e-mail: mihaeladican@yahoo.com **Introduction.** The aim of our study was to evaluate the chemical composition of the essential oils from two Romanian cultivated *Agastache* species and to investigate their antiproliferative effect on a panel of malignancies using different cell lines for triplenegative breast carcinoma (MDA-MB-231), colon adenocarcinoma (HCT116), lung adenocarcinoma (A549) and liver carcinoma (HEPG2).

**Material and methods.** The essential oils were obtained by hydrodistillation from the aerial parts of *Agastache foeniculum* "Aromat de Buzău" variety and *Agastache rugosa*. The chemical composition was evaluated using gas chromatography-mass spectrometry analysis. The antiproliferative effect was investigated using the MTT assay.

**Results.** The results of the study showed that estragole (63.27%) is the major compound in *A. foeniculum* essential oil, and menthone (39.60%) is the main component in *A. rugosa* essential oil. The investigation of the antiproliferative potential revealed that the essential oils display a significant cytotoxic effect on MDA-MB-231 and HEPG2 tumor lines, *A. foeniculum* essential oil having a higher cytotoxic activity compared to *A. rugosa* essential oil on all investigated tumor lines.

**Conclusion.** The essential oils of *A. foeniculum* "Aromat de Buzău" variety and *A. rugosa* showed important differences in their chemical composition and displayed a significant antiproliferative effect on MDA-MB-231 and HEPG2 tumor lines, thus opening new research directions on Romanian cultivated *Agastache* species.

Acknowledgement. This study was funded by Iuliu Hațieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania, grant number PCD 771/20/11.01.2023.

## Gastric pneumatosis in a septic shock patient with relapsed bladder cancer – a case report

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Corresponding Author: Radin-Darius Oniț e-mail: radin.onit@gmail.com Gastric pneumatosis (GP), a rather rare finding, is defined as the presence of intramural air in the stomach, potentially found in a benign condition such as gastric emphysema (GE) or in emphysematous gastritis (EG), a potentially deadly condition. I hereby report a case of a relapsed bladder cancer patient admitted via the emergency room, diagnosed with a stroke, who subsequently developed a state of shock with gastric pneumatosis and a suspicion of gastric perforation, as seen on the second abdominopelvic computed tomography (CT) scan following his admission. This case report aimed to showcase the CT aspect of GP and how several etiopathogenic mechanisms may be intertwined to produce this finding in a patient with multiple comorbidities who ultimately passed away shortly after GP had been diagnosed.



# Antimicrobial effects of phytosynthesized silver nanoparticles functionalized with fermented *Kombucha* tea: an *in vitro* and *in vivo* study

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Corresponding Author: Razvan Vlad Opris e-mail: razvan.opris@elearn.umfcluj.ro **Introduction.** Silver nanoparticles (AgNPs), owing to their small size, have been integrated into various products such as hydrocolloid bandages, food packaging materials, and cosmetic products, where they serve as antimicrobial agents. These applications are critical for protecting patients from hospital-acquired infections, preventing food spoilage, and extending the shelf life of cosmetic items. The objective of our study was to develop an economical and cost-effective method for producing AgNPs with potent antimicrobial properties against microorganisms responsible for nosocomial infections.

**Material and methods.** AgNPs were synthesized using a biological method that utilized the rich antioxidant content of *Kombucha* fermented black tea. The characterization of AgNPs was performed using UV-Visible (UV-Vis) spectrometry, while their shape and size were confirmed with transmission electron microscopy (TEM). The antibacterial efficacy was evaluated using 2 methods: determination of the minimal inhibitory concentration (MIC) with an ELISA plate reader and assessment of the minimal bactericidal concentration (MBC) through the MTT assay for *Acinetobacter baumannii* strains acquired from hospitals. *In vivo* toxicity experiments were conducted using a *Galleria mellonella* larvae model.

**Results.** The synthesized AgNPs had an average size of 20 nm and were predominantly spherical in shape. They exhibited a characteristic absorption peak at 410 nm in the UV-Vis spectrum. Both MIC and MBC were found at 0.076  $\mu$ g/  $\mu$ L. *G. mellonella* larvae exhibited an LD50 at 7 days at a concentration of 0.183  $\mu$ g/  $\mu$ L AgNPs proving that AgNPs have low toxicity.

**Conclusion.** The phytosynthesized AgNPs produced a greater antibacterial effect against Acinetobacter baumannii compared to colistin. The *in vivo* model of *G. mellonella* larvae proves to be extremely valuable in the discovery of new antimicrobial compounds especially nowadays when we're faced with an increase in multi-drug-resistant bacteria.

## **Predatory or legitimate? An example of a journal with an Impact Factor**

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Department of Medical Informatics and Biostatistics, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Multidisciplinary Digital Publishing Institute (MDPI) has emerged and hosts, as on October 28, 2023, 430 open access journals (421 peer-reviewed journals, and 9 conference journals) covering multiple disciplines. The aim of this study was to evaluate the time span from submission to acceptance, considering the hot papers and highly cited papers published in 2022 in Biomedicines MDPI journal.

Material and methods. We selected the Biomedicines MDPI journal considering

Corresponding Author: Sorana D. Bolboacă e-mail: sbolboaca@umfcluj.ro the list published in February 2023 - https://predatoryreports.org/news/f/list-of-all-mdpipredatory-publications. We selected and evaluated the hot papers and highly cited papers (type: review or article) published in 2022 and indexed by Web of Science and verified the time span from submission to publication and the validity of the academic editor who made the decision. The search string used was "Biomedicines [Publication Titles] and MDPI [Publisher]" (search done on October 30, 2023).

**Results.** We tested the legitimacy of the journal with an online algorithm and the results was "*Everything seems to indicate that this journal is very unlikely to be predatory*". Three thousand two-hundred and ninety-six articles were published in 2022 in Biomedicines, 3,232 articles and reviews (2,372 articles and 860 review articles). Twenty-four papers were identified as eligible (2 hot papers and 22 highly cited papers), but three were excluded since had been published in 2021. Six of the evaluated papers were classified as original studies. Half of the evaluated articles had at least 30 citations (ranging from 22 to 49, the highest number of citations obtained by an original study). The number of days from submission to revision ranged from 8 to 96 days, with a median of 26 days. The number of days from revision to acceptance ranged from 1 to 25 days, with a median of 4 days.

**Conclusion.** Although the overall editorial process seems legitimate, a review of 8 days raised suspicion of a breach of integrity in the editorial process. Violation of integrity in the editorial process can also appear in a legitimate journal.

### **Student Section – Scientific START**

## An uncommon clinical presentation of MTHFR C677T inherited thrombophilia

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Corresponding Author: Andrada Albu e-mail: andraada23@yahoo.com **Introduction.** The methylenetetrahydrofolate reductase enzyme has a key role in the metabolism of the methionine, being involved in the folate pathway. The general population prevalence for the homozygote C677T variant is estimated to be around 8.5%. We aimed to underline the importance of personalized healthcare regarding a rare cause of a coagulation disorder and an uncharacteristic clinical presentation.

**Case report.** An 18-year-old Caucasian female was referred to our clinic for further investigations regarding her 8-month history of paroxysmal oral bleeding. The episodes did not exhibit any consistent pattern regarding the exteriorised blood (fresh and coagulated were both noticed). Her recent medical history included congestive pangastritis positive for Helicobacter pylori, treated with the Levofloxacin-based triple therapy. On examination the patient had an ectomorphic constitution, presented hypermobility in her elbows and thumbs and had a positive Rumpel-Leede test. Relevant laboratory findings included elevated D-dimer level, prolonged activated partial thromboplastin time and decreased folic acid level. Given the presentation, the patient was further investigated for coagulation disorders. The MTHFR C677T variant was present in homozygote form. Follow-up recommendations included genetic testing and rheumatology consults regarding the clinical suspicion of a connective tissue disorder.

**Discussion.** Although hyperhomocysteinemia is a known cardiovascular risk factor, recent studies challenged this notion, proving otherwise. Recent guidelines do not advise MTHFR testing as routine evaluation of thrombophilias, however, for the present case, it proved to be an important step.

**Conclusions.** Early implementation of genetic testing and orienting the diagnosis based upon the patient's characteristics would be a step towards lowering the prevalence of major complications, such as thromboembolism or recurrent fetal loss.

### A rare disease exploration: cystathionine beta-synthase deficiency through a pyridoxine responsive case

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2) Department of Cell and Molecular Biology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Background.** Cystathionine-beta-synthase (CBS) deficiency, or classical homocystinuria, is a monogenic disorder affecting CBS gene, being the most common inborn error of sulfur amino acid metabolism. There are symptoms resulting from the impaired metabolism of homocysteine (Hcy) and methionine; this defect is a progressive disease, usually starting at school age.

**Material and methods.** We are presenting the main features of a 14 y.o. boy with Marfan-like appearance and myopia; the biochemical test was done using the thin-

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Corresponding Author: Tabita Alexa e-mail: alexa tabita25@yahoo.com layer-chromatography method adapted after Wadman et al. 1981, routinely used for the amino acids analysis. Besides, we conducted a review using the keywords "classical homocystinuria" AND "diagnostic" AND "pyridoxine responsive" on PubMed, which yielded 11 results (1999-2023).

**Results and conclusions.** The case was framed as pyridoxine-responsive classical homocystinuria, having a favorable prognostic; the biochemical evaluation should target a plasma Hcy level  $< 30 \ \mu$ mol/l (there are reported cases well controlled if Hcy was  $< 60 \ \mu$ mol/l). The review outlines that, without therapy, the toxic methionine metabolic intermediate known to be the primary culprit of complications: skeletal deformities, connective tissue defects, thromboembolism, progressive myopia and cognitive impairment. The current standard of care entails pyridoxine intake (50-100 mg/day) in responsive cases. In non-responsive cases, the indications are: methionine-restricted diet, intake of betaine, hydroxocobalamin. In recent years, the growing demand for improved therapy options has spurred the development of innovative enzyme or gene therapies, or the investigation of pharmacological strategies to rectify CBS folding defects.

In the absence of an expanded newborn screening, we outline the importance of amino acids evaluation in patients with a suggestive clinical picture for this disorder.

