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MEDICINE
Basic Sciences

The conal septum imaged in the developing heart by ultrasound and micro-MRI at 11.6 Tesla

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Introduction. A thorough knowledge of cardiac embryology is required to understand the mechanism of congenital anomaly development and accurately interpret images provided by current imaging technologies. The aim of this observational descriptive study of morphological research is to assess the conal septum within the developing heart using high-resolution ultrasonography and micro-MRI at 11.6 Tesla.

Material and methods. We studied 11 fetuses in the second and third trimesters of pregnancy using a Voluson E10, BT 15 ultrasound scanner (GE Healthcare, Zipf, Austria) with a mechanical high-frequency transducer (6-12 MHz/256-element 3D/4D). Both 2D and Doppler images of the fetal heart were obtained. We also examined ex vivo 8 human embryos aged 6 to 10 weeks, and 4 fetuses aged 11 to 14 weeks. Micro-MRI examination was conducted using a Bruker BioSpec scanner (Bruker BioSpin MRI GmbH, Ettlingen, Germany) at 11.6 Tesla.

Results. We used ultrasonography to depict the conal septum in fetuses. This structure is better seen in the section of the left ventricular outflow tract beginning from 16 gestational weeks. We discussed its relationship to the interventricular septum, infundibulum, and aortic valves. The conal septum was detected on micro-MRI images acquired at 11.6 Tesla in fetuses beginning from 11 gestational weeks. The ultrasound and micro-MRI images were compared to anatomical specimens and images from classical embryology atlases. We review the clinical significance of the conal septum in the context of conotruncal abnormalities.

Conclusion. Imaging of the conal septum is essential for the diagnosis of conotruncal abnormalities. Early ultrasound detection of cardiac congenital anomalies requires a solid understanding of the embryology and sonographic semiology of the developing heart. Micro-MRI provides embryologists with an alternative to classic histology procedures, which have the disadvantage of destroying specimens.

New catechol hydrazinyl-thiazole derivatives as potential retinoprotective compounds

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Introduction. As human life expectancy increases, there has also been a rise in age-related conditions. Among these, retinal degenerative diseases are a significant cause of blindness in older individuals, with age-related macular degeneration (AMD) being one of the most common. Currently, the non-neovascular form of AMD has a limited selection of therapeutic options, primarily consisting of antioxidant supplements.

Aim. Synthesis, characterization, and antioxidant capacity evaluation of two

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structurally analog compounds based on thiazole, catechol, and β-ionone. These compounds have demonstrated significant biological antioxidant and anti-inflammatory activity, and by effectively addressing oxidative stress, a well-known contributor to retinal diseases, they may offer therapeutic potential for treating retinal degeneration.

Material and methods. The compounds were obtained using the Hantzsch heterocyclisation of thiosemicarbazones. The antioxidant activity of the compounds was evaluated in vitro through various assays, including radical scavenging, electron transfer, ferrous ions chelation, and lipid peroxidation inhibition. In silico quantum and thermodynamics calculations were performed to evaluate how the structure of the compounds influences their antioxidant activity. The cytotoxic activity was assessed in vitro using a human retinal pigment epithelial cell line (ARPE-19).

Results. The results for the new substances indicated a high antioxidant activity compared to ascorbic acid and Trolox. When retinal cells were treated with a range of concentrations using two exposure protocols (24 hours and 48 hours), no toxic effects from the two compounds were observed. Further analysis of cytotoxicity revealed an unexpected pro-proliferative effect, suggesting a potential retinoprotective profile.

Conclusion. The two newly synthesized compounds have promising prospects concerning retinodegenerative processes.

Phytochemical analysis and antioxidant effects of *prunella vulgaris* in experimental acute inflammation

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Introduction. Prunella vulgaris (PV) is one of the most commonly used nutraceuticals as it has been proven to have anti-inflammatory and antioxidant properties. The aim of this study was to evaluate the phytochemical composition of PV and its in vivo antioxidant properties.

Material and methods. A phytochemical analysis measuring the total phenolic content (TPC), an HPLC-DAD-ESI of the phenolic compounds, and a DPPH assay of the extract were performed. The antioxidant effects on inflammation induced by turpentine oil were experimentally tested in rats. Seven groups with six animals each were used: a control group, the experimental inflammation treatment group, the experimental inflammation and diclofenac sodium (DS) treatment group, and four groups with their inflammation treated using different dilutions of the extract. Serum redox balance was assessed based on total oxidative status (TOS), nitric oxide content (NO), malondialdehyde content (MDA), total antioxidant capacity (TAC), total thiols content, and an oxidative stress index (OSI).

Results. The TPC was 0.28 mg gallic acid equivalents (GAE)/mL extract. The HPLC-DAD-ESI analysis showed phenolic compounds with antioxidant activities. The antioxidant activity of the extracts, determined using the DPPH assay, was 27.52 mmol Trolox/mL extract. The PV treatment reduced the oxidative stress by lowering the TOS, OSI, NO, and MDA and by increasing the TAC and thiols. The PV ethanol extract phytochemical analysis found compounds with antioxidant activities.

Conclusion. In acute inflammation, treatment with the PV extract reduced oxidative stress, with lower concentrations being more efficient and having a better effect than DS.

Acknowledgment. The authors thank the Iuliu Haţieganu University of Medicine and Pharmacy Cluj-Napoca, Romania, for their support and cooperation.

Human brain morphogenesis in the first trimester of pregnancy as assessed by ex vivo micro-MRI at 11.6 Tesla

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Introduction. Research teams across the world undertake studies on brain development. The objective of this observational descriptive study in morphological research is to demonstrate structures within the embryonic and early fetal brains that have not previously been cited in literature utilizing micro-MRI at 11.6 Tesla.

Material and methods. We examined 12 human embryos from 6 to 10 GW and 8 fetuses from 11 to 14 GW. The MRI examination used a Bruker BioSpec scanner (Bruker BioSpin MRI GmbH, Ettlingen, Germany) running at 11.6 Tesla.

Results. At 9 GW, the laminar structure of the ventral wall of the telencephalon was identified. The hippocampus was first noticed at 12 gestational weeks (GW). The putamen, globus pallidus, and claustrum were apparent at 12 GW. The medial and lateral portions of the globus pallidus, and the head of the caudate nucleus, were visible at 14 GW. The nucleus accumbens was observed at 10 GW. The subthalamic nucleus, red nucleus, and substantia nigra were first identified at 12 GW. The internal capsule was documented at 10 GW. The inferior olivary nuclei were identified in the medulla oblongata at 12 GW, whereas the nuclei gracilis and cuneatus were found at 14 SA.

Conclusion. Micro-MRI provides embryologists with an alternative to traditional histology procedures. We depicted neurological structures using micro-MRI, including the nucleus accumbens, subthalamic nucleus, red nucleus, internal capsule, and inferior olivary nucleus, which had not been reported in previous studies during the first trimester. Other neurological structures, including the lentiform nucleus, epiphysis, claustrum, anterior commissure, habenular commissure, and subpallial laminar structure, were depicted by micro-MRI at earlier gestational ages as previously reported in the literature. This new evidence for imaging brain morphogenesis in the first trimester of pregnancy can be used as a reference for future research.

Female pelvic fistulizing disease: case presentation of a vesico-vaginal fistula of benign etiology and arguments for the diagnostic use of MRI

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Introduction. Female pelvic fistulizing disease is a significant cause of morbidity, profoundly impacting patients' quality of life and leading to distressing symptoms. This condition poses a diagnostic challenge for healthcare providers because of the complex anatomy of the female pelvis. The major causes of genitourinary fistulas include surgical procedures, radiation therapy, inflammatory bowel diseases, infections, and malignancies. One specific type of fistula arises after surgical interventions and can manifest in the immediate postoperative period or up to six weeks after surgery.

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Higher rates of fistulas are commonly associated with hysterectomies, laparoscopic procedures, and significant oncological surgeries .Vaginal fistulas (VF) are the most common type of fistula, defined as abnormal epithelial-lined connections between the vagina and other pelvic organs . Iatrogenic vesico-vaginal fistulas (VVF) typically occur supratrigonal, resulting from thermal injuries that cause necrosis, followed by inflammation, collagen formation, and perifistula fibrosis. Patients present with continuous urine leakage, leading to mucosal irritation. Other symptoms include dyspareunia, painful perineal dermatitis, and excoriation. Clinical examination of the vagina can identify less than 80% of fistula orifices . Visualization techniques such as urethro-cystoscopy or cystography can help, but they offer limited insight into the complexity of the fistulous tract and underlying conditions . An enhanced role for radiologists has emerged, with computed tomography (CT) and magnetic resonance imaging (MRI) transitioning from conventional radiological techniques.

Material and methods. Case Presentation We present a 53-year-old postmenopausal woman with a recent total hysterectomy for a large uterine leiomyoma. Six weeks post-surgery, she began leaking urine, first during coughing or changing positions, and then on a nearly continuous basis. Despite a vaginoscopy, the fistulous orifice was not identified, and the patient experienced multiple urinary tract infections.

A diagnosis of VVF was established through urethro-cystoscopy and imaging studies, including excretory CT and pelvic contrast-enhanced MRI. Urethro-cystoscopy revealed the fistulous orifice on the posterior bladder wall, above the interureteric ridge, near the right ureteral ostium.

The CT scan confirmed the post-hysterectomy status, with no abdominal collections noted. Air was observed in the bladder, and the excretory phase showed the fistulous tract. The contrast-enhanced MRI displayed the fistulous tract in T2 weighted imaging (T2WI), revealing urine in the bladder, along the tract, and in the vagina. The fistulous tract measured 3.5 mm in length and 2 mm in diameter, connecting the posterior bladder wall to the anterior vaginal wall, with no additional pathological findings reported .

Results. Surgical Procedure The patient underwent a 3D laparoscopic repair of the VVF via a transperitoneal-transvesical approach, utilizing the O'Connor technique. Prior to laparoscopic intervention, endoscopy was performed for bilateral ureteral stenting and marking of the fistulous tract.

The total operative time was 150 minutes, with no intraoperative complications and estimated blood loss under 50 ml. Postoperative Results - Postoperatively, the patient had a favorable recovery, with the pelvic drain removed two days after surgery and the bladder catheter removed ten days later. Following catheter removal, the patient was continent and reported no additional complaints. Ureteral stents were subsequently taken out.

Conclusion. Despite vesico-vaginal fistulas being the most commonly diagnosed type of urinary tract fistula, consensus regarding their management remains elusive . A standardized imaging protocol for diagnostics is also lacking.MRI can easily offer all the information neeed for surgery planning with a high flexibility for the patients individualised needs.

Case presentation of a uterine Mullerian carcino-sarcoma

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Introduction. Uterine Mullerian carcino-sarcoma (UMCS) is a rare and aggressive gynecological malignancy with a poor prognosis. This case presentation aims to highlight the clinical presentation, diagnostic challenges, and management of UMCS in a 59-year-old female.

Material and methods. We present a retrospective analysis of the clinical, radiological, and histopathological findings of a 59-year-old female patient diagnosed with UMCS. The patient presented with abnormal uterine bleeding and underwent a comprehensive evaluation including pelvic examination, transvaginal ultrasound, and magnetic resonance imaging (MRI). Surgical staging was performed, followed by histopathological examination of the resected specimen.

Results. Transvaginal ultrasound and MRI revealed a heterogeneous endometrial mass suggesting a uterine malignant tumor. The patient underwent a total hysterectomy with bilateral salpingo-oophorectomy. Histopathological examination confirmed the diagnosis of UMCS, of high grade (G3), pT2L0V0Pn0R0 FIGO IIC, characterized by a mixture of carcinomatous and sarcomatous components.

Conclusion. UMCS is a rare and aggressive tumor with a poor prognosis. Early diagnosis and prompt surgical intervention followed by adjuvant therapy are crucial for improving patient outcomes. This case underscores the importance of a high index of suspicion for UMCS in postmenopausal women presenting with abnormal uterine bleeding.

Inflammatory markers role in predicting necrotizing enterocolitis

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Introduction. Necrotising Enterocolitis (NEC) remains one of the most significant complications of prematurity with a high mortality and morbidity rate. Identifying reliable markers that could predict the onset of NEC before clinical signs allow earlier interventions and improved clinical outcomes.

More than half of preterm births are triggered by inflammatory process on the feto-maternal site. Inflammation has an in important role in development on complications of preterm neonates like bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL).

The aim of our study was to analyze the role of inflammatory biomarkers on NEC incidence in preterm neonates.

Material and method. A prospective longitudinal study was done in the Neonatology Department of 1st Obstetrics Clinic, Cluj Napoca. In the study group were enrolled 74 preterm newborns, admitted between May 2022 and December 2022, gestational age <34 weeks + 6 days.