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### The rupture of a lateral ventricle dermoid cyst - a case report

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Corresponding Author: Alexandra-Maria Călăuz e-mail: calauz\_alexandra@yahoo.com **Introduction.** Dermoid cysts represent less then 1% of all intracranial tumors. They are characterized by slow growth, localization on the midline and their benign course. These cysts are derived from trapped somatic ectoderm during the embryological development in the 3rd to 5th week of gestation. They are composed of mature squamous epithelium and can contain apocrine, eccrine, and sebaceous glands, as well as other ectodermal structures such as hair follicles and teeth.

**Case.** We present the case of 30 y.o. female who came to our institution with no signs or symptoms. She had a CT scan done after minor head trauma in which a 4.2/3.2 cm mass was found. The lesion was located on the midline, starting from the clivus and going towards the mesial part of the left temporal lobe, engaging superiorly in the lateral ventricle, and inferiorly causing a small mass effect on the cerebral peduncle. Hydrocephalus and some masses at the level of the frontal horns of the lateral ventricles and in the subarachnoid space were also seen on the CT. For better differential diagnosis and further understanding of the exact localization of the tumor, an MRI scan was also performed.

Surgery was then performed in a seated position with a rectosigmoid craniotomy. An infratentorial supracerebellar approach was taken, with an encapsulated, slightly yellow mass visible in the intraoperative view. The cystic tumor was subtotally removed and the surgery concluded without any complications. On the post-op CT scan we can still see a hypodense remnant structure. Hydrocephalus as well as the fatty masses from the supposed rupture are still visible in the ventricles and the subarachnoid space. The morpho-phonology report confirms the diagnosis of a dermoid cyst. The cyst was covered with squamous epithelium and had sebaceous glands and hair follicles. She presented back for observation every year after surgery. The follow-up MRIs show a slow growth of the tumor, but since the patient has no symptoms, she is yet to undergo another surgical intervention.

**Discussion.** The imaging shows pathognomonic signs for the rupture of dermoid cysts: the fat-fluid levels in the ventricles and the subarachnoid space. Rupture frequently occurs spontaneously, only a handful of cases in the literature describe a relationship between head trauma and ruptured cysts. The rupture of a dermoid cyst with spillage of its contents into the subarachnoid space or ventricles like it was in our case is relatively rare. It can lead to serious complications such as chemical meningitis, seizures, cerebral vasospasm and hydrocephalus. The intraventricular or subarachnoid fat may persist for years after the time of rupture because they do not seem to reabsorb but it must be noted that even though it persists they do not cause any further harm to the patient.

When found within the ventricular system, dermoid cysts are typically located in the fourth ventricle, and only a handful of cases have been reported to have a 3rd ventricle or even less so a lateral ventricle involvement.

**Conclusion.** Intracranial dermoid cysts are rare benign lesions. Our case is one out of only a few reported cases of a dermoid cyst that presented with intraventricular elements as well as having ruptured after minor head trauma. Awareness of this pathology and early recognition of these pathognomic imaging findings are crucial to the management of these cysts in the future and the prevention of life-threatening complications.

### Fabry disease - a classic manifestation, but a challenging diagnosis

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Corresponding Author: Alin-Gavril Moldovan e-mail: amoldovan19@gmail.com **Introduction.** Fabry disease or Anderson-Fabry disease is a genetic lysosomal storage disease resulted by over 400 mutation of  $\alpha$ -galactosidase A (GLA) enzyme gene. The particularity of Fabry disease is that it is the only known X-linked sphingolipid storage disease and despite the locus of the gene, heterozygous females can also be affected, but usually present mild symptoms. The GLA mutations lead to  $\alpha$ -galactosidase A enzyme deficiency, thus the substrate is accumulated in various tissues, such as: kidney, heart, vascular endothelium (cerebral vessels are usually involved), perineurium, peripheral nerves, autonomic neurons and somatic afferent neurons.

**Case report.** We present the case of a 36-year-old male patient, in evidence of nephrology department with Fabry disease who was admitted for periodic re-evaluation and treatment administration. Impressive aspect of this case is the time passed between the symptoms debut and making a diagnosis. His symptoms start in childhood with angiokeratomas disseminated on his body, chronic fatigue, hypohydrosis continuing in adolescence with acroparesthesias and episodic severe pain crises at hand precipitated by cold. At 24-year-old he presented painful lower limb edema, decrease visual acuity and neurosensory hypoacusia. This was the moment when the Fabry disease diagnosis has been considering and admitted for the first time in nephrology department His condition is insignificant unchanged compared to that moment, due to the start of enzyme replacement therapy (ERT).

**Discussion.** For stopping the evolution of Fabry disease starting ERT is necessary, but for this the diagnosis is important to make as soon as possible and after every person diagnosed the screening is mandatory for all his relatives.

**Conclusion.** Fabry disease have various manifestations and these can occurs in early ages and can affect renal and extrarenal tissue including cardiac, vascular and nervous tissue with catastrophic effects on life quality or even to be lethal without properly therapy.



### **Recurrent acute pancreatitis in a young patient: pancreas divisum and biliary microlithiasis**

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Corresponding Author: Ioan-Cosmin Baroană e-mail: baroanacosmin@gmail.com **Introduction.** Pancreas divisum, the most common congenital malformation of the pancreas, occurs due to a failure of fusion of the ductal systems of the dorsal and ventral pancreatic buds. This anatomical variant is asymptomatic in 95% of the patients, however it is proven that co-existence of factors such as hypertriglyceridemia, alcohol, or biliary microlithiasis increase the risk of recurrent severe episodes.

**Case report.** We present the case of a 34-year-old woman with a history of recurrent acute pancreatitis. Her first episode occurred in April 2021, coinciding with elevated triglyceride levels and the use of oral contraceptives, which lead to the complication of developing type 2 Diabetes. A second episode of pancreatitis in May 2023 lead to her admission in our clinic and was graded E using the Balthazar score. Between the two episodes, her triglyceride levels were within the normal range, but she was still using oral contraceptives.

Given the patient's young age, the recurrence and the gravity of the episodes, the clinical presentation was suggestive for an underlying condition. Upon imagistic examination (MR-Cholangiopancreatography), an anatomical variant of the pancreas was discovered, leading to the diagnosis of pancreas divisum. Furthermore, the imaging revealed the presence of biliary microlithiasis, in addition to the two gallstones that were previously detected in prior examinations.

**Discussion.** Acute pancreatitis has a broad mortality rate ranging from 3% for the edematous type to at least 20% for the necrotizing type. Comparing our case to the literature, our patient had a fortunate recovery, even though she developed diabetes as a complication.

**Conclusions.** This case highlights the importance of considering and investigating potential underlying anatomical abnormalities and conditions when managing recurrent acute pancreatitis, particularly in younger patients experiencing severe episodes.

## Ankylosing spondylitis and cervical spine injury: is riding an e-scooter a death sentence?

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2) Department of Emergency Medicine, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Ankylosing spondylitis (AS) is a chronic, inflammatory disease affecting the axial spine, with an estimated incidence of 0.1%, which also causes individuals to be twice as likely to experience vertebral fragility fractures. Since the routine use of e-scooters, the incidence of traumatic injuries among the population has increased significantly, especially at the level of the face, limbs and spine. We will be presenting the case of a patient who suffered a low-velocity crash which unfortunately became fatal, under the aggravating circumstances of AS.

**Material and methods.** The patient was a 42-years-old male, with a history of stage 4 AS and exaggerated spinal curvature who suffered a cardiac arrest following an

Corresponding Author: Bogdan Borlea e-mail: bogdanborlea27@gmail.com e-scooter accident which resulted in a frontal collision. Once the ambulance arrived, CPR manoeuvres were applied with cervical spine support in 4 axes and additional posterior support. The initial injuries suggested an impact on the frontal bone with a flexion-extension mechanism on a rigid spine, without a protective helmet.

CT full body scan revealed a C1 comminuted fracture with complete medullar resection and a migrated fragment in the foramen magnum, diffuse cerebellar edema, displaced C2 fracture, epidural C1-C2 hematoma which had a mass effect on the medulla. Even with inotropic support, the patient continued to present hemodynamic instability after initial resuscitation.

**Results.** The patient remained critical, presenting multiple organ failure, central fever and severe spinal shock. After almost 19 hours in intensive therapy, the patient entered cardiac arrest and the resuscitation methods failed.

**Conclusion.** This case is unusual because of the location of the spinal fracture, as lower cervical fractures tend to be much more common in AS, and it also highlights the dangers of an increasingly popular vehicle. The post-traumatic management of AS patients remains a challenge due to the higher risk of fractures and disabling injuries.

## Unlocking the hidden secrets: exploring everyday MRI scans for incidental discoveries

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Corresponding Author: Bianca Gabriela Grigorie e-mail: biancagrigorie@yahoo.com **Introduction.** In imaging, an incidental finding, the so-called ,incidentaloma', is an unanticipated finding unrelated to the initial diagnosis. Dealing with them can be difficult as they represent a diagnostic, ethical and psychological dilemma.

**Material and methods.** A retrospective analysis of 460 patients (aged 25-75 years) from the Radiology Department of Cluj Emergency County Hospital with MRI examinations of the head, limbs, abdomen and pelvis was performed. We defined incidental finding as any abnormal finding not related to the chief complaint. The frequency of incidental findings was reported according to the International Classification of Diseases 10<sup>th</sup> Revision (ICD-10).

**Results.** Overall, 108 of 460 patients (23.47%) had a total number of 187 incidental findings (two patients having 5 incidentalomas each). The most frequent incidentalomas were those without indication for further follow-up, with a significant weight among men, while all 5 malign incidentalomas were found in women (p=0.04). There were no statistically significant differences in the follow-up indication of incidentalomas detected with or without contrast (p=0.27). The most frequent incidentalomas were found among genitourinary diseases (N00-N99 - 18.18%), followed by congenital malformations (Q00-Q99 - 17.11%) and respiratory diseases (J00-J99 - 15.51%). No differences were observed between ages by follow-up indication, neither in men (p=0.3) nor in women (p=0.29).

**Conclusion.** Incidental findings by MRI examinations were common and significant according to indication of follow-up and gender. The majority were benign and associated with diseases of the genitourinary system. An awareness of the prevalence of the incidental findings detected at MRI is helpful for diagnosing lesions not related to symptoms.

## Linking cell biology with neurology, or unraveling the molecular mechanisms of adrenoleukodystrophies: a tale of two onsets

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Corresponding Author: Maria Gruian e-mail: gruianmariateodora@yahoo.com **Introduction.** Adrenoleukodystrophy (ALD) encompass a spectrum of rare X-linked genetic disorders given by the accumulation of very long-chain fatty acids (VLCFAs), peroxisomes being responsible for VLCFA metabolisms; these lead to severe neurological and adrenal dysfunction arising from mutations in the ABCD1 gene.

**Material and methods.** We discuss the main features of a child suspected of ALD (frequent in boys between ages of 4 and 10 years, with progressive cognitive & neurological deterioration); we conducted a literature review based on a reference book (Inborn Metabolic Diseases, 2022) and on PubMed using the keywords 'Adrenoleukodystrophy' AND 'clinical onset' AND 'molecular mechanisms' yielding 7 results (1995-2023).

**Results.** ALD manifests in 2 forms, one is Childhood Cerebral ALD (CCALD) predominantly affecting young boys. The adult onset X-ALD typically presents with a broader range of clinical manifestations, including Adrenomyeloneuropathy and, less commonly, cerebral involvement. Some individuals with ALD may only experience isolated adrenal insufficiency, referred to as Addison disease. Early diagnosis and intervention are crucial in managing ALD. Lorenzo's oil, which is a treatment originally developed for ALD, had shown some promise in slowing the progression of the disease, mainly in its CCALD form, but it wasn't universally accepted as a definitive therapy for ALD. Treatment approaches involve a combination of therapies, including early hematopoietic stem cell transplantation (HSCT), HSC gene therapy, and symptom-specific interventions.

**Conclusions.** HSCT remains the sole established treatment capable of modifying the disease's course. Here we provide an overview of ALD, highlighting its various manifestations, emphasizing the importance of timely diagnosis and intervention, and pivotal role of peroxisomes in the disease. Many states have also started newborn screening for ALD (USA, Holland, Japan).

### Chronic trimalleolar fracture-dislocation: a complex case study

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2) Department of Pediatric Orthopedics and Traumatology, Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Complex ankle fractures are challenging and they demand rigorous preoperative planning. A neglected tibio-talar dislocation associated with a trimalleolar fracture is an uncommon injury seen in modern clinical practice and it is associated with posttraumatic arthritis, chronic pain, increased risks of infection and impaired functional outcomes. Patients with delayed diagnoses are more likely to experience postoperative complications and poorer results compared to those with acute injuries. The treatment involves a comprehensive approach that encompasses preoperative planning, specialized surgical techniques, and postoperative rehabilitation for functional recovery.

**Case presentation.** We are presenting the case of a 42-year-old male patient who was referred with a trimalleolar fracture of the left ankle associated with a posterior ankle

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Corresponding Author: Horia-Mihnea Fotescu e-mail: horiafotescu@gmail.com dislocation that was left untreated for 2 months. The cause of injury was represented by a fall from a height of approximately 2 meters. The patient underwent 3 staged surgical procedures at our institution. The first procedure was the application of an external fixator to elongate the ankle to progressively reduce the old posterior dislocation. Following the next 17 days, we progressively restored the length of the leg. A second surgical procedure was performed consisting of three steps: 1) open reduction of the posterior ankle dislocation followed by a tibiotalocalcaneal K-wire fixation; 2) open reduction and internal fixation (ORIF) of the posterior malleolus and medial malleolus fractures with 2 screws each; 3) ORIF of the lateral malleolus fracture using one K-Wire. A good anatomic reduction was obtained to achieve the reconstruction of the ankle. The third intervention was made after 6 weeks to remove the 2 Kirschner Wires that were used to stabilize the ankle and respectively the fibula fracture. The patient returned to daily activities after 3 months, at which point weight-bearing was possible.

**Conclusion.** Neglected ankle fracture-dislocation remains a challenge for the orthopedic surgeon, necessitating special surgical treatment plans. Due to its rarity, there is a lack of recommendations in the literature, highlighting the need for additional clinical research. Staged interventions and a gradual reduction approach employing an external fixator are widely acknowledged as the most effective treatment regimens for achieving a favorable result.

## Case report: Hashimoto's thyroiditis in monozygotic twins with different responses to treatment

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Corresponding Author: Mara Spătar e-mail: mara.spatar@yahoo.com **Introduction.** This case report aims to provide insights into the diverse clinical manifestations and treatment responses in Hashimoto's disease among monozygotic biviteline twin siblings, highlighting potential genetic and environmental factors influencing the disease's progression and management.

**Material and methods.** We selected a pair of 42-year-old monozygotic biviteline twin women diagnosed with Hashimoto's disease, further referred to as Patient A and Patient B. We obtained their medical histories, including any pre-existing conditions, as well as their treatment plan, including the dosages and types of thyroid replacement therapy (sodium levothyroxine), and their adherence to treatment and clinical outcomes. Additionally, we obtained the patient's familial background to identify possible predispositions to other autoimmune diseases. Informed consent was obtained from both patients regarding the publication of their medical data.

**Results.** Patient A, with a history of polycystic ovary syndrome (PCOS), irritable bowel syndrome, moderate anemia, and allergic reactions, was diagnosed with Hashimoto's at the age of 35. She has been effectively managed, with favorable clinical evolution and without notable side effects. Patient B was diagnosed at the age of 27 and has experienced inconsistent adherence to treatment for almost a decade. Presently, her clinical presentation remains suboptimal despite following a treatment regimen. Additionally, Patient B's medical history includes coexisting conditions such as PCOS, asthma, severe allergies, rheumatic arthritis and irritable bowel syndrome. Furthermore, there are several documented cases of Graves' disease, Hashimoto thyroiditis, rheumatic arthritis, psoriasis, and inflammatory diseases of the colon in their family.

**Conclusion.** The report sheds light upon the complexity of Hashimoto's disease and the need for personalized approach to diagnosis and management in similar familial settings.



### Neonatal cholelithiasis - case report

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Corresponding Author: Adriana Nistor e-mail: adriananistor028@gmail.com **Introduction.** Neonatal cholelithiasis is a rare disease, being usually associated with some predisposing factors like hemolysis, congenital anomalies of the biliary tree, hyperalimentation or prolonged fasting.

**Case report.** We describe the case of a 13 days girl who was admitted in our hospital for jaundice. Laboratory parameters revealed increased transaminase levels, conjugated hyperbilirubinemia and cholestasis. The abdominal ultrasound (US) highlighted a hyperechoic mass within gallbladder lumen with posterior acoustic shadowing, and normal common bile duct diameter (1.5 mm). We evaluated all the possible risk factors but her birth and family history were not significant. Complete blood count, reticulocyte number and peripheral smear were normal, direct coomb's test was negative. TORCH screening was negative, thyroid function was normal. Procalcitonine and C-reactive protein were negative as well as all cultures. The case was managed conservatively with ursodeoxicholic acid (15 mg/kg twice daily) and was monitorised weekly. Six weeks later her clinical features and laboratory parameters improved and the follow up US showed the absence of the stone.

**Conclusion.** In the absence of predisposing factors, neonatal cholelithiasis can be a self-limiting phenomenon. We chose to present this case to highlight that conservative therapy and a careful follow-up can be a sufficient approach to facilitating resolution of the lithiasis in non-complicated cases.

### A rapid onset of septic shock caused by obstructive renal calculi

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Corresponding Author: Raluca-Nicoleta Nițu e-mail: ralucannitu@gmail.com **Introduction.** Urosepsis is a life-threatening medical condition characterized by a systemic response to a urinary tract infection, resulting in the presence of pathogens in the bloodstream. On the other hand, obstructive urolithiasis refers to the urinary tract blockage caused by the presence of stones, which can obstruct the normal urine flow. The connection between the two lies in the fact that this obstruction can act as a nidus for infection, further increasing the risk of urosepsis.

**Material and methods.** A 25-year-old female patient presented to the emergency department at 6 a.m., complaining of right-sided lower back pain radiating into the abdomen, accompanied by nausea and vomiting, which began a day prior. During the consultation, the patient also reported pain in the hypogastric region.

**Results.** Following the investigations, the patient was diagnosed with right-sided renal colic and grade 2 right hydronephrosis (HN) with no echographic visible calculi and was discharged with a recommendation to undergo urine culture and antibiotic sensitivity testing, an outpatient Urology consultation, and a prescription for oral antibiotic.

Later that day, at 7 p.m., the patient was brought back to the emergency department by a B2 type ambulance due to an episode of loss of consciousness without associated trauma, which occurred following an episode of chills and vomiting. The patient denies the administration of any treatment after the morning consult. At the second consultation, the patient's condition had significantly deteriorated compared to the morning presentation. On physical examination, the patient exhibited an altered general state, pallor, and fever, but without focal neurological signs. Paraclinically, the patient displayed leukopenia, thrombocytopenia, elevated C-reactive protein (CRP) and Procalcitonin (PCT), leukocyturia, increased PT and INR, azotemic retention syndrome, and metabolic acidosis.

Ultrasound examinations and a native and contrast-enhanced CT scan were performed. The imaging findings led to the diagnosis of obstructive right-sided urinary lithiasis, grade 2 urohydronophrosis associated with right-sided pyelonephritis, and significant renal and perirenal changes. These diagnoses contributed to the final diagnosis of multiple organ dysfunction syndrome (cardiocirculatory insufficiency, hematologic dysfunction, acute kidney injury and hepatic dysfunction).

The recommendations received: admission to the intensive care unit, urethral stenting for deobstruction, appropriate antibiotic therapy, and hydroelectrolytic rebalancing.

**Conclusion.** This case underscores the critical consequences of non-compliance in patients with obstructive calculi. The fulminant progression from renal colic to septic shock due to pyelonephritis highlights the urgency of timely intervention and adherence to treatment recommendations, including antibiotic therapy and urological specific procedures. This case serves as a stark reminder of the potential severity when recommendations are not followed.