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For inflammation study of enrolled preterms we evaluated the interleukin 3 (IL-3) and matrix – metalloproteinase 9 by ELISA technique from blood sample obtained at birth. Also we followed up the reactive C protein (CRP) and procalcitonin value in the first day of life. We analyzed the correlation of the inflammatory markers with NEC incidence of the study group. Maternal inflammation was evaluated by CRP value and role of maternal chorioamnionitis on NEC incidence of the study group was followed up.

Results. Out of the 74 neonates enrolled 20(27%) developed NEC. IL-3 value at birth was higher at neonates which developed NEC. A positive correlation between maternal CRP value and IL-3 of neonates was found ($r=0.541$, $p<0.001$). Maternal CRP was significantly higher in the NEC group – almost 4 times of normal value. We found no correlation of choriomanionitis with NEC.We found no corelation of NEC with the type of feeding.

Conclusion. Increased inflammatory biomarkers value at birth corelates with a higher incidence of NEC. The intrauterine inflammatory condition will associate inflammatory process in preterm neonate and will increase the risk for NEC.

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Black cumin *(Nigella sativa L.)* oil protective effects in rats induced myocardial infarction

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Introduction. Black cumin *(Nigella sativa L.)* oil (NSO) has been shown to have beneficial effects on several cardiovascular risk factors, including diabetes, obesity, high blood pressure, high cholesterol, inflammation, and oxidative stress. This study used a rat in vivo model of isoproterenol-induced myocardial infarction (MI) to assess the NSO impact.

Material and methods. The fatty acids in NSO were characterized using gas chromatography-mass spectrometry (GC-MS) analysis. Fifty rats were split into five groups: two negative control groups that received carboxymethylcellulose by oral gavage (0.4 mL/100 g) (one for 2 weeks and one for 4 weeks), two groups that received NSO (0.4 mL/100 g) (one for 2 weeks and one for 4 weeks) and one positive control group (that received 0.1 mg/100 g ramipril for 4 weeks). MI was induced in all groups on the 14th day of the experiment by subcutaneous isoproterenol (ISO) (45 mg/kg) administration. To evaluate the MI, electrocardiograms, histopathological analysis, serum biochemical creatine kinase-myocardial band (CK-MB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and serum inflammatory markers tumor necrosis factor-alpha (TNF-a), interleukin 1 beta (IL-1b), and interleukin 6 (IL-6) were evaluated.

Results. NSO was rich in linoleic and oleic acids which accounted for 89.49% of the total identified fatty acids. ECG records and histological examination showed distinct alterations associated with acute MI following ISO injection. NSO treatment before MI did not prevent the increment of CK-MB serum levels, but prevented ALT

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and AST increment. The levels of the pro-inflammatory cytokines IL-6 and IL-1b were decreased only after long-term administration of NSO.

Conclusion. NSO treatment might help the modulation of inflammatory processes following MI induction in rats, but more studies are necessary to evidence their potential as therapeutic options in the treatment of myocardial infarction.

Inflammatory profiles in severe COVID-19 and influenza: potential biomarkers for disease severity

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Introduction. Effective management of COVID-19 and influenza requires identifying differences in clinical presentation and disease severity. This study investigates the association between specific inflammatory markers and severity in COVID-19 and severe influenza patients to enhance insights into immunopathogenesis and support clinical decision-making.

Material and methods. This cross-sectional observational study was conducted at two hospitals specializing in COVID-19 care. Adult patients with confirmed moderate to severe COVID-19 or severe influenza were enrolled. Data collected included demographic details, clinical characteristics, laboratory findings, and imaging results. Inflammatory biomarkers—IL-1β, IFN-α2, IFN-γ, TNF-α, MCP-1, IL-6, IL-8, IL-10, IL-12p70, IL-17A, IL-18, IL-23, and IL-33—were analyzed, with statistical significance set at $p < 0.05$.

Results. Median inflammatory marker levels varied across these groups, with generally higher values in severe cases. IL-8, IL-17A and IL-18 showed statistically significant differences between groups, suggesting their role in distinguishing disease severity (p-values: IL-8 = 0.012, IL-17A = 0.013, IL-18 = 0.034). Other markers showed no significant differences ($p > 0.05$), indicating limited utility in severity differentiation.

Conclusions. This study highlights that IL-8, IL-17A, and IL-18 are significantly elevated in severe cases of COVID-19 and influenza, suggesting their potential as biomarkers for disease severity. Although other markers, including IL-1β, IFN-α2, and TNF-α, were elevated in severe cases, these differences were not statistically significant, indicating a limited role in severity assessment. Monitoring IL-8, IL-17A and IL-18 could enhance clinical management and prognosis in severe respiratory infections.

Acknowledgement. We thank the Department of Translational Medicine, Institute of Medical Research and Life Sciences – MEDFUTURE for assistance with flow cytometry and data analysis.

Role of vitamin D in respiratory viral infections

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Introduction. Respiratory viral infections, such as COVID-19 and influenza, challenge global health, particularly in winter. Differentiating them by clinical presentation and severity is essential for effective management. This study investigates the relationship between serum vitamin D levels, vitamin D receptor gene polymorphisms (rs1544410, rs731236, rs7975232), and disease severity in COVID-19 and severe influenza patients during 2023-2024.

Material and methods. This cross-sectional observational study was conducted at an Infectious Diseases Hospital during the 2023-2024 winter season. The study enrolled adult patients diagnosed with COVID-19 (classified as mild, moderate, or severe) and severe influenza, with diagnoses confirmed through PCR or rapid antigen tests. Data collected included demographics, clinical characteristics, laboratory results, and imaging findings. Biomarkers analyzed were serum vitamin D levels, with insufficiency defined as <20 ng/ml, and three vitamin D receptor SNPs: rs1544410, rs731236, and rs7975232. Statistical significance was set at $p < 0.05$.

Results. Among 73 patients divided into four groups (Mild, Moderate, Severe COVID-19 and Influenza), vitamin D levels were lowest in patients with severe COVID-19. Inflammatory markers were significantly higher in the vitamin D-insufficient group, with elevated leukocytes, neutrophils, and CRP (p-values: 0.009, 0.001, and 0.035, respectively). No significant differences in lymphocytes, monocytes, or platelets were observed based on vitamin D status, indicating that vitamin D insufficiency is linked to increased inflammation, especially in severe COVID-19.

Conclusions. Patients with severe COVID-19 had significantly lower serum vitamin D levels compared to those with mild/moderate COVID-19 and severe influenza. This suggests that vitamin D deficiency may contribute to more severe COVID-19 progression. The studied SNPs (rs1544410, rs731236, rs7975232) did not significantly impact disease severity.

Assessment of specific tumoral markers, inflammatory status before and after the first chemotherapy cycle in patients with lung cancer

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Introduction. Our pilot study aimed to investigate a possible association between the inflammatory status (reflected by circulating levels of chitotriosidase and neopterin) and tumoral markers, NSE and SCCA before and after one cycle of chemotherapy.

Material and methods. Inclusion criteria: This observational study included twenty patients with lung cancer, consecutively selected from the medical files of the above-mentioned clinics in Cluj-Napoca. The diagnosis of lung cancer and its complications was established according to the Tumor, Node, Metastasis (TNM) staging system, thoracic computer tomography (CT) imaging, lung biopsy puncture, and pathological examination.

The inclusion criteria were defined by the diagnosis of lung cancer, regardless of disease staging, before the first cycle of chemotherapy. After chemotherapy, patients were evaluated according to RECIST criteria 1.1, which is the gold standard for assessment of treatment response in solid tumors. Exclusion criteria: Age under eighteen and immunocompromised patients were the main exclusion criteria. Sample preparation and determination: Blood samples obtained from freshly drawn blood were centrifuged and stored at −80 °C. The second blood sample was obtained after seven days or three weeks from the first cycle of chemotherapy. An enzyme-linked immunosorbent assay for the quantification of serum levels of neopterin, NSE, SCCA were performed according to the instructions of the manufacturers. The enzymatic activity of CHT was measured by a fluorometric method using an artificial substrate. Statistical analysis: Statistical analysis was performed in three different ways: for all patients (N = 20), for those who followed a seven-day treatment scheme, and for those who followed a three-week treatment scheme, as patients were stratified by the duration of the treatment. Data analysis was performed using IBM SPSS v. 25.0.

Results. Pre- and post-treatment values of chitotriosidase did not show statistically significant variations. Post-treatment values of NSE were significantly lower compared to pre-treatment values. A similar trend in neopterin levels could be noticed, but the difference was only marginally significant. On the contrary, the variations of circulating SCCA, chitotriosidase, neopterin, before and after treatment, did not reach statistical significance. In all analyzed markers, we did not find any significant difference between patients who followed a seven-day treatment scheme compared to those who followed the three-week treatment scheme. Finally, when we compared post-treatment values of the specific laboratory markers by the type of cancer, we did not find any statistically significant differences.

Conclusion. In patients with lung cancer, serum levels of NSE were significantly decreased after the first chemotherapy cycle compared with pre-treatment values. In addition, the post-treatment values of neopterin were lower as well, but with marginal statistical significance. Conversely, circulating levels of chitotriosidase, SCCA were not significantly modified in response to the first chemotherapy cycle.

Nanomedicine use in gastrointestinal pathology induced by non-steroidal anti-inflammatory drugs

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Introduction. Non-steroidal anti-inflammatory drugs (NSAIDs), which are extremely useful due to their anti-inflammatory and analgesic effects, are accompanied by several drawbacks related to adverse reactions, particularly gastrointestinal ones. The aim of this study was to evaluate the oral administration of iron oxide magnetic nanoparticles loaded with ibuprofen (IMNPs), compared to standard treatment with ibuprofen in the delivery of a higher dose of medication, with good biocompatibility and lower rates of GI adverse effects.

Material and methods. An experimental model was used that included 30 healthy Wistar albino rats, 15 males and 15 females, divided into three equal groups of ten subjects each, who were treated for 10 days, with either sodium chloride saline solution (Group A), or simple ibuprofen (Group B) or IMNPs (Group C). The evaluation of the response involved quantifying oxidative stress in gastric, duodenal, colonic,

splenic, hepatic, and renal tissues by measuring oxidative stress markers and through histological analyses of collected tissues.

Results. In measuring the oxidative stress parameters at the blood level, a favorable antioxidant response was observed with the administration of IMNPs compared to the control group, as well as to the ibuprofen-treated group. By encapsulating ibuprofen in MNPs, a reduction in oxidative stress at the duodenojejunal junction was achieved, along with additional antioxidant action. Furthermore, in the measurement of hepatic transaminases across the three groups, IMNPs reduced the degree of hepatic toxicity, compared to the ibuprofen-treated group with statistically significant differences.

Conclusions. The use of iron oxide magnetic nanoparticles as delivery systems for drug or genetic treatments represents a means to enhance therapeutic response and reduce adverse reactions in the gastrointestinal setting. The generalization of these very promising results can be achieved through future, more heterogeneous and comprehensive studies.

MEDICINE
Medical Specialties

The hidden patient - quality of life and caregiver burden in palliative care

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The primary caregiver is the person who cares for the patient with a progressive chronic disease in the palliative care stage. Caregiving burden is a difficult ‚syndrome' to assess, with multiple responsibilities ultimately causing physical, psycho-emotional distress in the primary caregiver and affecting their social life.

The main objective of the study is to assess the quality of life of the primary caregiver by measuring the burden of caregiving and assessing their depression and anxiety.

The research enrolled caregivers over the age of 18 who gave written consent to participate in the research. The evaluation of the subjects was performed monthly during 3 months using the following instruments: Burden Scale for Family, Hospital Anxiety and Depression Scale and MOS-SF36.

The difference between the mean values of two variables was analyzed by the chi-square test for independent samples. The Mann-Whitney U test and the Kruskal-Wallis test were used to highlight differences between two and three or more variables, respectively.

The burden of care increased statistically significantly during the three months of evolution, being significantly higher in the group of those who cared for patients with non-oncological conditions (p=0.01). They perceive more strongly the deterioration of their health, the reduction of time for themselves, the standard of living, and the abandonment of plans.

Primary caregivers of cancer patients experience anxiety that increases significantly as the disease progresses (p=0.03).

Depression and anxiety are significantly correlated with the degree of burden (p=0.001).

Pain and decreased vitality are present in caregivers of both subgroups.

Social life is similarly affected regardless of the pathology of the patient being cared for.

The main caregiver represents a hidden patient who gradually turns into a real patient prone to somatic and mental ailments.

Assessing caregiver burden can detect decreased quality of life and early symptoms of depression and anxiety.

Pulmonary embolism - a potentially fatal condition associated with psychiatric disorders

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Introduction. Pulmonary embolism represents a serious condition with a potentially fatal evolution. In psychiatric patients this risk of developing a pulmonary embolism is associated with the prescription of antipsychotic drugs.

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Objective. The aim of the study was to explore the association between different psychiatric diagnosis and the complication of developing a pulmonary embolism.

Method. We analyzed the number of all cases of thromboembolism reported in the Psychiatry clinics within SCJU Cluj-Napoca, during the last 10 years. The cases selected for analysis had as a selection criterion the main diagnosis at discharge of a psychiatric type and a secondary diagnosis of pulmonary thromboembolism. The clinical data were taken from the AtlasMed information system.

Results. Several factors that influence the risk of developing a pulmonary embolism have been identified including immobilization, oral contraception, genetics and the prescription of antipsychotic drugs. All of the patients were started on anticoagulation drugs and progressed well.

Conclusion. It can be suggested that the use of antipsychotics, mainly Olanzapine and Risperidone, could determine an additional risk factor for pulmonary embolism in psychiatric patients.

Prevalence of bordereline personality disorder in a clinical population

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Introduction. Borderline personality disorder (BPD) is a serious mental disorder characterized by emotional dysregulation, interpersonal dysfunction, unstable identity, and behavioral impulsivity. The estimated prevalence of BPD in the general U.S. population is between 0.5 % and 5.9 % . Data from European studies reported an estimated the prevalence of borderline personality disorder to be 1.6% in the general population and 20% of the psychiatric inpatient population. BPD is characterized by instability of self-image, interpersonal relationships and affects. Further symptoms include impulsivity, intense anger, feelings of emptiness, strong abandonment fears, suicidal or self-mutilation behavior, and transient stress-related paranoid ideation or severe dissociative symptoms. High rates of suicide are also reported, with at least three-quarters of these individuals attempting suicide and 10 % dying by suicide. Additionally, BPD is associated with high rates of psychiatric comorbidity and treatment utilization, as well as functional impairment. Furthermore, patients with BPD often engage in maladaptive behaviors to cope with negative emotional states. These behaviors can include altered eating behaviors, alcohol or drug use, impulsive spending, reckless driving, risky sexual behavior, and nonsuicidal self-injury

Material and method. We conducted a research using the Emergency Clinical Hospital Cluj-Napoca database from 2022 to 2024 in order to assess the prevalence of BPD and changes in the prevalence in the last 2 years.

Results. Results showed an increase in the number of patients with BPD, with prevalence being higher in female patients. Also, our data revealed a higher frequency of hospital admission for patients diagnosed with BPD.

Conclusions. BPD prevalence shows a rising tendency in the recent years, requiring complex psychiatric and non-psychiatric interventions and also a multimodal therapeutic approach.

Drug use among adolescents - prevention programs

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Introduction. Drug use among adolescents is a significant social and public health issue, impacting young people's psychological and physical development. This paper examines the importance of prevention programs and the effectiveness of various strategies aimed at reducing risky behaviors in adolescents.

Material and methods. The study analyzed specialized literature on drug prevention programs for adolescents, selecting articles from academic sources and government reports. Key strategies used in drug prevention, including educational campaigns, community-level interventions, and family counseling programs, were identified.

Results. Prevention programs focused on education and counseling proved effective in reducing the incidence of drug use among adolescents. Awareness campaigns involving both youth and their families showed positive impacts in increasing awareness of risks. Social skills and peer pressure resistance interventions were essential in reducing risky behaviors.

Conclusions. Drug prevention programs for adolescents are crucial for public health, reducing both substance use prevalence and associated risks. An integrated approach is recommended, combining educational information, family support, and social skills-building activities.

Autoimmune diseases and psychotic disorders

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Introduction. The notion of immunological pathways playing a role in the etiology of a subset of psychotic disorders has received increased interest in the last decades.

Material and methods. In this review we will summarize the epidemiologic evidence on associations between autoimmune diseases and psychosis. Possible mechanisms accountable for the association will be discussed, amongst others the probable role of shared genetic risk factors, the impact of infections on both autoimmunity and the development of psychotic disorders, and the potential role of the microbiome.

Results. Several large-scale epidemiologic studies have found positive associations between autoimmune diseases and psychosis. Particularly, autoimmune diseases as multiple sclerosis and lupus are known to have higher frequencies of neuropsychiatric symptoms, including psychosis, compared to healthy controls. Cross sectional studies have found higher prevalence of psychiatric diagnoses among those with autoimmune diseases, and longitudinal studies have shown bidirectional associations between several autoimmune diseases and increased risks associated with schizophrenia.

Conclusions. In addition to the potential importance of autoimmunity in etiological mechanisms of psychotic disorders, the association also brings important attention to somatic comorbidity in patients with psychotic disorders.

Assessing the inflammatory profile of the negative symptoms in schizophrenia

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Introduction. Consistent but disparate evidence indicates a pro-inflammatory status in schizophrenia (SCZ) patients. A growing tendency in the literature indicates particular associations of these immune perturbations such as peripheral cytokine levels with the negative symptoms (NS), which may highlight a particular immune type for the deficit SCZ subgroups.In this cross-sectional study, we aim to identify distinct SCZ subgroups based on NS scores along with testing for the validity of an inflammatory profile concerning NS subgroups.

Material and methods. A total of 60 SCZ in patients and healthy controls (HCs), with no history of immune disease were included in the study. The peripheral inflammation was assessed by measuring IL-6, IL-10, and TNF-α protein levels from the peripheral blood samples using ELISAs. In parallel,we stratified SCZ subjects based on NS scores using the PANSS and BNSS scales. Two main subgroups emerged 1. Predominant negative symptoms subgroup (PNS) and 2. Non-negative subtype subgroup (nPNS). The protein levels will be compared between the two subgroups and HCs. Further more, them RNA levels of IL-6 and TNF-α will be measured from the peripheral blood samples using quantitative RT-PCR and the correlation coefficient between the cytokine transcript and protein levels and BNSS scores will be tested.

Results. Distinct cytokine levels between the two measurements are expected and we hypothesize higher transcript and protein levels in the blood of PNS subjects, followed by nPNS subjects and HCs. Also, we expect significant correlations between cytokine levels and BNSS symptom domains.

Conclusions. In this study, we aim to assess the association between NS and inflammation as a deconstructing model for distinct endophenotypes in SCZ. BNSS conceptualization of NS might be a “croppingtool” for the deficit of SCZ into homogenous phenotypes that can be easily assessed in terms of biological variables such as cytokine perturbations.

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Alternative DSM-5 model of personality disorders

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Introduction. Authoritative classification systems for psychopathology such as DSM and ICD are shifting toward more dimensional approaches in the area of Personality Disorders. The concept of personality functioning (alternative DSM-5 Model of Personality Disorders-AMPD) combines dimensional assessment with personality traits domains, providing more nuanced view of personality pathology.

Material and methods. In the present paper, we reviewed studies on personality functioning, personality structure, and personality organization with a focus on categorical

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PDs and similarities and differences among the concepts themselves.

Results. The benefits of the alternative model are a greater flexibility and precision (it accommodates a wider range of personality presentations, reducing reliance on rigid categories), dimensional approach (recognizes that personality traits exists on a continuum) and treatment planning (focusing on specific traits and functioning levels can aid in developing personalized treatment plans).

Conclusions. This model represents a hybrid approach that combines dimensional assessment with categorial elements, aimed at capturing the complexity of personality pathology more efectively than the traditional model.

An overview of the students' lifestyle and behavior assessment study

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Introduction. Lifestyle and behaviors are modifiable determinants factors of health status. Their detailed study may contribute to the establishment of algorithms for early risk factors identification, for chronic conditions which may occur later in life. The purpose of this paper was to present an overview of the students' lifestyle and behaviors assessment study, in the tenth year of its implementation.

Material and methods. We carried out a cross-sectional study, repeated in each academic year starting from 2015 until now. Data was collected by an anonymous online questionnaire offered to all students in our university. The questionnaire explores multiple dimensions concerning the current state of the person's characteristics, substance use such as alcohol, smoking, eating disorders, mental health, physical activity and sleep quality. The statistical analysis was performed with Excel and Epi Info software.

Results. Every year the number of participants in the survey was consistently different. The students who filled questionnaires were mostly females (around 80%), in the 2nd and 6th academic study year at the faculty of Medicine. Most students had good considerations about their academic Results, but more than half used different preparation for the purpose of neuroenhancement. Less than a quarter smoke, and rarely drink excessively alcohol or use other recreational substances. Students are concerned about their eating disorders and excessive weight, but they rarely practice sports regularly. Stress is felt by around a third of students, and up to a quarter of them admit to poor sleep quality.

Conclusion. The survey was easily implemented, but the students' interest was heterogeneous, rather skeptical about its usefulness. Further analysis is needed for using the survey in students' health status evaluation and the screening for risk factors that can alter health.

Presentation of patients with NOD2 gene variants - a case series

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Introduction. NOD2 is an intracellular receptor involved in the innate defense against bacteria, which induces an inflammatory response through various pathways, including NF-κB, caspase 1, IL-1, and type 1 interferon (1). Most commonly, mutations in the genes encoding NOD2 are associated with Crohn's disease, Blau syndrome, early-onset sarcoidosis, and Yao syndrome (2).

Objectives. To describe the clinical phenotypes of patients with NOD2 gene variants and symptoms of autoinflammatory diseases, as well as the treatments they received.

Material and methods. Adult patients with NOD2 gene variants were selected from the databases of the authors' institutions, members of the Romanian Autoinflammatory Disease Group (GRAI).

Results. Ten cases were diagnosed (6 females and 4 males), with a mean age of onset of 27.2 years (3-50) and a mean age at molecular diagnosis of 41 years (25-60). Presentations included vasculitis (leukocytoclastic, Behcet's or Behcet-like disease, Cogan syndrome, aortitis) (5/10), Blau syndrome (3/10), Yao syndrome (2/10), relapsing polychondritis, recurrent panniculitis, chronic recurrent multifocal osteitis, undifferentiated spondyloarthritis, juvenile idiopathic arthritis, psoriatic arthritis, sarcoidosis, recurrent serositis, autoimmune hepatitis, or recurrent lower limb edema. Fever was inconsistently present (6/10 patients, brief episodes). Inflammatory bowel disease was excluded in all cases. Most patients had heterozygous variants of uncertain significance (VUS) of the NOD2 gene; only one patient, with Blau syndrome and recurrent granulomatous uveitis and arthritis, carried a pathogenic NOD2 mutation. The most common variant was c.2104C>T (p.Arg704Trp), found in 4 unrelated patients-2 presenting with vasculitis and 2 with Yao syndrome. Treatments, in addition to glucocorticoids and non-steroidal anti-inflammatory drugs, included colchicine, azathioprine, methotrexate, sulfasalazine, or leflunomide.

Conclusion. Patients with NOD2 gene variants and suspected autoinflammatory disease may present with a wide range of clinical manifestations. Even variants of uncertain significance could be relevant in this context, necessitating further genotype-phenotype correlation studies.

The management of antipsychotic induced weight gain, a major risk factor for non-compliance

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Introduction. Obesity and metabolic syndrome are common and serious issues among psychiatric patients prescribed atypical antipsychotics. Weight gain can cause signifficant health complications frequently leads to non-compliance. The goal of the study is to examine potential treatment options for antipsychotic-induced weight gain (AIWG).

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Material and methods. We conducted a thorough review of current literature to identify pharmacological interventions aimed at managing AIWG. The analysis focused on the effectiveness and safety profiles of various drug classes, including antidiabetic agents, antiepileptics, opioid receptor agonists and histamine H1 agonists.

Results. Antidiabetic drugs showed the most promise in addressing AIWG. Specifically, glucagon-like peptide 1 (GLP-1) receptor agonists outperformed traditional options like metformin. The antiepileptic drug topiramate was also linked to significant weight loss, but cognitive side effects may limit its use. Other medications, such as reboxetine, ranitidine, aripiprazole, samidorphan, and betahistine, displayed encouraging results, although further research is necessary for conclusive findings. By contrast, naltrexone-bupropion had notable contraindications that make them less suitable for psychotic patients.

Conclusion. Addressing weight gain related to atypical antipsychotics is vital for improving the health of psychiatric patients. It is important to tailor treatment plans to individual patients, taking into account contraindications and specific needs. Continued research and a good collaboration with different medical specialties, such as Diabetes, nutritional and metabolic diseases, are essential for optimizing management strategies for AIWG and improving patient outcomes.

Metabolomic markers in attention-deficit/hyperactivity disorder (ADHD) among children and adolescents - a systematic review

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Introduction. Research has shown that children and adolescents with ADHD exhibit altered levels of kynurenine pathway metabolites, indicating their potential as biomarkers. However, findings across studies have been inconsistent. This study aims to consolidate existing evidence into a cohesive framework.

Material and methods. A systematic search of the PubMed and Web of Science databases yielded 11 relevant studies.