### **Clinical insights into hepatorenal syndrome: a case presentation**

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Corresponding Author: Rareş-Sebastian Ciumbrudean e-mail: raresciumbrudean@gmail.com **Introduction.** Hepatorenal syndrome (HRS) is a condition characterized by potentially reversible kidney failure in patients known with advanced liver cirrhosis where every other cause of renal insufficiency has been excluded. Being a serious complication of a fairly complex disease that alters the function of various systems and poses a threat to the life of patients, HRS constitutes a challenge in both diagnosis and treatment.

**Material and methods.** A 50-year-old woman with a history of chronic alcohol consumption and liver cirrhosis presented to the emergency department with dyspnea, dizziness, nausea and lower limb pain. Additionally, she was disoriented and drowsy.

**Results.** The clinical findings included an afebrile, hemodynamically stable patient with tachycardia, tachypnea, a non-painful distended abdomen and scleral jaundice. Blood tests revealed mild metabolic acidosis, severe thrombocytopenia, hepatocellular injury, hyponatremia and elevated creatinine levels suggesting renal failure. Proteinuria was not present, there were no signs of an UTI and no pathological structural modifications of the kidneys was found. Based on the clinical, laboratory and imagistic findings, a high degree of suspicion for HRS was raised and the patient was started on an albumin infusion and assessed for a response. As there was no improvement in kidney function after the albumin administration, the diagnosis of HRS was confirmed and treatment was initiated. Management comprised correction of hyponatremia and acidosis and improving renal blood flow through administration of terlipressin. Examination of the ascitic fluid confirmed spontaneous bacterial peritonitis (SBP) with E. coli, which fully explained the debut of HRS. Consecutively,



treatment with Ceftriaxone was started. Furthermore, Lactulose and Rifaximin were administered for the reversal of the hepatic encephalopathy that was also starting to emerge.

**Conclusion.** Hepatorenal syndrome is a serious complication of portal hypertension. Most of the time, its onset is precipitated by an acute stressor such as an infection (in this case SBP), bleeding or surgery. Although its recognition and management are often challenging, it remains a fully reversible condition, provided that a thorough diagnostic process and a multidisciplinary intervention are carried out.

## Biomarkers in maple syrup urine disease, implications for pediatricians and medical geneticists - a case-based review

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Corresponding Author: Irina Maria Rusu e-mail: irinarusu2003@gmail.com **Introduction.** Maple syrup urine disease (MSUD) is caused by deficient branched-chain keto acid dehydrogenase activity, leading to elevated levels of plasma branched-chain amino acids (BCAA) and their corresponding keto-acids. MSUD has five subtypes, the classical form being frequent, with neonatal onset.

**Material and methods.** We summarize the features of an 11-day-old boy with rapid deterioration of the general condition, who had been admitted to the ICU with cardiorespiratory arrest. He was diagnosed post-resuscitation with metabolic acidosis and ketonuria, and was referred for amino acids analysis. The chromatography (2D-TLC) for amino acids showed abnormal pattern for plasma, and was non-informative for urine. We also conducted a literature review based on two reference books and on PubMed using the keywords 'Maple Syrup Urine Disease' AND 'diagnostic' AND 'biomarkers' that yielded 17 results (2013-2023).

**Results.** The plasma elevated BCAA levels (leucine, isoleucine, valine) is indicative of MSUD, even though allo-isoleucine cannot be distinguished. The absence of expanded newborn screening (NBS) along with lack of rapid intervention led to the early death of the child.

**Conclusion.** The case was included in classical form of MSUD (and later molecularly confirmed). Other biomarkers are branched-chain keto- (and hydroxy-) acids;  $\alpha$ -ketoisocaproic acid is the most toxic substance in MSUD. The urinary amino acids 2D-TLC was inconclusive, because urinary ketoacids resulted from BCAA are ninhydrin-negative. We also outline the value of NBS for prompt interventions to mitigate the risk of leucine encephalopathy. The prognosis is satisfactory with prompt (before 5th day of life) and specific therapy. The protocol should include trial of thiamine (for patients responding to vit. B1). When lacking expanded NBS, the rapid plasma amino acids analysis is useful in relevant patients.

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### The spectrum of PROP-1-related pituitary insufficiency

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Corresponding Author: Silviu-Ionuț Zgîmbău e-mail: silviuzgimbau@yahoo.com **Introduction.** Pituitary insufficiency occurs when one or more pituitary hormones are completely or partially lost, leading to various clinical symptoms based on the severity and number of hormone deficiencies. Combined pituitary hormone deficiency (CPHD) manifests as deficiencies in growth hormone (GH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH) and prolactin (PrL).

**Case report.** A 52-year-old female presents in the Endocrinology department after being referred from the Pneumology department where low levels of TSH, FT4 and cortisol were detected. Her complaints were asthenia, loss of appetite, concentration difficulties, cold intolerance and primary amenorrhea.

The clinical examination reveals: below average weight, height; blood pressure – 90/50 mmHg; pale, cold and dry skin, eyelid oedema, brittle hair, Tanner stage 2 breast, lack of pilosity. No secondary sexual characters were found.

The hormonal profile shows low levels of IGF-1; LH, FSH and estradiol; TSH and FT4; ACTH and cortisol. The contrast-enhanced pituitary MRI detects an "empty sella" aspect. Eventually, genetic testing is performed describing the PROP-1 gene mutation (301-302delAG).

**Discussion.** Compared to other causes of CPHD, newborns with PROP-1 mutations don't have hypopituitarism signs. This mutation's phenotype is characterized by a variable time of onset and severity of pituitary deficiencies. The hormonal deficiencies onsets usually follow the next pattern: GH deficiency in the first months after birth, followed by TSH deficiency. FSH and LH deficiencies occur at puberty. ACTH deficiency onset can be in adolescence or adulthood.

**Conclusion.** PROP-1-related CPHD is a rare condition with polymorph clinical features, which is usually diagnosed in infancy or early childhood. The particularity of this case is the late diagnosis, which emphasizes the idea of "spectrum" when we talk about pituitary insufficiency.

### Two separate aortopathies: the intersection of genetics and cellmolecular biology in clinical practice

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 Rheumatology, Center for Rare Autoimmune and Autoinflammatory Diseases, Emergency, Clinical County Hospital Cluj, Romania **Introduction**. Aortopathies are a group of conditions that encompass thoracic aortic aneurysms (TAA) and abdominal aortic aneurysms (AAA). The genetic peculiarities of the two pathologies we summarize are related to Vascular Ehlers-Danlos Syndrome (vEDS) and Loeys-Dietz syndrome (LDS), respectively, both involving thoracic aortic aneurysms.



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Corresponding Author: Maria-Cristina Simian e-mail: simianmariacristina@gmail.com **Material and methods.** We did an extensive search on PubMed as the preferred database. The keywords used are "Aortopathy", "Vascular Ehlers–Danlos Syndrome", and "Loeys-Dietz syndrome", connected by the Boolean operator "OR". Only the papers published in the last six years were considered for this work (1559 results after search). We compared several features of two patients with aortopathies diagnosed with vEDS and LDS, respectively.

**Results.** Vascular Ehlers-Danlos Syndrome is an autosomal dominant genetic disorder implying dysfunction of collagen typically caused by pathogenic variants in the COL3A1 (and rarely in COL1A1) gene. The outcome of these defects is soft connective tissue vulnerability, which means arterial, intestinal, or uterine fragility. The Loeys-Dietz syndrome is also an autosomal dominant aortic aneurysm disease accompanied by vascular tortuosity. In terms of genetics, the cause is heterogeneous, with mutations in genes encoding components of the transforming growth factor beta (TGF $\beta$ ) signalling pathway (as are TGFBR1, SMAD2, and TGFB2).

Regarding a few clinical signs, both patients present skin marks. The one with LDS shows sternal scars with secondary healing and dehiscence following surgery, and the patient suffering from EDS presents stretch marks at the level of the lower back. The common aortic histopathology shows severe degeneration of the aortic media and underscores the importance of genetic testing for accurate diagnosis in both conditions.

**Conclusion.** We are stressing the biological and clinical similarities between vEDS and LDS, underlining the importance of molecular genetics within this domain.

### Effects of different antiarrhythmic drugs on the QT interval in patients with supraventricular arrhythmias

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Corresponding Author: Simon Picker e-mail: simonpicker@gmail.com **Introduction.** Prolonged QT intervals induced by drugs such as Amiodarone and Class 1C antiarrhythmics are known to increase the risk of a potentially fatal arrhythmia known as Torsades de Pointes.

**Methods.** This retrospective clinical study, conducted during the course of 2023 investigates whether Amiodarone, Flecainide, and Propafenone significantly increase QTc interval times in patients compared to a control group not receiving antiarrhythmics. The 70 patients included in the study were selected from the Rehabilitation Clinic Hospital Cluj-Napoca database, including individuals treated with Amiodarone, Flecainide, or Propafenone for a minimum of three months and diagnosed with supraventricular arrhythmias such as Atrial Fibrillation, Atrial Flutter, Atrial Tachycardia or PSVT. The Control group was slightly larger and selected from the same hospital and had ECGs available, excluding those receiving any kind of antiarrhythmic treatment.

**Results.** The research came to the result that among patients receiving antiarrhythmics, 60% of the males had prolonged QT intervals over 450 ms and 40% in the female group had longer intervals than 460 ms, compared to 20.45% in males and 7,89% in females of the control group. Also Male patients over all showed an average QTc interval of 462.94 ms, 10.72 ms longer than female patients (452.22 ms), though this difference was not statistically significant. Furthermore Amiodarone-treated

patients exhibited the highest rate of QTc prolongation, followed by Propafenone and Flecainide. Notably, Amiodarone significantly prolonged the QTc interval compared to Class 1C antiarrhythmics.

**Conclusion.** Amiodarone, Propafenone, and Flecainide significantly prolong the QTc interval in a Romanian population, with Amiodarone exhibiting the highest risk. The results of this study aligns with previous research, affirming the risk of QT interval prolongation induced by these antiarrhythmics.