Results. Reduced levels of 3-hydroxykynurenine, associated with neural maturation, were observed in children and adolescents with ADHD, suggesting a potential delay in brain development. Although some studies reported elevated levels of tryptophan and kynurenine, a biochemical pattern resembling epilepsy, these findings were not consistently replicated. Additionally, kynurenine pathway compounds are closely linked to other metabolic processes implicated in ADHD pathophysiology, such as oxidative stress, amino acid metabolism, and neurotransmitter synthesis. Methodological limitations and considerable variability were noted among the studies reviewed.

Conclusions. While kynurenine pathway metabolites may have clinical relevance, larger studies are essential to reach definitive conclusions.

The utility of blood-based biomarkers in stratifying patients with psychotic disorders

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Introduction. Psychotic disorders have been associated with a pro-inflammatory endophenotype. Blood-based biomarkers are accessible and cost-effective indicators that may be useful for characterizing systemic inflammation and aiding inthe stratification of patients with psychotic disorders.

Material and methods. We aim to retrospectively evaluate several blood-based biomarkers (neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, monocyte-lymphocyte ratio, systemic immune-inflammation index, and systemic inflammation response index) in patients with both non-affective and affective psychoses over a period of five years. We will compare the two groups and analyze the various ratios in relation to the number of prior episodes, the length of hospital stay, and other inflammatory biomarkers, such as C-reactive protein. Additionally, we will evaluate how treatment impacts these ratios throughout the course of the disorder.

Results. We expect to find increased blood-based biomarkers in both first-episode and chronic psychoses. Moreover, we predict that patients with non-affective psychoses will have higher ratios than patients with affective psychoses. Lastly, we expect that patients with high ratios will exhibit more relapses.

Conclusion. We predict that blood-based biomarkers will be accessible and reliable indicatorsfor characterizing the systemic inflammation state in patients with psychotic disorders, aiding intheir stratification.

Guidelines data – are they all we need to control hypertension?

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Introduction. The European Society of Cardiology Guidelines for management of arterial hypertension contains customized recommendations for hypertension treatment, based upon large controlled, randomized studies and reviews that sum up the most compelling evidences. Clinical practice, however, shows that, in spite of many trials and review, almost 55% of patients receiving treatment still have high blood pressure (BP) (systolic BP of at least 140 mmHg and/or diastolic BP of at least 90 mmHg).

Material and methods. A HOTMAN F100 system for hemodynamic monitoring uses the TEB (Thoracic Electrical Bioimpedance) Technology (manufactured by HEMO SAPIENS, INC) was used to evaluate hypertensive patients. One group of patients were monitored before treatment initiation, using medication suggested by the monitoring system, although it wasn't always fully according to the guidelines. Another group of patients was monitored to evaluate the efficacy of treatment initiated irrespective of hemodynamic monitoring; their treatment was changed or tuned according to the hemodynamic monitoring and "virtual therapy".

Results. We present several case studies. For example, P.C. a 42 year-old male

with obesity, dyslipidemia and moderate hypertension (160/100) treated for one month with perindopril 5mg od, presents with fatigue. BP on first monitoring was 140/85 mmHg. The guidelines recommend increasing perindopril dose or adding a second medication (beta-blocker, diuretic, etc.). Patient age and occupational stress would favor the beta-blocker. Hemodynamic monitoring with the HOTMAN system reveals (9:44/03.02.09) a low cardiac output, 87% hypervolemia, 109% hypoinotropy and 84% vasoconstriction. The "virtual therapy" allow us to make the right treatment choice. The beta-blocker would worsen patient's hemodynamic status by worsening inotropism, while the diuretic would produce a 74% hypodynamic status, although reducing hypervolemia. "Virtual therapy" allows us to increase the vasodilator dose.

Conclusion. Hemodynamic monitoring of hypertension using the HOTMAN system provides valuable data for hypertension treatment. Therapeutic recommendation sometimes (apparently) "contradicts" the "best solution" suggested by the guidelines. Selecting and using it allows a quick stabilization of the patient and shortens the initiation (sometimes frustrating, both for the doctor and for the patient) period.

Challenges in the diagnosis and management of biliary atresia in a patient with multiple congenital malformations

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Introduction. Biliary atresia is a severe neonatal disease caused by an inflammatory and fibrotic obliteration of the extrahepatic biliary tree, resulting in cholestasis and progressive hepatic failure. If untreated, progressive liver cirrhosis leads to death by the age of 2 years. Biliary atresia is the most common indication for liver transplantation in children, accounting for about 75% of transplantations in those younger than 2 years.

Case report. We present the case of a 7-month-old infant diagnosed with liver cirrhosis, esophageal atresia, and tracheoesophageal fistula that were surgically treated in the neonatal period, pulmonary necrosis of the superior and middle of the right lung and occipital encephalocele. The patient presented jaundice and cholestasis from the early days of life, which were initially interpreted as caused by the associated digestive pathology and the prolonged parenteral nutrition that was necessary in the first 4 weeks postoperatively. Subsequently, he developed acholic stools, hepatosplenomegaly, and ascites. The laboratory findings showed severe cholestasis, while the abdominal ultrasonography and the liver biopsy confirmed the biliary atresia and liver cirrhosis diagnosis.

Treatment of biliary atresia is mainly surgical. In the first weeks of life, the Kasai operation aims to bypass the obstructed extrahepatic bile ducts and restore the biliary flow. When this procedure fails, or complications associated with biliary cirrhosis appear, liver transplantation is needed.

Conclusions. Early diagnosis of biliary atresia is essential, as increased age at the moment of surgery has a negative impact on the result of the Kasai portoenterostomy. The evaluation of infants with conjugated hyperbilirubinemia must aim to identify possible biliary atresia in order to initiate surgical treatment as soon as possible and postpone the need for liver transplantation.

Five-year multidisciplinary assessment of genetic predisposition in hereditary breast cancer

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Introduction. Breast cancer remains a major health problem being the most common neoplasia, being overtaken in terms of mortality only by lung cancer. An upward trend in the incidence of breast cancer has been shown, with an annual increase of 1-4%. Estimating that by 2050, it will reach 3.2 million annually. The vast majority of forms of breast cancer (80%) are diagnosed sporadically in women without an oncological family history. Approximately 10-15% of cases appear in the context of a hereditary predisposition, the most common secondary to some germline mutations at the level of some genes involved in breast carcinogenesis.

Material and methods. The present study is the largest ever conducted in Romania. We will present the Results of a retrospective, longitudinal, carried out in IOCN Cluj, which includes a group of 150 patients with criteria of eligibility for germline testing in hereditary breast cancer. Molecular analysis (NGS panel 125 genes), performed in within the RSP Regina Maria Central Laboratory, Bucharest, revealed the presence of predisposing defects in 28% of the test patients. There will be a detailed presentation of the characteristics of the identified mutations as well as the associations with the other clinical and paraclinical variables (subtype molecular, oncological AHC, oncological therapy and prophylaxis).

Conclusions. Oncogenetic assement and germline testing have become an indispensable tool in breast cancer management because they allow correct performance of personalized oncological screening, therapy and prophylaxis recommendations.

Mediastinal tumors - differential diagnosis in pediatric respiratory pathology

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Introduction. A good part of the pediatric malignant pathology is associated with mediastinal tumor masses. Diagnosis is often delayed because respiratory symptoms are initially interpreted as infectious pathology, considering the higher prevalence of respiratory infections compared to malignant pathology.

Case series. We present a series of four cases of malignant mediastinal tumors from the Pediatric oncology and hematology unit of the 2nd Pediatric Clinic, where diagnosis and treatment were delayed due to their interpretation as respiratory tract infections. The first case is a 3-year-old boy presented with odinophagia and submandibular swelling. He was treated with anti-inflammatory medication but showed unfavorable evolution, developing marked agitation and shortness of breath, therefore it was interpreted as pleuro-pneumonia, and he was given antibiotics and corticosteroid therapy. The symptoms initially subsided, but after a week without corticosteroids, the symptoms reappeared. A chest imaging was

performed, revealing an enlarged mediastinum with irregular contours. He was referred to our clinic, where he was diagnosed with T-cell acute lymphoblastic leukemia. The second case involves a 1-year-old boy with difficult breathing, productive cough, and fatigue that began three weeks earlier. His family doctor prescribed home treatment for bronchiolitis, but symptoms worsened. He presented to the emergency department, where a chest CT scan showed a giant mediastinal tumor with characteristics of neuroblastoma. The third case is a 6-year-old boy who had been diagnosed with chickenpox six weeks earlier, and afterward, he continued to have a persistent productive cough, night sweats, and a decreased appetite. He was treated for bacterial lung infection, with unfavorable progress. The chest imaging revealed a large tumor in the anterior mediastinum, with vascular invasion and pleural metastasis. Later in our unit, he was diagnosed with non-Hodgkin lymphoma. The final case is a 12-year-old patient with shortness of breath and a productive cough lasting two months, for which he was treated with antibiotics. Over time, he developed supraclavicular and lateral cervical adenopathy, which led to a chest X-ray showing a giant mediastinal mass. In our clinic, a lymph node biopsy confirmed the diagnosis of thymic carcinoma.

Due to the high frequency of respiratory infections in the pediatric population, respiratory symptoms are initially interpreted in an infectious context. Imaging studies that could rule out malignant pathology are often delayed due to the risks of radiation exposure and the need for sedation at young ages. Furthermore, corticosteroid treatment in respiratory diseases temporarily alleviates symptoms, also delaying diagnosis and treatment.

Conclusion. Persistent respiratory symptoms despite anti-infective treatment should raise suspicion of a compressive tumor pathology, for which imaging investigations are essential.

Multisystem hemangiomatosis in infancy: a case of cutaneous, hepatic, and splenic involvement with complex management challenges

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Background. Hemangiomatosis is a rare condition characterized by the presence of multiple benign vascular tumors, involving various organs, including the skin, liver, spleen and other tissues. It can lead to complications depending on the location and size of the lesions.

Case-report. We present the case of a newborn with hemangiomas scattered across the body and on the oral mucosa. Diagnostic tests confirmed cutaneous, hepatic, and splenic hemangiomatosis with secondary cholestasis . Ultrasound evaluations revealed slightly dilated hepatic veins and minor mitral, aortic, and tricuspid insufficiencies. Treatment with propranolol was initiated at an increasing dose up to 2.6 mg/kg/day, along with prednisone up to 2 mg/kg/day, a decision made in collaboration with the pediatric hematology experts.

The evolution was slowly favorable, no new hemangiomas appeared and those on the face and limbs were largely in remission. The splenic and hepatic hemangiomas regressed more slowly than the cutaneous ones, but their size reduction and the improvement of cholestasis syndrome were consistent. Due to significant iatrogenic Cushing's syndrome, the predisone doses were progressively reduced until stopping, the patient is currently only under treatment with propranolol.

Conclusions. This case of multiorgan hemangiomatosis is notable for several reasons. The presence of multiple disseminated hemangiomas is rare and associated with significant risks of complications, including cholestasis and minor cardiac valvular insufficiencies. The patient exhibited a slow but favorable response to a combination of propranolol and prednisone, highlighting the need for a tailored therapeutic approach. The slower regression of hepatic and splenic hemangiomas compared to cutaneous lesions underscores the challenges in treating visceral hemangiomas, necessitating ongoing monitoring and adjustments in therapy.

Sudden cardiac death in a patient with Steinert disease - a case report

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We present the case of a 55-year-old female patient admitted to our department after being successfully resuscitated from a cardiac arrest. Our patient had already been diagnosed with Steinert Disease, the most common form of myotonic dystrophy in adults. Because the left ventricular ejection fraction was severely decreased after the resuscitation without an obvious explanation, the case interpretation was of Tako-Tsobo cardiomyopathy. Three months later, echicardiographic reevaluation showed almost complete recovery of the left ventricular systolic function. The patient had an indication for secondary prevention of sudden cardiac death considering the history of torsade-du-point that caused the cardiac arrest and also the presence of a prolonged QT interval that persisted on repeated ECG recordings and holter ECG monitoring. Patients with Steinert Disease frequently suffer for cardiac complications, including atrioventricular conduction disturbances that require permanent cardiac pacing. For all the above-mentioned reasons, we decided to Implant a dual chamber cardiac defibrillator. Although the short and mid term evolution of our patient was favorable, their life expectancy is decreased.

Breaking therapeutic inertia with PCSK9 inhibitor and sRNA in familial hypercholesterolemia: case report

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Background. Therapeutic inertia is an important barrier limiting optimal care in patients with familial hypercholesterolemia. New lipid lowering medications are available, but the injectable administration and prescription rules might be challenging.

Case description. 55 years old male attended our outpatient clinic at the Centre of Diabetes, Nutrition and Metabolic Diseases, Emergency Clinical County Hospital of Cluj-Napoca, Romania. The patient was referred by the family physician because of persistently high LDL-cholesterol levels and statin intolerance. The patient has a history

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of elevated transaminases (>100 UI/L) after treatment with Atorvastatin and Rosuvastatin which lead to statins discontinuation. LDL-cholesterol of 226 mg/dl (total-cholesterol 332 mg/dl) was measured starting 5 years ago, in the absence of secondary causes of hypercholesterolemia. The patient has no history of atherosclerotic cardiovascular disease and had a high cardiovascular risk according to 2021 recommendation guidelines of the European Society of Cardiology for cardiovascular prevention, with a target of LDL-cholesterol<70 mg/dL and a decrease of at least 50%. Treatment with Alirocumab, a proprotein convertase subtilisin–kexin type 9 inhibitor (PCSK9 inhibitor), in the dose of 75 mg administered subcutaneously every 2 weeks was initiated in June 2022 for achieving LDL-cholesterol target. After 6 months of treatment, LDL-cholesterol decreased to 56 mg/dL, with no adverse reactions. The patient was switched on Inclisiran, PCSK9-targeting small interfering RNA (siRNA), in the dose of 248 mg administered subcutaneously every 6 months in June 2024. The reason for lipid-lowering drug change was related to easier prescription and administration which can result in better long term medication adherence. After 3 months, LDL-cholesterol was 79 mg/dL and the second Inclisiran administration was performed, with no adverse reaction.

Conclusion. Our clinical case report describes a patient with high LDL-cholesterol left untreated because of statin intolerance, in whom therapeutic inertia maintained a high cardiovascular risk profile. Initiation of new injectable lipid-lowering drugs, PCSK9 inhibitor followed by siRNA, led to significant decrease in LDL-cholesterol.

Extreme prematurity: where are we now? The experience of a 3rd degree center in Romania

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Introduction. Alfred Rusescu INSMC report 2021: 0.21% of live births had weights between 500-999 g. The population deficit increased, reaching -6% in 1st semester of 2022.

Aim. The authors want to asses the incidence of premature babies under 28 weeks of gestation in Cluj-Napoca, in a 3rd level unit. We evaluated the prognostic elements of premature babies based on determined maternal factors, type of birth and complications.

Material and methods. We conducted a retrospective analytical study on 108 patients ≤28 weeks of gestation, hospitalized in Neonatology I, County Emergency Clinical Hospital Cluj-Napoca, during January 2020 - December 2023. Group was divided in 2 subgroups: delivered by caesarean section or by vaginal delivery. We performed analysis of the clinical medical records of pregnant women and premature babies. All patients had signed the informed consent.

Results. The incidence of extreme prematurity was increasing in study period from 1,5% to 2,95% in 2023. Premature birth prevention therapies were complex: cerclage in 6.5%, oral or IV magnesium administration, progesterone, lipoic acid and probiotics in 100% of the mothers. SA was significantly lower in vaginal delivery group (p=0.03). The severity of respiratory distress syndrome (RDS) was significantly lower in C-section group (0.001). Persistence of ductus arteriosus (PDA) had an incidence of 77.4%. The chance of PDA is 5.16 times higher in C-section group. NEC had significantly lower incidence in C-section group (p=0.002). The incidence of ROP was 10.3%. Group C- section had a significantly lower mortality 21.7% compared to vaginal delivery 26.11% (p=0.045).

Conclusions. Risk factor significantly involved in death - the cerclage (p=0.04). RDS had significantly lower severity in the C-section group. The chance of developing PDA is 5.16 times higher in C-section group. ROP had smaller incidence in C-section group. The survival was significantly higher in those born by C-section: 78.3% vs. 72.89%.

Atrial fibrillation recurrence after accessory pathways ablation in Wolff-Parkinson-White Syndrome

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Introduction. Wolff Parkinson White Syndrome (WPW) is considered to be a congenital abnormality that involves the presence of abnormal electrical conductive circuits between the atria and ventricles. The disorder includes accessory electrical pathways that bypass the AV node.

Atrial fibrillation (AF) can develop in up to one third of patients with WPW syndrome and can be potentially life threatening if rapid ventricular rate develops as a result of antegrade conduction over accessory pathway. Mechanisms postulated are spontaneous degeneration of AVRT to AF, intrinsic atrial muscle vulnerability and effect of accessory pathway (AP) on atrial musculature.

Episodes of atrial fibrillation occur in patients with WPW syndrome but frequently disappear after successful radiofrequency ablation. Some studies concluded that successful catheter ablation of accessory pathways prevents further recurrence of AF in 91% of patients.

Our study evaluated incidence, clinical features, electrophysiological characteristics and atrial fibrillation recurrence after successful catheter of accessory pathways compared to patients in whom catheter ablation failed to eliminate the accessory pathway.

Material and methods. This is a retrospective observational study. Data were collected retrospectively over last 10 year. We included in the study only the patients who presented with WPW syndrome or ventricular preexcitation on surface ECG, in whom complete required clinical and electrophysiological study data was available were included in the study. Eight French 4 mm tip ablation catheter was used for ablation. Criteria for successful ablation were loss of preexcitation on atrial stimulation protocol, decremental VA conduction through AV node during ventricular pacing and non-induction of tachycardia. Electrophysiological features like anterograde conduction, retrograde conduction, localization of pathway and outcomes of ablation were analysed.

The patients were divided into 2 groups, the first group with successful catheter ablation of accessory pathway and the second group that did not fulfill the criteria for successful ablation. The patients were monitored after the procedure with 24 hours Holter after the procedure and clinically for the rest of the motorization period. AL the clinical arrhythmias documented as atrial fibrillation were noted down in the patient's history. Mean duration of follow up was 3 ± 2 years.

Results. Out of 35 patients of WPW syndrome, 20 had successful ablation of accessory pathways and the rest of 15 did not fulfill the criteria for successful ablation. In the group of patients with a successful catheter ablation, only one patient experienced symptomatic atrial fibrillation that had to be medically converted. In the second group out of 15 patient that still presented the accessory pathways 10 experienced symptomatic paroxysmal or persistent atrial fibrillation with a P value of 0.04.

Conclusion. Our study concluded that successful catheter ablation of accessory pathways prevents further recurrence of AF. Recurrence rates for AF after successful ablation of WPW vary, but studies suggest they can be around 10-30%, depending on individual patient factors and the thoroughness of the procedure. In case of recurrence, further evaluation and a potential repeat ablation may be considered, and ongoing monitoring by a healthcare provider is essential to manage symptoms and maintain heart health and also to prevent an unnecessary atrial fibrillation ablation.

The last days of life - needs, barriers, approach

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Introduction. Palliative care is essential for patients with advanced cancer, with the aim to improve quality of life.

Case report. We present the case of LV, a 70-year-old non-smoking former teacher diagnosed with stage IV bronchopulmonary cancer, radio-chemotherapy treated, associated with grade II post-radiotherapy esophagitis and a history of operated abdominal melanoma (2014). She was admitted to the Cluj-Napoca Pneumology Clinic with the clinical and imaging picture of bronchopneumonia. On admission, the patient reported severe dyspnea at rest (VAS=7), cough with mucopurulent sputum, generalized pain, dysphagia, anorexia, significant weight loss, marked fatigue (ESAS=9), and anxiety. The ECOG was 3. Nutritional difficulties secondary to the post-radiotherapy esophagitis were initially conservatively addressed with a pureed diet allowing the patient to eat independently. As fatigue, dysphagia, and the overall health status worsened, the placement of a nasogastric tube was needed. Dyspnea progressively worsened, requiring constant titration of oxygen therapy and the addition of low doses of opioids alongside inhaled bronchodilators and systemic corticotherapy. Pain and fatigue were initially managed with non-opioid analgesics and adjuvant co-analgesics. Controlling psycho-emotional symptoms was a real challenge, but the presence of the family (especially the husband), along with the psychological and spiritual counseling, had a favorable impact on anxiety, dyspnea, and the patient's overall suffering. In the last hours of life, the focus of palliative care was not only on symptom control, but also on the patient comfort, on family communication and support. After the patient's death, in the bereavement period, close contact with the family was maintained.

Conclusions. Recognizing the final days/hours of life is an important clinical skill, as many patients die in the hospital with uncontrolled symptoms and unfulfilled emotional and spiritual needs.

Evaluation of the vascular proliferation factor (VEGF) in the pathology of premature with a gestation age under 33 weeks

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Aim and objectives. In vasculogenesis and angiogenesis, VEGF plays an important but not yet fully elucidated role in the neonatal period. The study aims to evaluate the relationship between the complications of prematurity and the serum VEGF value at birth, 7 days postnatally, and at one month of age.

Material and method. The study was conducted in the Neonatal Intensive Care Unit at the Cluj-Napoca County Emergency Clinical Hospital from April 2022- December 2023. Inclusion criteria were gestational age under 33 weeks and signing the informed consent.

Results. Thirty-three premature infants with an average gestational age of 29.24±0.75 weeks and an average weight of 1327.96±106.8 grams were included in the study. The value of VEGF at birth was 206.41±21.4 pg/ml, with an increase at 7 days of life to 390.6 ± 14.1 pg/ml and to 406.32±23.4 pg/ml at the age of 1 month, with significant differences both at 7 days and at 1-month-old ($p<0.05$). Oxygen requirement (FiO2) was 40.46±4.1% at birth, decreasing to 26.69 ± 3.1% at 7 days and to 33.60 ± 1.3% at one month. We obtained a significant correlation between FiO2 on the first day of life and the VEGF value at 1 month of age ($p=0.03$). We obtained a significant correlation between the value of VEGF at birth and retinopathy of prematurity ($p=0.04$).

Conclusions. The serum level of VEGF increases in direct proportion to postnatal age. Oxygen requirement in the preterm neonate is higher at birth and at 1 month of age compared to FiO2 at 7 days of life. Increased FiO2 at birth correlates with VEGF at 1 month. The level of VEGF at birth correlates with the risk of developing retinopathy of prematurity.

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Challenges in the diagnosis and management of bacterial endocarditis

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Background. Bacterial endocarditis is a rare but potentially severe infection involving the endocardium or valves. Early diagnosis and prompt treatment are important, and in some cases, extracardiac manifestations may also occur. Rarely bacterial endocarditis occurs in children without known chronic conditions or congenital heart disease, and they may have a worse prognosis.

Case report. We present the case of a 17-year-old female admitted to our hospital for fever, dizziness, and myalgia. Clinically, she exhibits nodular skin lesions of varying

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sizes, erythematous and painful on palpation, and a grade II systolic murmur. Laboratory tests revealed a marked inflammatory syndrome and two blood cultures were positive for Staphylococcus aureus infection.

Cerebral MRI revealed infectious foci in the fovea and septic emboli. We had one major criterion (positive blood cultures) and three minor criteria (fever, septic cerebral emboli, and Roth spots) for bacterial endocarditis but the first echocardiogram showed no significant changes. Treatment with high doses of Vancomycin and Meropenem was administered for 6 weeks. Three weeks after the start of therapy, the control echocardiography revealed the presence of a mitral valve abscess. Evolution was favourable after antibiotherapy, with the resolution of cutaneous nodules and brain lesions. The last echocardiography showed important mitral insufficiency which will require surgical treatment.

Conclusions. The particularity of this case is the onset of mitral valve involvement approximately three weeks after initiating antibiotic therapy in a previously healthy adolescent, without any other risk factors.

BASM syndrome - a rare form of biliary atresia

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Background. Biliary atresia is a life-limiting fibro-obliterative disorder of the bile ducts that can advance to end-stage liver disease. Biliary atresia with splenic malformation syndrome (BASM) designates the association of biliary atresia and splenic abnormalities (mainly polysplenia and, less frequently, asplenia or double spleen). Cardiac defect, situs inversus, and a preduodenal portal vein can also be present. It represents the embryonal or syndromic form of biliary atresia.

Case report. We present the case of a newborn patient who presented jaundice, pale stools, and dark urine early postnatally, with conjugated hyperbilirubinemia, whereas complex cardiac abnormalities were diagnosed prenatally. Besides jaundice, the physical examination showed dysmorphic facial features (broad nasal root, low-set ears, and hypertelorism), hepatomegaly, and splenomegaly. CT angiography described the presence of symmetric hepatic tissue on both sides of the spine, stomach located on the right side of the spine, and polysplenia situated in the right hypochondrium. Echocardiography revealed complex cardiac malformation. Intraoperatively, at the age of 3 weeks, heterotaxy was described; the liver was cirrhotic, the gallbladder was hypoplasic, and the common hepatic, right, and left hepatic ducts were atretic. Thus the Kasai portoenterostomy was performed. Postoperative, the patient experienced an episode of acute cholangitis. The rest of the recovery was uneventful. The stools gradually became colored, and the liver function improved. She is currently on regular follow-up.

Conclusions. BASM syndrome is a rare form of biliary atresia associated with complex anomalies. The syndrome can lead to end-stage cirrhosis and liver failure if left untreated; therefore, timely Kasai portoenterostomy is considered the standard treatment. Early diagnosis and treatment are essential in the management of these cases. Moreover, the patients need careful follow-up.