### The importance of a multidisciplinary approach in a head and neck squamous cell carcinoma patient - a case report

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Corresponding Author: Teodor-Marian Vancea e-mail: vanceateodor@gmail.com **Introduction.** Oral cancers are a rapidly increasing health issue with an incidence of 11.5 adults per 100,000, a vast majority of whom present risk factors such as heavy smoking, alcohol consumption and a prior infection with human papilloma virus. In these patients a high rate of complications can occur obliging the therapists to take a multidisciplinary approach.

**Case report.** We present the case of a 68-year-old male patient known with cardiac comorbidities, who presented in 2022 with a large solid mass emerging outside of the oral cavity. The histopathological examination concluded that the lesion was specific for a squamous cell carcinoma, that required an imagistic evaluation for staging. The computed tomography evaluation has shown a voluminous tumoral mass in the anterior half of the oral floor, symmetrical to the median septum invading the mandible at alveolar margin and extending in the oral vestibule and in the submandibular region. Since the physiological act of nutrition was impaired, the patient was presented in the ear-nose-throat committee that decided the insertion of a gastrostomy. Given the context and the staging cT4N0M0 (stage IVa), a systemic therapy with Gemcitabine and Carboplatin was implemented with a favourable response after only three cycles making external radiotherapy (ERT) possible. Post ERT an anti-epidermal growth factor receptor (EGFR) was added to the current treatment with good tumour response, without major toxicities.

**Discussion.** Head and neck cancers can have a mutilating effect on patients due to the self-stigma, the involvement of the physiological alimentation pathway, which leads to not only psycho-social scars but also altered nutritional status. It is thus advisable to manage the previously mentioned issues, the underlying pathologies and the side effects of the treatment.

**Conclusions.** A multidisciplinary approach in this type of cases should be taken into consideration in order to increase the quality of life and to prevent and treat possible side effects that could occur.

## Encountered challenges in therapeutical management of a NSCLC patient

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Corresponding Author: Bogdan Cristian Venter e-mail: bogdanventer@yahoo.com **Introduction.** Lung cancer is a very important health issue as its 5-year survival rate of 12-15% turns it into the first cause of cancer death worldwide. Despite the implementation of new therapeutic agents, the management of non-small cell lung cancer (NSCLC) patient still remains challenging due to the numerous adverse effects.

**Case report.** We present a case of a 66 year old female patient known with chronic obstructive pulmonary disease (COPD), type 2 diabetes, essential 3rd grade hypertension with a history of surgically treated right lobe pulmonary mucinous adenocarcinoma (pT1bN0M0- stage I) in 2016 who, during an imagistic follow-up examination in 2019 presented a suspicious nodular lesion (6/4cm) in the 3rd segment of the right superior pulmonary lobe. The clinical and histopathological examination characterized it as metachronous metastasis of the initial mucinous adenocarcinoma. Multiple lines of systemic chemotherapy have been applied, such as platinum agents, immune checkpoints inhibitors (targeted therapy with Pembrolizumab) and taxanes over 4 years of evolution due to constant disease progression and the encounter of several adverse effects most notable being severe anemia, intense lumbago and autoimmune thyroiditis. In present, by controlling the tumor growth with an maintenance treatment and treating the side effects the patient has a good quality of life.

**Discussions.** Literature says that genetic testing is mandatory in the therapeutic choice process as it is proven to increase the survival rate by the efficiency of targeted therapy: anti-EGFR, anti-ALK, anti-PD-L1. However, targeted therapies come with the cost of a wide pallet of side effects that can alter the patient's quality of life bringing new difficulties in the therapeutic management. The importance of this case report is to highlight the complex approach of this type of cancer since we have to cease the progression of the disease, but also to manage the adverse effects of both systemic and targeted therapy

**Conclusions.** Considering the overall infaust prognosis, the multiple treatment choices with different side effects the management of lung cancer is complex, requires multidicipllinary approaches in order to increase both the survival rate and the quality of life.

## The unseen signals: recognizing altered urine pigmentation in two inherited metabolic diseases

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1) Faculty of Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Alkaptonuria (AKU) is a genetic disorder in which homogentisic acid is not metabolized; several fatty acid oxidation disorders (FAODs) may present rhabdomyolysis caused by injury of skeletal muscle and leakage of potentially toxic contents into plasma, both having, as a common sign the dark urine. We emphasize the fact that one sign present in different metabolic pathologies leads to different approaches.

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Corresponding Author: Alin-Ștefan Vizitiu e-mail: vizitiu.23@yahoo.com **Material and methods.** Starting with several signs of an AKU patient, we compare and contrast the main aspects of diagnostic and treatments in AKU and rhabdomyolysis due to FAODs [i.e. Carnitine Palmitoyltransferase II (CPT II)], using a reference book Inborn Metabolic Diseases, edited in 2022 and a review based on 8 relevant articles found on Pubmed using the keywords: Alkaptonuria, Rhabdomyolysis, Treatment, Dark Urine published during the last 10 years.

**Results.** Both AKU and rhabdomyolysis due to FAODs affect the musculoskeletal system: in AKU the joints and connective tissue, and in CPT II the presentation is related to energy metabolism- muscle weakness, hypoglycemia and fatigue. However, their complete presentation is different: joints limitations, ochronosis present in the cornea in AKU, whereas the muscle pain and weakness are typical for few FAODs. AKU is managed with nitisinone and dietary restriction, while in FAODs therapy focus on the types and amounts of fats and carbohydrates consumed. The biochemical and genetic tests are are important for their early diagnosis. The markers identified in newborn screening (NBS) for CPT II defect (using mass spectrometry) include elevated long-chain acylcarnitines. AKU is not typically identified through NBS.

**Conclusions.** Dark urine is one of the first signs that occur in few inborn metabolic diseases. Even it helps to orientate the diagnostic, it is crucial to take into account the two different biochemical defects.

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## **Correlations between type 2 diabetes, obesity and alcohol use in the context of bariatric surgery**

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Corresponding Author: Théo Chopard-Vilhem e-mail: theochopardvilhem@gmail.com **Introduction.** Obesity, type 2 diabetes (T2D), and alcohol use pose public health concerns. The link between T2D, obesity and alcohol use in the context of bariatric surgery and their impact need a proper characterization in order to properly identify and treat these conditions.

**Material and methods.** We conducted an extensive literature search using various research strategies covering obesity, T2D, alcohol consumption, and bariatric surgery. We consulted medical and scientific databases to identify relevant studies. The results of these searches were summarized, analyzed, and categorized based on the specific relationships between the variables.

**Results.** The link between obesity, T2D, alcohol, and bariatric surgery are complex. Managing T2D in obese individuals remains challenging. Bariatric surgery offers promise with weight loss and glycemic control. More research is vital. Alcohol's impact on metabolic health in obese and diabetic patients is significant. Better understanding can guide clinical recommendations.

In regards to bariatric surgery outcomes may significantly vary. Further research is needed to comprehend the implications, including influencing factors and risks related to alcohol consumption.

**Conclusion.** This study highlights the importance of better understanding the relationships between obesity, T2D, alcohol consumption, and bariatric surgery.



The results suggest that these variables are intricately intertwined, necessitating a multidisciplinary approach to the management of obese patients with T2D.

Bariatric surgery can play a pivotal role in managing obesity and diabetes. Nevertheless, its effects on alcohol consumption and metabolic health exhibit considerable variation. Additionally, the involvement of alcohol in these contexts requires further exploration. The findings of this study offer insights for more nuanced clinical recommendations and guidance for future research to better comprehend and manage these complex public health issues.

### HLA Studio: an R platform to analyze associations of human leucocyte antigen alleles and haplotypes with pathologies

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Corresponding Author: Vlad-Florin Chelaru e-mail: vladflorinchelaru@gmail.com **Introduction.** Human leucocyte antigen (HLA) genes have a pleiotropic effect on the physiologic and pathologic processes, especially in the development of diseases with autoimmune components such as type 1 diabetes mellitus (T1DM). Given the high number of alleles available for each gene in this region, statistical modelling of the effect implies intensive computational resources. We described a statistical analysis platform written in R which allows such analysis, and we provided results for the analysis of HLA associations with T1DM in end-stage renal disease (ESRD) patients.

**Material and methods.** The HLA Studio platform enables the detection of all unique alleles available for a user-defined number of genes. Differences between cases of interest and controls are computed at allele and patient level, and the platform allows for controlling for combined effects of different alleles through multivariate regression models. Possible theoretical haplotypes are computed using the haplo.stats package. For demonstration, we used a database of 2392 patients with ESRD (of which 118 with T1DM as cases and the remainder as controls) and 3274 disease-free donors as controls, having complete information for loci HLA-A, HLA-B and HLA-DRB1.

**Results.** By controlling for allele interaction, we identified HLA-A\*34, HLA-B\*41, HLA-B\*50, HLA-DRB1\*03 and HLA-DRB1\*04 as posing a risk for T1DM causing ESRD, while HLA-DRB1\*11, HLA-DRB1\*13 and HLA-DRB1\*15 were protective against ESRD caused by T1DM. The first three haplotypes posing a statistically significant risk for the pathology were A\*01-B\*08-DRB1\*03, A\*02-B\*08-DRB1\*03 and A\*24-B\*08-DRB1\*03.

**Conclusion.** We described an R-based platform for the analysis of HLA allele and haplotype association with pathologies, as well as proving its use through a study on ESRD caused by T1DM, identifying risk and protective alleles and haplotypes. Specific improvements for further versions of the platform were stated.

### Hypertensive emergencies and urgencies: impact of medication administration on blood pressure reduction and discharge status

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Corresponding Author: Elena-Diana Gâbroveanu e-mail: diagabroveanu@yahoo.com **Introduction.** Hypertensive emergencies and urgencies are critical conditions that require prompt management to prevent acute end-organ damage. The study aimed to analyze the effectiveness of treatment interventions and their impact on blood pressure.

**Material and methods.** Patient information, including symptoms, medication administered, and blood pressure measurements, were gathered from hospital records over a period of one month.