Evaluation of the efficacy of recombinant human growth hormone treatment in patients with pituitary dwarfism

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Introduction. Pituitary dwarfism (PD) is a rare endocrine condition that affects 1 in 4,000 to 10,000 individuals and leads to proportionate short stature. The etiology of PD includes genetic or acquired causes (hypothalamic-pituitary tumors, brain trauma, pituitary surgery/radiotherapy, etc). PD is treatable with recombinant human growth hormone (rhGH) therapy.

Material and methods. We conducted a retrospective case-control study over a 5-year period (2019-2023) within the Endocrinology Clinic Cluj-Napoca, in which we included 36 pediatric patients with PD (group A) versus 53 patients with short stature due to other causes (e.g., Turner syndrome and idiopathic dwarfism) (group B). All patients received treatment with rhGH, their height being evaluated after 6 and 12 months from the initiation of therapy.

Results. Group A (29 boys, 7 girls, median age of 11 years and 3 months) presented a median height of 125.1 cm (-2.62 SD) versus group B (24 boys, 29 girls, median age of 12 years) which presented a median height of 130 cm (-3.13 SD) ($p>0.05$). The delayed bone age in group A was 2 years and 4 months compared to 1 year and 8 months in group B ($p<0.05$). The IGF-1 level was significantly lower in group A (98.8 ng/ml) compared to group B (189.3 ng/ml) ($p<0.05$). RhGH therapy determined in group A an increase in height from -2.62 SD to -2.35 SD at 6 months ($p<0.05$) and to -2.02 SD at 12 months ($p<0.05$). Treatment with rhGH led to an increase in height in group B from -3.13 SD to -2.84 SD at 6 months ($p<0.05$) and to -2.6 SD at 12 months ($p<0.05$). There was no statistically significant difference between the height velocity in the two groups after 12 months of rhGH treatment (4.3±1.6 cm, 0.60 SD in group A versus 4.1±1.7 cm, 0.53 SD in group B; $p>0.05$).

Conclusion. RhGH treatment not only improves short stature caused by PD but also enhances height in cases of short stature due to other endocrine and non-endocrine causes.

Abnormal dexamethasone suppression test in a patient undergoing chronic treatment with rifampicin for ulcerative cellulitis of the left calf

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Introduction. The dexamethasone suppression test (DST) is one of the best diagnostic tools for Cushing's syndrome (CS). False-positive Results of the DST can be caused by various factors such as alcohol withdrawal, stress, weight loss, and certain drugs (carbamazepine, phenobarbital, phenytoin, and rifampicin) which induce CYP3A4 and increase the hepatic clearance of dexamethasone.

Case report. The 54-year-old female patient known with hypertension, grade 3 obesity and T12 compression fracture was referred to the Endocrinology Department with suspected CS, presenting unsuppressed cortisol levels after the overnight DST (11.3

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mcg/dl and 11.6 mcg/dl; normal values <1.8 mcg/dl). A year ago, the patient developed ulcerative cellulitis of the left calf, for which she has been on continuous antibiotic treatment with various preparations (currently under therapy with rifampicin 600 mg/day for approximately 7 months). She also has subtalar dislocation with extensive erosions at the fibular, calcaneocuboid, and talonavicular levels, partial fibrillar tears of the left long and short fibular tendons, left flexor hallucis tenosynovitis, and left ankle osteoarthritis. The physical examination revealed grade 3 obesity (BMI=41.91 kg/m²), a „moon face" appearance, erythema and edema of the skin on the left calf associated with an ulcerated area, the left ankle with advanced valgus deformity, BP=152/87 mmHg. The hormonal profile revealed normal values for: basal serum cortisol (7.47 mcg/dl), ACTH (24.4 pg/ml), midnight plasma cortisol (3.4 mcg/dl), and free urinary cortisol/24 h (49.3 mcg/24 h); however, there was unsuppressed cortisol after the low-DST (7.31 mcg/dl) interpreted as a false-positive result in the context of treatment with rifampicin. The pituitary MRI and abdominal CT scan did not describe any pituitary lesions or tumors/hyperplasia of the adrenal glands.

Conclusion. The diagnosis of CS based on DST can be very misleading in patients treated with rifampicin.

Technology and innovation in psychiatry: diagnosis and treatment

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Introduction. Technology is revolutionizing psychiatry, offering new methods of diagnosis and treatment. AI, VR, wearable, mobile apps are just some examples of the evolving technology used nowadays in medical setting. Benefits include increased accessibility, customization and continuous monitoring. Challenges include data privacy and uneven access.

Material and methods. A literature review regarding the technological innovations in psychiatry and their benefits and challenges will be presented.

Results. AI analyzes complex data to identify risks, VR simulates anxious situations, and wearables monitor the condition of patients. rTMS and TEC are innovative therapies, and mobile apps provide accessibility to treatment.

Conclusion. Technology has the potential to significantly improve mental health care.

A rare and unusual cause of ischemic stroke: kinking of the internal carotid artery

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Introduction. Kinking or tortuosity of the internal carotid artery (ICA) is associated with an increased risk of stroke, though the mechanism and risk magnitude can vary based on several factors, including the severity of the kinking, patient age, and presence of other

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comorbidities. Cervical arterial kinking is relatively common, especially among older adults, with a prevalence ranging from 22% to 58%, as reported in past studies.

Material and methods. A 58-year-old male patient, smoker, with no significant medical history, presented to our neurological department for multiple episodes of reduced muscle strength on the right side of the body, sensory impairments on the same side, and right-sided facial asymmetry. The symptoms had a sudden onset, lasting approximately 10-15 minutes, and fully resolved afterwards. At the time of the consultation, NIHSS score was 0 points. After a while, the neurological examination highlighted permanent right central facial paresis, hemiplegia, muscle hypotonia, positive Babinski sign and exteroceptive hypoesthesia on the right side of the body. For that, a CT-Angiography of the head and neck was performed in the ICU, which didn't reveal areas of acute infarction at the time of examination (ASPECTS -10). Considering the severe symptomatology, it was decided to start intravenous thrombolysis. The second CT-Angiography after 24h revealed a subcortical lesion in the right anterior frontal region and left capsulo-lenticular hypodense lesion. The cardiology consultation, including echocardiography, transesophageal echocardiography and ECG-Holter for 48h, did not reveal any significant valvulopathies, intracardiac masses, embolic sources, or significant arithmia, and the carotid Doppler ultrasound showed non-significant carotid atherosclerosis. Additionally, we indicated a MR-Angiography of the brain and supra-aortic arteries with contrast which revealed the acute ischemic stroke in the left capsulo-lenticular region, chronic ischemic microangiopathy, filling defect in the V4 segment of the right vertebral artery, with maintained distal patency and arterial kinking in the C1 segment on the left side. After many laboratory tests, we found a newly diagnosed uncontrolled diabetes mellitus type II, newly diagnosed mixed dyslipidemia and we excluded multiple other causes that could have been involved in the occurrence of the ischemic stroke.

Conclusions. In summary, ICA kinking is associated with increased stroke risk, primarily due to its effects on hemodynamics and predisposition to vascular complications. The risk is compounded in the presence of other cardiovascular risk factors, also the severity of the kink can influence the likelihood of stroke or TIA.

Emergency medicine at 30 years of existence - the current perspective of professionals in the field, a bridge between human resources and future management

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Introduction. Emergency Medicine is a young specialty and according to legislation, specialist physicians in emergency, intensive care and pediatrician may practice in the Emergency Department. The actual data estimate a major shortage of emergency physicians (ED doctors) at country level of 35%. The active medical staff must compensate for the lack of human resources. Starting from these premises, the objectives were to identify what is the opinion of professionals in the field and to identify the precipitating factors that can lead to abandoning the specialty.

Material and methods. This observational study was based on the opinion questionnaire and evaluated the answers of 577 participants, nurses and doctors. Statistical analysis was performed using MedCalc®Statistical Software version 22.021. P <0.05 was

considered statistically significant.

Results. The average age of the respondents was 40.06 years. The nurses were part of professional category with the highest managerial support ($p<0.001$). ED doctors had the highest non-participation in working groups for procedures/protocols/guidelines ($p<0.001$). Intensive care and ED doctors represented the majority of respondents where the employer did not provide them with the resources to overcome conflict situations ($p<0.001$). Difficult collaboration with colleagues, lack of respect, appreciation and managerial support, overwork were the answers that motivated disappointment for ED doctors and report practicing defensive medicine, disregarding the specialty in terms of education and lack of work protocols. Psycho-emotional, physical overwork at work ($p<0.001$), supports professional reorientation for 26.0% of ED and intensive doctors.

Conclusions. The study highlights 4 ideas which represent the pillars of the reconsolidation of a perspective healthcare system: development of procedures/protocols; managerial reorganization; identification of new strategies to restore the trust of the medical staff in the system and academic development.

Effects of treadmill and ground walk training on improving gait in Parkinson's disease

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Introduction. Parkinson's disease is a common neurodegenerative disorder caused by the loss of dopaminergic neurons, the most disabling symptoms being the gait disturbances. Gait recovery in these patients is complex and there is no standardised rehabilitation program up to now. The aim of this study was to compare the effects of treadmill training (TT) and ground walk training (GWT) programs on improving gait in Parkinson's disease.

Material and methods. 32 patients with Parkinson's disease stages I-III (age between 56 and 77 years, 10 women and 22 men) were included in a prospective randomized clinical trial. Patients were randomly assigned to TT group (16 patients) or to GWT group (16 patients). Each type of rehabilitation program was applied for 30 minutes / day, 5 days / week, for 2 weeks. timed-up-and-go (TUG). Gait was assessed on the first and on the last day of by the timed up-and-go (TUG) test.

Results. After the rehabilitation programme, gait significantly improved in TT group (TUG decreased from 18.1 s to 14.4 s, $p<0.05$), but not in GWT group (TUG decresed from 23.8 s to 22.9 s, $p>0.05$).

Conclusion. Treadmill training could represent an effective rehabilitation method for improving gait in Parkinson's disease patients.

Benefits of blood flow restriction in athletes with supraspinatus tendinitis

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Introduction. Blood Flow Restriction (BFR) is a training and rehabilitation technique consisting in compressing one limb to reduce venous (but not arterial) blood flow to the muscles during exercise. The purpose of this technique is to induce hypoxia and, subsequently, metabolite accumulation in the muscles, leading to increase in muscle mass and strength at lower exercise intensity than typically required. The aim of this study was, therefore, to prove the advantages of BFR over the classical kinesitherapy (KT) techniques in athletes with supraspinatus tendinitis.

Material and methods. 60 patients with supraspinatus tendinitis (age between 19 and 32 years, 19 women and 11 men) participated in this prospective randomized clinical trial. Patients were assigned to BFR group (n=30) or to KY group (n=30). Study participants received 18 sessions of BFR or KT therapy, 3 days / week, for 6 weeks. All patients were assessed on the first and on the last day of treatment, by: visual analogue scale (VAS) for pain, manual muscle testing (MMT), Shoulder Pain and Disability Index (SPADI) 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 7.1 ± 1.2 to 1.0 ± 0.7, $p<0.05$ in BFR group, and from 6.9 ± 1.5 to 3.1 ± 1.7, $p<0.05$ in KT group), abductor muscle strength (MMT increased from 3.6 ± 1.7 to 4.73 ± 1.3, $p<0.05$ in BFR group, and from 3.47 ± 1.3 to 3.93 ± 1.2, $p<0.05$ in KT group), function (SPADI decreased from 70.2 ± 4.8 to 11.9 ± 1.6, $p<0.05$ in BFR group, and from 68.5 ± 6.8 to 26.1 ± 2.4, $p<0.05$ in KT group). No significant difference was found between the final Results of the 2 groups ($p>0.05$) in muscle strength, although pain and function improved significantly better in the BFR group.

Conclusion. Both BFR and classical KT were effective in the rehabilitation of the athletes with supraspinatus tendinitis. Nevertheless, BFR supplementarily relieved pain and improved function, representing a promising therapeutic option in these patients.

A rare case report of spinal cord ependymoma

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Introduction. Spinal cord ependymomas are rare tumors that are usually low-grade. Patients generally present with non-specific symptoms, progressive over a period of several months or several years. In rare cases, patients may present with acute-onset symptoms if intratumoral haemorrhage occurs. Ependymomas account for about 1.9% of primary tumors of the central nervous system. It usually occurs in the ventricular system and spinal canal, but can also develop intraparenchymal and paraventricular systems. In pediatric age, ependymomas develop predominantly intracranially, and the location at the spinal level is more prevalent in adulthood. The male sex has a slightly increased prevalence. The 2021 WHO classification has reclassified ependymal tumors according to their location and methylation profiles.

Material and methods. A 52-year-old man was referred to our service for motor deficit progressively installed in the lower limbs and sphincter incontinence. The MRI examination revealed a spindle-shaped intramedullary lesion, well defined, at the level of D8-D9, intensely gadophilic, which occupies almost the entire spinal cord. Neurosurgery was performed, with laminectomy and macroscopic ablation of the dorsal intramedullary tumor formation. Histopathological examination was suggestive of ependymoma. Post-surgery, the patient's sphincter deficiency and incontinence persisted, with no favorable evolution at 6 months post-intervention.

Conclusion. Surgical resection is the first therapeutic measure, but adjuvant radiotherapy can be used. Chemotherapy is usually left as a life-saving therapy in recurrent cases, but the result is mostly modest.

Negative symptoms of schizophrenia - treatment options

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Introduction. Schizophrenia is a severe psychiatric disorder affecting approximately 1% of the global population. Diagnosis typically occurs through the identification of positive symptoms, which are most markedly manifest at the disease onset. While psychopharmacology offers various treatment options, many pharmacological agents can exacerbate negative and cognitive symptoms that often persist throughout a patient's life. Notably, approximately 60% of patients experience negative symptoms such as avolition, anhedonia, alogia, social withdrawal, and affective flattening. This study aims to explore effective contemporary treatment methods for alleviating these negative symptoms.

Material and methods. A systematic review was conducted using the PubMed and Embase databases, focusing on literature published within the past decade.

Results. The review revealed several key therapeutic approaches, including atypical antipsychotics (Aripiprazole, Cariprazine, Amisulpride), antidepressants (SSRIs, Mirtazapine), glutamatergic compounds (Glycine, D-Serine, D-Cycloserine), dopaminergic agonists (Selegiline, Modafinil), and acetylcholinesterase inhibitors (Donepezil). Psychotherapeutic modalities, both individual and group, along with psychosocial therapies (such as art therapy, occupational therapy, and family therapy) and lifestyle modifications, play a significant role in improving negative symptoms.

Conclusions. There remains a lack of consensus in the literature regarding the most effective therapeutic interventions for negative symptoms of schizophrenia. Given the high prevalence and substantial impact on patients' quality of life, further investigation into this subject is critical to identify optimal treatment strategies that can enhance patient well-being and promote a life closer to normalcy.

Serous ovarian cystadenoma in a patient with secondary biliary cirrhosis – case report

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Background. Secondary biliary cirrhosis is a particular form of liver cirrhosis that develops secondary to chronic inflammation caused by obstruction or narrowing of the extrahepatic bile ducts. Over time, periportal fibrosis leads to scarring and, ultimately, cirrhosis. Some patients may also present with associated comorbidities that may have potential malignant characteristics.

Case presentation. We present the case of a 13-year-old female patient with known secondary biliary cirrhosis, choledochal cyst, and multiple obstructive gallstones, surgically treated, who has been periodically monitored in our clinic for supportive care. She presented with an increase in abdominal girth over the past two weeks, abdominal pain, early satiety, constipation, and dysuria. Clinically, the patient was in a generally affected state, with a distended, firm, non-depressible abdomen, insensitive to palpation, and paraclinically, with signs of worsening cholestasis and a normal urinalysis. An abdominal ultrasound revealed a right ovarian tumor and substantial ascites. Subsequent MRI identified an exophytic mass with solid papillary projections, diffusion restriction, and intense contrast uptake in the right ovary, suggestive of a borderline serous cystadenoma. Surgical intervention was performed, including excision of the right ovarian tumor and partial right oophorectomy, and histopathological analysis confirmed the diagnosis. The patient was subsequently transferred to the Institute of Oncology for further treatment and continues to return to our clinic for periodic evaluations concerning secondary biliary cirrhosis, with a favorable evolution to date.

Conclusions. This case was chosen due to the complexity involved in managing these patients: on the one hand, the challenge of addressing secondary biliary cirrhosis and its potential long-term complications, and on the other, the presence of a tumor, which, despite its benign nature, may follow an unfavorable course. Furthermore, the potential malignancy associated with secondary biliary cirrhosis in pediatric patients calls for a multidisciplinary approach, both in terms of the therapeutic plan and quality of life considerations.

Understanding stroke mimics - recognizing the signs

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Introduction. Ischemic stroke is the leading cause of disability and one of the primary causes of death. The effectiveness of revascularization treatments, such as intravenous thrombolysis, is time-dependent, making it crucial to reduce the door-to-needle time (from patient arrival to treatment administration). However, the increased accessibility to thrombolysis and shortened intervention times have led to incorrect treatment of non-stroke patients. The term „stroke mimics" encompasses various conditions that present with similar symptoms but are not due to ischemic stroke. Studies indicate that approximately one-third of patients admitted for stroke evaluation might be experiencing mimics, with findings from a review of over 60,000 patients showing about 25% of admissions could be unnecessary.

Material and methods. The PubMed online medical database was used to extract the necessary data regarding the topic of this poster, alongside a concrete clinical case that was encountered during common medical practice in our department. No real name was used in the presentation so as to offer anonymity to the person in case.

Results. This poster aimed to identify the most common medical conditions that are commonly mistaken in the ER as a stroke. Peripheral vestibular disfunction being the leading cause of a stroke misdiagnosis, followed by seizures, functional disorders, migraines and other causes.

Conclusion. In case of suspicion of an acute stroke, the history of the patient and a comprehensive clinical examination is critical to make the differential diagnosis between an actual stroke and a stroke mimic, which will later inform the establishment of management plan and achieve the best of outcomes.

Capillaroscopy – a handy tool for identifying rare connective tissue diseases

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Introduction. The use of capillaroscopy in the screening and monitoring of inflammatory rheumatic diseases is gaining more ground. Controversies regarding the diagnosis of mixed connective tissue disease remain a current issue, and difficulties in clearly defining the onset and progression of this pathology persist.

Objectives. The research aims to evaluate the role of capillaroscopy in the early identification of certain disease phenotypes, as well as in the subsequent monitoring of the disease and organ involvement.

Material and methods. The study conducted at the Rheumatology Clinic in Cluj-Napoca from May 1, 2023, to May 31, 2024 is an observational, retrospective study that included 300 patients with various collagenoses. Eligible participants were those who had positive anti-U1-RNP antibodies in at least one test and at least one capillaroscopic evaluation.

Results. Of the 49 subjects who met the inclusion criteria, 42 were women, with a mean age of 51 ± 1.2 years. The Raynaud phenomenon was present in 61.2% of patients since the onset of the disease, and 32.6% were initially diagnosed with SLE and showed fewer capillaroscopic changes compared to the rest of the sample. Among the cohort of patients initially diagnosed with scleroderma (38.7%), the presence of avascular areas was associated with a 2.188-fold increased risk of developing pulmonary arterial hypertension ($p=0.588$). Among those identified with MCTD and megacapillaries, the risk of developing interstitial lung disease was 1.538 times greater.

Conclusions. The capillaroscopic appearance varies depending on the predominant clinical manifestations at onset, providing insights into the development of organic pathology, particularly pulmonary involvement.

Traps of over / underdiagnosis in psychiatry

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Introduction. Psychiatric diagnosis records a vivid dynamic, whether being unrecognized, hesitant or overdiagnosed.

Material and methods. An analysis of the main examples of these tendencies are ruled out.

Results. This study outlines the dynamics of the main psychiatric diagnosis such as psychotic disorders, bipolar disorder, personality disorder, anxiety disorders, alcohol and other psychoactive use/abuse disorders, cognitive disorders/dementia, gender dysphoria.

We emphasize the natural course of some disorders towards a more complex disorder or the evoluiton facettes, the comorbidities and complication of the initial diagnosis, the overlaps of these conditions.

Conclusion. The cutoff or dynamic analysis of the journey of psychiatric diagnosis should be analised comprehensively, taking into consideration all clinical, psychometric, evolutionary aspects, argumentating a complex viewpoints.

A case of severe vasculitis with neurological onset: a tricky road to diagnosis

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Introduction. Polyarteritis nodosa (PAN) is a rare necrotizing vasculitis affecting medium-sized arteries, requiring high clinical suspicion for early diagnosis due to diverse presentations. We present a 43-year-old female with complex diagnostic pathways and treatment-related complications.

Case presentation. In December 2023, the patient developed sudden severe peripheral neurological symptoms, initially unilateral sensory, rapidly progressing to bilateral motor impairment with distal paresis and gait difficulties. After a week, skin lesions appeared on the legs, evolving from a livedoid pattern to hemorrhagic bullae with ulceration and necrosis, accompanied by asthenia, fatigue, and weight loss. Investigations revealed bilateral tibial and right peroneal arterial occlusions due to serial thrombotic stenoses, right femoropopliteal venous thrombosis, chronic thromboembolism with pulmonary infarction, and severe mononeuritis multiplex. Lab Results showed leukocytosis with eosinophilia, thrombocytopenia, and anemia. Endovascular revascularization attempts failed. Etiological tests excluded thrombophilias, connective tissue diseases, neoplasms, and infections (fluctuating CMV serologies, undetectable viremia). Imaging revealed irregularly sized arteries with stenoses and occlusions. Sural nerve biopsy confirmed medium-vessel vasculitis. In the absence of other organ involvement and ANCA negativity, a diagnosis of PAN was confirmed, and corticosteroids with cyclophosphamide (CYC) were initiated. A favorable response was observed, but hemorrhagic cystitis required CYC discontinuation after the third dose. The active, severe and progressive disease (BVAS=27, VDI=10), and CYC side effects led to Rituximab initiation.

The atypical presentation with eosinophilia, thrombocytopenia, and DVT created diagnostic challenges. The abrupt symptom onset suggested an infectious trigger, with CMV identified in literature as a potential PAN agent. Treatment complications and limited access to Rituximab were additional challenges.

Conclusions. This case highlights the diagnostic and treatment challenges in PAN, underscoring the need for a multidisciplinary approach to optimize therapeutic outcomes.

Diagnosing thromboangiitis obliterans: a case of critical ischemia in a 53-year-old female patient

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Introduction. Thromboangiitis obliterans (TAO), or Buerger's disease, is a segmental vasculitis predominantly affecting small and medium-sized arteries and veins, primarily observed in young male smokers. This condition manifests with ischemic symptoms in the extremities, often leading to critical limb ischemia. This report presents a case of critical ischemia in the fingers of a 53-year-old female patient with a complex medical history, including multiple cardiovascular and metabolic comorbidities.

Case report. A 53-year-old female, with a significant history of bilateral coxarthrosis, early-stage lumbar spondylosis, type II diabetes mellitus, and chronic obstructive pulmonary disease (COPD), was referred to our clinic for evaluation of bilateral acrocyanosis accompanied by pain, paresthesias, and sensory disturbances in the distal phalanges. On examination, the patient demonstrated cyanotic discoloration of the fingers with preserved range of motion, absence of peripheral edema, and no evidence of synovitis. Diagnostic workup revealed moderate leukocytosis, hyperuricemia, mixed dyslipidemia, and a mildly elevated HbA1c level (6.03%). Autoimmune markers, including anti-nuclear antibodies and profiles for myositis and scleroderma, were negative. Capillaroscopy indicated decreased capillary density and multiple hemorrhages in several digits. Doppler ultrasound findings suggested reduced flow in the ulnar arteries, indicative of significant vascular compromise.

The clinical presentation and the patient's extensive history of chronic tobacco use led to the diagnosis of thromboangiitis obliterans, as other potential etiologies, including systemic sclerosis and vasculitis, were excluded. The management included the initiation of a pharmacological regimen comprising Pridax, nifedipine, cilostazol, and macitentan, with favorable tolerance and without significant adverse effects. This case illustrates the importance of recognizing TAO in female patients and emphasizes the necessity of a comprehensive assessment in those presenting with ischemic symptoms in the context of significant comorbid conditions.

Conclusion. Thromboangiitis obliterans should be considered in the differential diagnosis of critical limb ischemia, particularly among individuals with a history of smoking. Early identification and tailored treatment strategies are crucial in managing this condition and preventing progression to severe ischemic events. The patient will continue to receive multidisciplinary care to monitor her vascular health and address her comorbidities effectively.

Adult-onset Still's disease presenting in early pregnancy: a case report

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Introduction. Adult-onset Still's Disease (AOSD) is an uncommon autoinflammatory disorder marked by quotidian fevers, evanescent salmon-colored rash, polyarthritis, and leukocytosis. Diagnosing AOSD is complex due to nonspecific biomarkers and its overlap with other inflammatory conditions. Hormonal and immunologic changes associated with pregnancy and the postpartum period may act as triggers for AOSD onset or exacerbation. This report presents a case of postpartum AOSD with significant systemic and cutaneous involvement, effectively managed with corticosteroid therapy.