**Results.** This study included 64 hypertensive urgencies and 45 emergencies. Common complaints were headache (26.61%), dyspnea (15.6%), nausea, dizziness, focal neurological signs (14.68% each). Enalaprilat (37.5%), captopril (20.31%), nifedipine (18.75%) were among the commonly used medications for hypertensive urgencies. For hypertensive emergencies, furosemide (33.33%), enalaprilat (26.66%), urapidil (22.22%) were the most frequently administered drugs. For hypertensive emergencies and respectively, urgencies, a notable reduction was observed in both systolic and diastolic blood pressure, as well as the mean arterial pressure, when measured one hour after medication administration compared to admission (p < 0.01). These reductions were also evident at the time of discharge (p<0.001). We found a significant correlation between nifedipine administration and improved discharge status (p=0.038). Statistically significant differences (p<0.001) were observed in the mean arterial pressure decrease one hour after medication between patients who received furosemide and those who did not. Furthermore, we found statistically significant differences in mean arterial pressure decreases at patient discharge for those who received furosemide vs without (p=0.032), and, respectively, nifedipine vs without it (p=0.007).

**Conclusion.** Appropriate medications such as nifedipine and furosemide effectively lower blood pressure for hypertensive emergencies and urgencies, with noticeable results within one hour of administration and at the time of discharge.

## QSAP: an R platform for statistical analysis of quantitative encephalography features and their correlations with clinical data

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2) RoNeuro Institute for Neurological Research and Diagnostic, Cluj-Napoca, Romania **Introduction.** Quantitative encephalography (qEEG) is used to extract meaningful information from brain electrical activity data, aiding in the interpretation of neurophysiological phenomena. We developed a statistical analysis platform written in R to automate such analysis, and we provided results for the analysis using network-based statistics (NBS) methods in the CAPTAIN-rTMS randomized clinical trial.

Material and methods. The QSAP (QEEG Statistical Analysis Platform) enables the conversion of qEEG features, computed by Brainstorm, to interoperable formats



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Corresponding Author: Vlad-Florin Chelaru e-mail: vlad.chelaru@brainscience.ro; vladflorinchelaru@gmail.com such as R image files or longform comma-separated values files. The platform computes the means of individual features, consolidating individual electrode information into larger brain areas, and, among others, determines the network integration based on the minimum spanning tree algorithm ran on individual electrode correlation matrices. For demonstration, we studied three groups of patients: cerebrolysin + repetitive transcranial magnetic stimulation (CRB+rTMS, N=16), cerebrolysin + sham (CRB+sham, N=15) and placebo + sham (PLC+sham, N=19). EEG recordings were taken at baseline (30 days after traumatic brain injury - TBI, before treatment) and 180 days after TBI.

**Results.** Using the QSAP, we rendered individual connectomics maps and computed five NBS features. We observed statistically significant differences only in the highest degree in node index (decrease of network integration in the CRB+sham group compared to baseline, p=0.042; higher increase in the CRB+rTMS group compared to CRB+sham, p=0.018). No significant differences were observed in the other four indexes. At both visits, Fz and PO10 were the electrodes corresponding to the center of most of the identified networks.

**Conclusion.** We described an R-based platform for the analysis of qEEG features, and we evaluated whether the treatment after TBI can influence BNI. Our findings suggested no clinically relevant differences.

## Metastatic renal cell carcinoma 12 years after nephrectomy: a case report

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Corresponding Author: Paul-Alexandru Milea e-mail: alex.milea2000@gmail.com **Introduction.** The most common type of malignancy originating in the kidney is renal cell carcinoma (RCC), accounting for 90% of adult renal cancers. Patients with RCC develop metastatic spread in approximately one-third of cases. While common sites of metastases include the lung, liver, bone, brain, and adrenal glands, a few case reports detail the capacity of RCC to appear almost anywhere throughout the body. Metastases may be found at diagnosis or, rarely, several years post-nephrectomy.

**Case report.** A 70-year-old patient presented to the otolaryngology department with the sensation of a lump in his throat and odynophagia on October 25, 2023. The patient's history included a curative intervention, a left nephrectomy, in 2011 followed by the removal of a secondary supraglottic RCC determination in March 2023 and the excision of a secondary determination in the right pyriform sinus and in the upper lip in July 2023 and September 2023, respectively. With all these in mind, the symptoms raise a high suspicion of another secondary determination of the RCC. Objective examination reveals a pedunculated formation located in the right valecula, with no other pathological laryngeal changes. Surgical excision of the mass is decided and the histopathological examination of the resection specimen revealed a metastasis of clear cell renal cell carcinoma. Given his good performance status, associated with the multiple surgeries, the patient's treatment is combined with Axitunib/Avelumab.

**Discussion.** Following breast and lung cancers, RCC is the third most frequent cancer to metastasise to the head and neck region, though such cases are rarely reported. Patients with this type of metastatic RCC face a dismal prognosis, but the median overall survival with the targeted therapies is now greater than two years, doubling the survival rate seen during the interferon- $\alpha$  era.

**Conclusion.** This case aims to underscore the significance of identifying rare metastatic sites in RCC, despite the significantly negative impact on the prognosis. A good performance status may offer the chance for proper treatment options that may prologue survival rates.

### Sustained complete response to immune checkpoint inhibitor therapy in patient with metastatic melanoma

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Corresponding Author: Eliza Maria Bob e-mail: bob.eliza@yahoo.com **Introduction.** Metastatic melanoma has long presented a significant challenge in the field of oncology. Historically, the prognosis has been grim, with limited treatment options and poor survival rates of only a few months. However, the landscape of melanoma treatment has been transformed in recent years, owing to the advent of immunotherapy and targeted therapy. It is well known that tumor cells developed various mechanisms to evade immune response. In this context, immune checkpoint inhibitors (ICIs) enable lymphocytes to recognize and destroy cancer cells again. Immunotherapy achieves long-term survival in about 50% of metastatic melanoma patients. However, not all patients benefit equally and efforts to identify predictive factors of clinical response are ongoing.

Case report. We present the case of a 45-year-old female patient diagnosed with a pigmented tumor of the left anterior thigh in 2010. The histopathological result described a superficial spreading melanoma Clark II, Breslow 1,6 mm, L0V0R0 (pT2a) with little peritumoral inflammatory infiltrate and a wild type BRAF. Clinically, no suspicious lymph nodes were detected and no SLNB was performed. Eight years later, in July 2018, she presented with left adenopathy with malignant characteristics, so a left inguinal and iliac lymphadenectomy was performed, which revealed three positive lymph nodes with melanoma metastases. A PET-CT showed no metabolically active lesions, so the patient received adjuvant therapy with Interferon until February 2019. In March 2019, a CT scan showed three hepatic lesions suspicious for metastases, confirmed by a subsequent PET-CT, which also revealed metabolically active renal, adrenal, and osseous (sacral) lesions. Therefore, first line immune therapy with ICIs Nivolumab and Ipilimumab was started. At that point, the patient had an LDH of normal range (191) and the NLR was 3,46. After receiving three cycles of combined ICI therapy, the patient presented with a severe diarrheic syndrome and diffuse abdominal pain diagnosed as autoimmune colitis (digestive toxicity grade 3), for which corticosteroid therapy was instituted. After remission of the symptoms, the therapy was resumed with Nivolumab alone. In November 2019, after 6 months of immune therapy, a PET-CT revealed partial response. The patient continued Nivolumab monotherapy and had no further adverse effects. A restaging PET-CT from July 2020 revealed complete metabolic response and a CT from December 2020 could not identify any secondary lesions. The patient received 36 cycles of Nivolumab in total, with discontinuation after 2 years, since the complete response was sustained at all o the following imagistic reevaluations, the last one being in May 2023.

**Discussion.** In this case, there are multiple intriguing particularities. The relapse, which involved loco-regional lymph nodes, but later also distant sites occurred after a long time (8 years), even though the patient was initially diagnosed with a thin (<2 mm Breslow) melanoma and did not have additional risk factors for relapse.

However, it is important to mention that the patient did not benefit from a SLNB at the moment of diagnosis. On the other hand, the patient was closely monitored, so the relapse was quickly identified, and treatment was promptly started. At the beginning of her ICI treatment, the patient had an LDH value in the normal range, which is a good prognostic factor and relatively low NLR, which in literature has been linked to a good response to the immunotherapy. On the other hand, the initial histopathology of the tumor showed a low, non-brisk lymphocyte infiltration rate, which suggests a lower immunogenicity of the tumor and might lead to a poorer response to ICIs. Nonetheless, it has been shown in multiple studies that the immune related adverse events (in this case autoimmune colitis) occur at a higher rate in patients with better tumor response to treatment with ICIs.

## A case of sudden-onset flaccid paralysis in a previously healthy person

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Corresponding Author: Iasmina-Andreea Toader e-mail: iasmina toader@yahoo.com **Introduction.** Flaccid paraplegia is defined as a clinical syndrome, with rapid and symmetrical onset of weakness in both lower limbs, progressing to a maximum severity within several days to weeks. It is a clinical occurrence with significant importance, due to the dramatic presentation, the severity of the underlying disorder, and the generally poor prognosis that follows such a condition.

**Material and methods.** A 19-year-old woman presented to the Emergency Department complaining of prolonged fatigue and tetrameric muscle weakness. After an episode of syncope, she became suddenly paraplegic without any identifiable traumatic events. In her medical history, she has a documented case of hypothyroidism for which she is receiving replacement therapy, is currently under treatment for polycystic ovarian syndrome with oral contraceptives and has a folic acid deficiency. Furthermore, she was complaining of metrorrhagia, so a gynecological examination was performed without any pathological results discovered.

**Results.** The clinical examination revealed flaccid quadriplegia with a predominance of paraplegia. Neurologic examination showed motor power grade 0/5 proximal and 1/5 distal in both arms and 0/5 in both legs and decreased deep tendon reflex. A cranial CT scan and a cerebral CT angiography with contrast were performed and they were without significant modifications. Moreover, the spinal cord was investigated. The doctors performed a CT scan and IRM native and with contrast, revealing no pathological modifications. In addition, EEG and Lumbar Puncture were performed and they were both negative. The patient was admitted to the Neurological Department for one month. Moreover, as part of the comprehensive rehabilitation program, she performed kinetotherapy during which her condition has significantly improved, now being fully recovered.

**Conclusion.** Acute paraplegia is an emergency condition that requires proper diagnosis and treatment in a very short time. To make an accurate diagnosis, immediate neurologic assessments, imaging rok-ups, EEG and lumbar punction are mandatory.

### Ethnicity and pediatric ADHD management: a challenging case

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Corresponding Author: Ştefania-Maria Mocrei-Rebrean e-mail: stefania.mocrei@gmail.com **Introduction.** Attention deficit hyperactivity disorder (ADHD) is one of the most common findings in child psychiatry and often has comorbidities, including learning and anxiety disorders. Outcomes depend on the successful implementation of psychosocial and pharmacological interventions.

**Case presentation.** A seven year-old male patient of Roma ethnicity presented in October 2022 with hyperactivity, educational maladjustment and mixed disorder of conduct and emotions. Symptom onset was during his final year of kindergarten with deterioration upon first grade introduction, when his behavior became heteroaggressive. History revealed institutionalization between the ages of one and four due to biological family abuse and subsequent adoption into a supportive Romanian family. In January 2023, risperidone 0,25mg was prescribed, leading to behavioral improvement. After six months, treatment was ceased due to urinary retention and symptoms relapsed, prompting aripiprazole initiation.

**Discussion.** The first line of treatment for ADHD and conduct disorders are psychosocial interventions, followed by pharmacotherapy. In this case, psychosocial measures are especially difficult to implement as a result of ethnic discrimination both on peer and administrative level, which led to adoption status-related bullying (and self-harm risk), education institution disregard of psychiatric assessment reports and parents being pressured into considering a transfer. Moreover, while opting for a low-dose antipsychotic instead of usual ADHD drugs like methylphenidate did improve aggression and hyperactivity via mild sedation, it led to the less frequently reported side-effect of urinary retention and to the discovery of preexisting urethral stricture to be considered in future monitoring.

**Conclusion.** ADHD management remains problematic due to social integration issues affecting ethnic minorities and institutionalized children especially, limiting psychological intervention effectiveness.

### Inflammatory biomarkers and their role in predicting the response to anti-EGFR therapy in metastatic colorectal cancer

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2) Institute of Oncology, Cluj-Napoca, Romania **Introduction.** Targeted therapies have shown remarkable outcomes in disease control and survival for metastatic colorectal cancer (mCRC). Discerning the patients who stand to have a better treatment response remains a challenge. Our retrospective single-center study aimed to evaluate the prognostic utility of inflammatory biomarkers when implementing standard doublet chemotherapy plus anti-EGFR monoclonal antibodies (Cetuximab) and share our center's experience.

**Materials and methods.** Out of 226 mCRC patients for whom standard doublet chemotherapy plus anti-EGFR monoclonal antibodies (Cetuximab) were initiated at our center between 2014 and 2023, 38 cases met inclusion criteria: unresectable stage IV



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Corresponding Author: Alexandru Necula e-mail: necula.alexandru@elearn.umfcluj.ro mCRC, KRAS-wt status, left-sided primary tumor, 3 months follow-up CT imaging with RECIST criteria, accessible histology, and availability of pre-treatment peripheral blood counts. We focused on assessing the role of Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR), which were quantified 1 day previous to the commencement of the regimen. To evaluate treatment response, we relied on follow-up CT conducted at the three-month mark and the RECIST criteria, thus diving next the patients in three distinct groups based on response: remission (R), stable disease (SD), and progressive disease (PD). To assess for any cut-off value between response (R, SD) and no response (PD) to treatment, we performed ROC curve analysis. Furthermore, we divided the NLR and PLR groups based on the median value into high and low NLR and high and low PLR, respectively, and tried to assess if there is any difference in terms of response to treatment between the two. Statistical analysis was performed using GraphPad Prism 9.0.1 software.

**Results.** We observed the lowest NLR values in the R group, followed by progressively increasing values in the SD group and the PD group. The cut-off after ROC curve analysis was not very conclusive, with an NLR > 1.54 (Se:75%, Sp:61%), but when separated based on the median NLR (=1.90), there was a significant difference in response between the high and low-value NLR groups (p < 0.0001).

With regard to PLR, a distinct upward trend from the R group to the PD group wasn't as evident, however, the lowest values corresponded to the R group. After ROC curve analysis, the indicated cut-off was PLR > 95.90 (Se:70%, Sp:66%), and when dividing based on the median PLR (=99) into high and low-value PLR groups, we found again a significant difference in terms of treatment response (p = 0.03). With regard to demographics, male patients demonstrated an improved treatment response, with 15% achieving remission compared to 11% in the female subgroup. We found no discernible correlation between patient age and treatment response (p = 0.96).

**Conclusions.** Inflammatory biomarkers hold value in managing systemic treatment for mCRC patients, as emerging data show the interplay between different infiltrating tumor leukocytes and the tumor microenvironment. From our data, low NLR and PLR values correspond to better treatment response, while high values are associated more with progressive disease. These findings are consistent with the literature and recent trials examining the role of leukocytes and platelets play in tumor progression, while at the same time high levels of tumor infiltrating lymphocytes, mostly due to their cytotoxic effect, correspond to tumor suppression and better overall survival. These findings emphasize the utility of biomarker use in the therapeutic strategy, as seen in our center's experience.

## Is there a predictive value of gender in the response of metastatic melanoma patients treated with immunotherapy?

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2) Institute of Oncology, Cluj-Napoca, Romania **Introduction.** There is a growing awareness concerning gender influences on the response of cancer to immunotherapy that is reflected by an increasing number of studies in many tumors, including melanoma. A new revolution was marked by immunotherapy in this setting, but neither predictive factors were identified in response, nor any selection criteria for targeted therapy of immunotherapy.

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Corresponding Author: Alexandru Necula e-mail: necula.alexandru@elearn.umfcluj.ro **Material and methods.** A retrospective study was initiated with the hypothesis of comparing the impact of gender on the response in cancer patients diagnosed with metastatic melanoma. For the inclusion, the patients were selected independently of BRAF status, treated with the combination checkpoint inhibitor drugs PD-1 inhibitor/ CTLA-4 inhibitor: NIVOLUMAB/ IPILIMUMAB.

For each patient, at the inclusion the performance status was assessed along with the ratio neutrophils/lymphocytes (NLR), trombocytes/neutrophils, the value of LDH. Every patient was evaluated after 4 cycles of double immunotherapy and then every 3 months during the maintenance treatment. Statistical analyses will be assessed to evaluate if there exists a statistical gender difference in response to double immunotherapy.

**Results.** The initial clinical population had more men than woman with melanoma. The top 3 sites for metastases were lymph nodes followed by the lungs then by the liver in both sexes (with more numbers for lungs and liver in men). More women are affected by the toxicity of the treatment (13 versus 11). In our study, we have found an overall good response to treatment in both subgroups. We found useful the NLR cut-off in the range 0,7-3 as the range for positive outcomes in response to treatment. (A normal range of NLR is between 1-2, the values higher than 3.0 and below 0.7 in adults are pathological. NLR in a grey zone between 2.3-3.0 may serve as early warning of pathological state or process such like cancer, atherosclerosis, infection, inflammation, psychiatric disorders and stress).

**Conclusion.** The majority of our findings tend to support the literature about the melanoma, especially in terms of incidence, metastasis distribution, toxicity of immunotherapy and the poor outcome of treatment in relation to a high baseline NLR. We didn't find an overall less effective response to treatment in females, this might be due to the limitations of the study such the number of patients.

However, in the era of personalized care, more studies are needed in order to understand, for instance, which treatment can suit better not only a woman versus a man, but even at an individual level by taking into account multiple variables.

## Therapeutic conundrums in a case of aggressive fibromatosis with exponential postoperative growth

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Corresponding Author: Vlad Răzniceanu e-mail: vlad.razniceanu@yahoo.com **Introduction.** Desmoid tumors are rare mesenchymal neoplasms developing from locally invasive fibroblasts. They lack metastatic potential but have high local recurrence rates and are particularly destructive to surrounding tissues. We present the case of a 39-year-old woman whose tumor exhibited rapid proliferation requiring surgical treatment after partial resection.

**Material and methods.** The patient presented with symptoms suggestive of peptic ulcer disease and a palpable mass in the left hemithorax. History includes cervical neoplasia CIN III (cervical intraepithelial neoplasia) treated via conization a month prior. During the physical examination, a firm painless tumoral mass was perceived on the superior part of the left rectus abdominis muscle, at the level of the left hypochondrium and hemithorax, adherent to nearby anatomical planes. Imagistic evaluations were performed, including CT and MRI, the former rendering tumoral mass size at



22/48/55mm (LL/AP/CC). Soft-tissue sonography and a tru-cut biopsy were carried out. The histopathological and immunohistochemical evaluation revealed a spindle cell mesenchymal tumor suggestive of aggressive fibromatosis. A patient-requested surgical intervention for partial growth removal was performed, but 12 months later an expanding mass (75/40/84mm) in the same location was found infiltrating the 5th and 6th intercostal spaces near the sternum.

**Results.** After its relapse, major surgery was needed to remove the mass, the affected sternum segment and ribs, followed by reconstruction via an autologous myocutaneous flap. Although desmoid tumor management is primarily surgical for low surgical morbidity individuals, microscopically negative margins can be hard to achieve, hence many patients suffer from local recurrence after initial surgery.

**Conclusion.** Our case puts invasive treatment under scrutiny and makes an argument for conservative approaches to desmoid tumors before the necessity of other interventions is considered.

### Pembrolizumab: a cause of immune-mediated type 1 diabetes mellitus in a cancer patient - a case report

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Corresponding Author: Bianca-Alexandra Savin e-mail: savin.bianca.alexandra@gmail.com **Introduction.** The Food and Drug Administration approved pembrolizumab, a programmed death receptor-1 (PD-1) blocking antibody, in April 2019, for treatment in non-small cell lung cancer (NSCLC).

Immune checkpoint inhibitors (ICIs), like pembrolizumab, have a profound impact on oncologic care by enhancing immune responses for anti-tumor activity. However, ICIs may also induce immune-related adverse events (irAE). This case report highlights the iatrogenic impact of pembrolizumab in an NSCLC patient, leading to the development of type 1 diabetes mellitus.

**Case report.** Disease onset occurred in February 2023 in a 56-year-old male with no suggestive symptoms. A MRI screening revealed a left pulmonary tumoral mass. Following a CT, a biopsy is taken, leading to the histopathological diagnosis of PD-1 positive, EGFR negative, ALK negative, T4N3M1b Pancoast adenocarcinoma. The patient consequently underwent immunological and chemotherapeutical treatment with pembrolizumab, pemetrexed and carboplatin in 8 courses. In August 2023, a CT exposed tumoral invasion in the mediastinum and in the lateral thoracic wall resulting in osteolysis of the posterior aspect of the second rib. Subsequent to the uncontrolled thoracic algic syndrome, morphine therapy and 2 courses of radiotherapy have been administered.

Blood sugar levels started to gradually increase throughout the immunotherapy and chemotherapy, reaching the value of 400 mg/dL in October 2023. It led to the temporary interruption of the oncological treatment. The male presented polydipsia, polyuria and weight loss. The 11% HbA1c levels, the significant glycosuria and ketones in the urinalysis support the diagnosis of type 1 diabetes mellitus. The treatment imposed fast-acting and long-acting insulin.

Discussion. In contrast with the favorable clinical responses regarding the
antitumor immunity, anti-PD-1 therapy can cause type 1 diabetes mellitus. It develops and progresses rapidly in a manner different from conventional autoimmune diabetes through inappropriate activation of T cells. It is reported to occur in 0.4% of patients. Unfortunately, discontinuing the oncological treatment has a negative impact on the prognosis and amplifies the psychosocial distress of the patient.

**Conclusions.** Physicians should be aware of the complex medical challenges that may occur in pembrolizumab-treated NSCLC and act promptly to offer the patient the utmost favorable outcome.

### Belated metachronous relapse of invasive mammary carcinoma raising awareness for lifelong monitoring of breast cancer survivors

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Corresponding Author: Andrada Olivia Țăpîrdea e-mail: tapirdeaandrada@gmail.com **Introduction.** Breast cancer in women under the age of 40 represents a very rare (under 7% of all breast cancers) and challenging disease as it generally evolves more aggressively than in older patients. Also, the most common invasions and recurrences are in bones, liver and lungs and they usually appear within less than 5 years after the primary tumor.

Case report. We present a case of a 76-year-old female patient with a history of left mammary invasive carcinoma treated curatively with chemotherapy and surgery in 1983, at the patient's age of 36, who, in 2018, underwent a thoracic computed tomography (CT) scan which revealed a 6-cm-high pleural effusion in the right lung. Biopsies were extracted and histopathological results determined an NST invasive mammary carcinoma metastasis with receptor profiling classification as Luminal A type, indicating further pleurodesis with Bleomicin. Further investigations concerning a cancer relapse showed no significant signs of local or regional recurrence. Thus, on abdominal ultrasound, low-grade ascites and peritoneal nodules were observed and their biopsies' results confirmed the association with mammary carcinoma. Considering the genetic profile of the tumor and the metachronous manifestations in the pleura and peritoneum, systemic and hormonal therapy was implemented at a level of CA15-3 of 76 U/ml. The under-treatment evaluation revealed an initial disease regression (CA15-3=36 U/ml, minor decrease of ascites and pleurisy) followed by a spontaneous relapse mirrored in massive ascites accumulation and increasing levels of CA15-3 (up to 100 U/ml). Therefore, the therapy changes for cyclin-kinases inhibitors (Pablociclib) and estrogenic receptors antagonists (Fulvestrant), the patient being monitored in evolution.

**Discussion.** Literature shows a roughly maximum of 20 years from the primary tumor as period in which a relapse can occur. Our case presents a metachronous metastasis fortuitously discovered after 40 years from a curatively treated Luminal A breast cancer appeared early in the life of the patient.

**Conclusions.** Thus, lifelong monitoring of breast cancer survivors is advisable not only to investigate the presence of local or regional relapsing, but also to consider multiple potential metastatic sites.

#### Posture awareness while using the cell phone

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Corresponding Author: Denisa-Paula Oniea e-mail: denisa.paula11@yahoo.ro **Introduction.** The improper position in front of the phone, became one of the main health problems our society has to face. The purpose of this study is to verify if drawing attention over an incorrect posture is or is not an important factor in maintaining a correct attitude. The objectives include the highlighting of unwanted effects, which may appear because of the aforementioned posture, but also several methods which help in acquiring a healthier stance.

**Material and methods.** We have edited a questionnaire which has been completed by 143 individuals who have access to a mobile phone, and use it daily. Out of these persons 28.7% are males and 71.3% females.

**Results.** The statistics show that those who completed our set of questions, 68.5% felt cervical pain after a certain time spent on the phone. While completing our survey, 62.9% of the respondents were with their head in flexion, however, 51% corrected their position after their attention has been drawn to this aspect. When finishing the survey, 49.7% of the persons had re-adopted the initial position. On the other hand, 82.4% of those who have completed our questionnaire are eager to find out useful tips about their stance, but also interested in correcting their vicious posture with physical therapy.

**Conclusion.** Mobile phones have become vital instruments in our everyday life. Thereby, there is no need to quit using it, but to become more aware of our posture while running errands. In addition, it is quintessential to know that simply drawing attention, doing a few physical therapy exercises can have an important role in maintaining a healthy posture while using our cellular phone.

## Shrinkable polystyrene decorated with gold nanostars for SERS applications

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Corresponding Author: Amalia-Simona Iacob e-mail: iacobamalia03@gmail.com **Introduction.** This study presents the facile synthesis of a SERS substrate using polystyrene sheets decorated with gold star shaped nanoparticles (AuNSs) for analytical applications. Polystyrene shrinks when heated leading to the aggregation of the deposited colloid, enhancing the SERS signal of the analyte. 4-aminothiophenol (p-ATP) was used as Raman probe for the characterization of the substrate.

**Material and methods.** AuNSs were synthesized through a one-pot seedless protocol in aqueous solution using tetrachlorauric (III) acid, silver nitrate and ascorbic acid as reducing agent. Small polystyrene disks were washed before use with Milli-Q water and ethanol (1:1) to remove all impurities, then air dried. The colloidal AuNSs were centrifuged and concentrated. Then, a given volume of AuNSs concentrate, either in the presence or the absence of the Raman probe, is placed on a polystyrene disk and heated on a hot plate until full contraction to generate a continuous and compact AuNS layer. SERS data were collected using a Raman spectrometer (Avantes, 785 nm laser).

**Results.** The optimum dimension for the polystyrene disks was found to be 5 mm, which will shrink upon heat exposure to 2 mm. The best results leading to a reproducible nanostructured gold surface were obtained by the deposition of 10  $\mu$ L of AuNSs able to fully cover the 5 mm disk. The optimum temperature for thermal contraction was 100°C allowing the disc to shrink evenly and the AuNSs colloid to dry properly.

**Conclusion.** In this study, the potential of polystyrene sheets to be used as roboust SERS substrates following a modification with AuNSs was demonstrated. The singleuse, cost-effective and reproducible SERS substrates, prone to mass production, were explored for the detection of various environmental pollutants.

#### The succes of prosthetic rehabilitations through occlusal records

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Corresponding Author: Mirela Ioana Flueraşu e-mail: mfluerasu@yahoo.com **Introduction.** The success of prosthetic rehabilitations through occlusal records is determined by an optimal functionality. This is crucial in ensuring a correct distribution of occlusal forces on teeth and soft tissues. An incorrect occlusion might lead to instability of dental prostheses or the occurrence of dental and TMJ trauma. The aim of the study was to investigate the role of different occlusal records technologies, analogue, as well as digital, in order to choose the optimal technique.

**Material and methods.** A literature review has been made on different platforms. Articles published between 2018 and 2023 were included looking for the results in occlusal records, using digital systems of recording, such as T-scan, Mo-jaw, etc. Obtained results have been analyzed statistically.

**Results.** All digital systems bring benefits to the practitioner as well as to the patient, facilitate workflow, they are easy to use having reproductible and predictable results, with the condition of the knowledge in detail of that technology and application.

**Conclusion.** This study reveals that digital technologies for occlusion recording provide highly accurate, predictable information to ensure the success of prosthetic rehabilitations. A good result is conditioned by solid foundations in terms of occlusion knowledge and good knowledge of the indicated recording system.

# Prosthetic treatment outcome preview in complex oral rehabilitations

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1) Department of Dental Propedeutics and Esthetics, Faculty of Dental Medicine, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania **Introduction.** Previewing the prosthetic treatment outcome is a task that is often performed in complex oral rehabilitations, especially in aesthetically demanding patients. Today there are multiple digital programs that can be used by the practitioners to make these predictions. The objective of the study was to evaluate the most commonly used digital smile design programs, for predicting the final result.

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Corresponding Author: Călina Dobocan e-mail: dobocancalina1@gmail.com **Material and method.** A number of 5 digital smile design programs used in dentistry for previewing the prosthetic treatment outcome were evaluated according to several specific parameters: data acquisition method, aesthetic and diagnostic analysis, assistance in making prostheses through CAD/CAM, opened or closed system and price. The data was organized in tables, classified and analysed.

**Results.** Cerec Smile Design - Sirona is not a standalone system, it is actually a module integrated directly into the CAD/CAM software. NemoDSD 2D and NemoDSD 3D – NemoTec makes it easy to create a digital smile design either from a photo or based on an optical impression. Romexis Smile Design - Planmeca automatically measures the width and height of the teeth, then automatically calculates the ideal proportions. Smile Designer Pro - Tasty Tech offers twelve pre-designed tooth shape templates, but also offers the possibility to draw freely on the program, after the aesthetic analysis phase. Digital Smile System - Dental Team allows the superimposition of face photos with those of a model or a wax-up.

**Conclusion.** Within the limits of this study, the choice of the digital smile design program used to predict the prosthetic treatment outcome is made according to several parameters and it is not always an easy task for the medic.