Case report. A 27-year-old female, recently postpartum following delivery on 28th of September 2024, developed cyclical fever, polyarthritis, and an evanescent salmon-colored rash early in pregnancy, around four weeks of gestation. Initially limited to select areas, the rash expanded to involve the entire body, including the face, following childbirth. Early pregnancy was marked by intermittent chills and polyarthritis, progressing to high fevers up to 40°C post-delivery. Physical examination revealed splenomegaly, and laboratory evaluation demonstrated leukocytosis with neutrophilia, thrombocytosis, elevated ferritin, and hepatic enzyme elevation during pregnancy, normalizing postpartum. A comprehensive immunologic workup, including ANA, anti-dsDNA, and other markers, was negative, aligning with the Yamaguchi criteria for AOSD diagnosis. The patient received intravenous methylprednisolone (250 mg daily for three days), resulting in rapid remission of systemic and cutaneous symptoms. She was discharged on oral Medrol 16 mg daily, with lactation counseling and a scheduled follow-up for continued management.

AOSD should be considered in postpartum patients presenting with a constellation of cyclical fever, polyarthritis, and a widespread salmon-colored rash, particularly when laboratory findings reveal leukocytosis and hyperferritinemia. This case highlights the role of pregnancy-related immunologic shifts as potential triggers for AOSD. Corticosteroids remain the mainstay of treatment, providing effective control of systemic inflammation and cutaneous manifestations. Management in the postpartum period, especially for lactating patients, necessitates a tailored approach to balance therapeutic efficacy and safety.

Conclusion. This case underscores the importance of considering AOSD in postpartum women with systemic symptoms, widespread rash, and arthritis. Prompt recognition and corticosteroid therapy are essential for symptom control and prevention of complications. Further studies are warranted to explore the relationship between pregnancy and AOSD pathogenesis and to establish guidelines for postpartum management, particularly in lactating patients.

Variations of the genetic profile – prominent tissue-specific features of papillary thyroid carcinoma subtypes

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Introduction. Papillary thyroid cancer (PTC) is the most frequent type of thyroid cancer. Although characterized by a very good prognosis, the rarely unpredictable evolution of PTC may be due to the mutational profile.

Aim. Comparatively analyze the key genes involved in the conventional variant of PTC (cPTC) versus the infiltrative follicular variant of PTC (iFVPTC), in order to evidence distinguishing genetic alterations.

Material and methods. Total DNA was extracted from paraffin-embedded tissues of 63 patients, 16 with iFVPTC and 47 with cPTC. A panel of 50 genes commonly mutated in cancer were sequenced in 24 patients (12 cPTC and 12 iFVPTC) using the NGS technique and 3 specific mutations were validated in all cohort by qRT-PCR.

Results. There were significant differences in the frequency of the genetic alterations among the two histologic variants of PTC. The following mutations were identified in both groups of patients: ERBB4 c.421+58A>G, FLT3 c.1310-3T>C, c.2053+23A>G, MET c.3029C>T, PIK3CA c.3196G>A, PTEN c.847C>T and SMAD4 c.955+58C>T. We observed six specific pathogenic mutations in BRAF, NRAS, PTEN, VHL, and TP53 genes for PTC and four pathogenic mutations in TP53, PTEN, and NRAS genes for iFVPTC, according to ClinVar database. BRAFV600E and MET c.3029C>T were identified only in cPTC samples as heterozygote mutations, and NRAS rs121434596 was observed in both PTC subtypes as a heterozygote mutation.

Conclusions. The present study describes the mutational profile of the two histological subtypes of PTC, pointing out variations in its genetic alterations. Our results suggest new perspectives on the mechanisms of development and evolution of specific subtypes of PTC.

MEDICINE
Surgical Specialties

Twice the scars, twice the challenge: a case report of abnormally invasive placenta praevia

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Introduction. Abnormally invasive placenta praevia (AIPP) poses significant risks, especially in women with prior C-sections. The growing global incidence of this pathological entity has drawn attention lately. We present the case of a 21-year-old, G2P2, with central placenta praevia and suspected AIPP following two previous C-sections.

Material and methods. The patient was referred to our department at 25 weeks of gestation (WG) for low-lying placenta. Ultrasound showed anterior low-lying placenta, covering the internal cervical ostium, placental lacunae, abnormal vascular flow at the site of previous scars, thinning of the myometrium and partial absence of the "clear zone" – the plane between the myometrium and underlying placenta. MRI was planned at 28WG but cancelled due to prior orthopaedic shoulder surgery and clips insertion. The patient was asymptomatic (no bleeding / contractions) until 34 weeks, when mild contractions prompted admission for corticosteroids. She was scheduled for elective C-section at 36/37WG.

Results. Intraoperatively, bladder adhesions complicated dissection. An extensive area of dilated vessels was observed in the lower segment. Foetal extraction was uneventful (2740g, Apgar 9/10) via midline uterine incision, away from the placenta. Hysterorrhaphy was carried out with the placenta in situ and subtotal hysterectomy was then performed. Estimated blood loss was 1L, and the procedure lasted 100 minutes. Postoperatively, 500 ml of blood suddenly drained 12 hours after surgery, but the patient remained stable, and her evolution was otherwise uneventful. She was discharged on postoperative day 3.

Conclusion. This case underscores the complexity of managing AIPP in young women with prior C-sections. Careful preoperative planning was key to achieving good outcomes. Although complex, subtotal hysterectomy with preservation of the adnexa allowed for successful management of the condition, while minimizing complications.

Sequential presentation of two rare pathologies: Meckel's diverticulum followed by intestinal lymphoma in a young adult – case report and literature review

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Introduction. Meckel's diverticulum, affecting about 2% of the population, is often asymptomatic but can lead to serious complications. Primary intestinal lymphomas, particularly diffuse large B-cell lymphoma (DLBCL), are rare, comprising less than 1% of gastrointestinal cancers. The sequential occurrence of Meckel's diverticulum followed

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by intestinal lymphoma in the same patient is exceedingly rare. This report aims to demonstrate the importance of a comprehensive approach in managing two uncommon gastrointestinal conditions.

Material and methods. A 19-year-old male initially presented with acute right iliac fossa pain, abdominal distension, and nausea. Clinical and imaging findings suggested small bowel obstruction, prompting emergency laparoscopy. Four years later, at age 23, the same patient presented with chronic right flank pain, altered bowel habits, and rectal bleeding. Diagnostic investigations included colonoscopy and computed tomography (CT), which identified a mass in the ileocecal region.

Results. The first surgical intervention revealed a Meckel's diverticulum obstructed by an impacted food bolus, managed with segmental enterectomy. Histopathology confirmed a diverticulum with heterotopic gastric mucosa. During the second presentation, a polypoid mass causing intussusception in the terminal ileum was discovered, requiring a right hemicolectomy. Histology confirmed DLBCL, and the patient subsequently underwent six cycles of R-CHOP chemotherapy, achieving complete remission with no recurrence at 12-month follow-up.

Conclusion. This case underscores the importance of considering Meckel's diverticulum in differential diagnoses for acute abdomen in young adults and highlights the need for vigilant evaluation of persistent gastrointestinal symptoms, which may indicate underlying malignancy. A multidisciplinary approach involving surgical and oncological collaboration is essential for favorable patient outcomes.

Traumatic fracture of the stapes and perilymph fistula: report of a case

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Introduction. Traumatic injuries to middle ear structures, often caused by direct force through the external auditory canal, can result in tympanic membrane perforations, typically managed conservatively due to high spontaneous healing rates. However, in cases of severe conductive deafness, continuous vertigo, sensorineural hearing loss, ossicular chain disruption, or perilymph fistula, immediate surgical intervention may be necessary to prevent irreversible inner ear damage.

Material and methods. Two cases of male patients presented în emergency room with traumatic injury to the tympanic membrane following an accidental penetration with a comb tip in one case and with small three branch, leading to severe ear pain, vertigo, and vomiting. Initial conservative treatment provided no improvement. Further assessment, including audiometry and high-resolution computed tomography (HRCT), revealed mixed hearing loss, ossicular dislocation, and a suspected perilymph fistula. Exploratory tympanotomy was performed 4 udays post-injury, during which middle ear structures were examined and surgical repair was initiated.

Results. Surgical exploration confirmed a disrupted incudostapedial joint, fractured stapes crura, and depressed stapes footplate with perilymph leakage. The fractured stapes components were removed, and a connective tissue graft was applied to seal the vestibular window. Postoperatively, the patient showed marked improvement in vertigo and hearing.

Conclusion. These cases underscore the importance of timely surgical intervention for traumatic ossicular and inner ear injuries, particularly with perilymph fistula. Early surgical exploration and meticulous repair can significantly improve outcomes, preserving hearing and reducing vestibular symptoms, even in cases with suspected irreversible sensorineural loss.

Tailgut cyst in a postmenopausal woman: a rare but peculiar cause of pelvic pain

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Introduction. A tailgut cyst is typically discovered as an incidental finding while imaging other pelvic conditions. Meanwhile, this tumor might cause symptoms, particularly pelvic pain, mass effect, and septic complications. Although there is a substantial amount of knowledge on this tumor, several issues remain unresolved, including its potential for malignancy.

We report the case of a 73-year-old postmenopausal woman who underwent surgery for vaginal prolapse. A month after the intervention, she complained of pelvic pain radiating to sacrum. A transvaginal ultrasound exam indicated a poorly defined tumor anterior to the sacrum which had no Doppler signal. The prior pelvic surgery made diagnosis challenging, considering a postoperative pelvic abscess or hematoma. MRI revealed a presacral cystic tumor measuring 70x76x42 mm in size, with a mass effect on the rectum that was moved anteriorly. The tumor contained parietal swellings and papillary projections measuring up to 7 mm. The MRI scans suggested a teratoma or a cystic hamartoma (tailgut cyst). Surgery was decided because of pelvic pain. Based on the imagistic appearance, laparoscopy was performed, followed by dissection and excision of the tumor. The frozen sections exam revealed a benign tumor. Histopathology confirmed that the tumor was a retrorectal cystic hamartoma filled with a yellowish-blackish liquid. The postoperative outcome was uneventful. The follow-up period is one year, and no evidence of recurrence is found.

Conclusion. Currently, there is no conventional treatment for tailgut cysts. Given their malignant potential, an extensive anterior excision according to oncological principles was suggested. Laparoscopy could be employed in selected cases. However, the Kraske technique is still used. Regardless of the type of intervention, we believe that the tumor's frozen sections are required to be examined because of the potential for malignancy.

Hepatic alveolar echinococcosis in a HIV+ patient – a case report

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Introduction. Hepatic alveolar echinococcosis, a rare and aggressive parasitic infection, is particularly uncommon in immunocompromised populations, including HIV+ patients. With an incidence of 0.03-1.2 cases per 100,000 in endemic regions, this disease's infiltrative growth mimics malignant tumors, posing significant diagnostic and therapeutic challenges. This report presents a 44-year-old HIV+ patient, illustrating the complexities of diagnosis and management.

Material and methods. A stage C3 HIV patient presented with mild symptoms, including right upper quadrant pain and low-grade fevers, without other systemic signs. Abdominal MRI revealed a 13 cm multilocular hepatic cyst with central necrosis in segments IV, V, and VI, a smaller lesion in segment VIII, and additional cysts of 2-3 cm in the left lobe. Following diagnosis, the patient underwent a four-week preoperative course of albendazole. Surgical intervention included atypical hepatic resection in segments V and VI, cholecystectomy, and extensive drainage. Histopathology confirmed alveolar echinococcosis, with granulomas and Langhans giant cells.

Results. Both intraoperative and postoperative courses were uneventful, with no complications encountered. Intestinal transit resumed by day 3, and surgical drains were removed at discharge. Postoperative albendazole therapy continued for two months, along with follow-up care.

Conclusion. Alveolar echinococcosis in HIV+ patients requires a customized approach. This case highlights the importance of combining surgical and anti-parasitic therapy to manage the infection effectively and prevent complications. Interdisciplinary collaboration and diligent postoperative monitoring are essential to optimize outcomes.

Evaluation of inpatient satisfaction for chemotherapy chamber implantation

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Introduction. The study focuses on the analysis of the experience and level of satisfaction of patients who have undergone the procedure of implantation of chambers for the administration of chemotherapy. These devices, also known as chemotherapy ports, are used to facilitate the administration of treatment and reduce discomfort caused by repeated stitches

Material and methods. Research methods include questionnaires and interviews with patients after implantation, and analyzes of the results highlight positive and negative factors related to the hospitalization experience.

Results. The study's findings emphasize the importance of adequate psychological support, good communication from medical staff and pain management in increasing patient satisfaction.

Conclusion. The authors recommend the implementation of some strategies for needing this type of intervention.

Non-resectional management of splenic injuries in laparoscopic surgery

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Introduction. Splenic iatrogenic injuries in abdominal surgery represent an underestimated complication and it is important to be recognised intraoperatively to assure a proper management. Among surgical procedures with the highest rate of splenic injuries the following are to be mentioned: left hemicolectomy (1-8%), open anti-reflux procedures (3-20%), left nephrectomy (4-13%) and reconstruction of the proximal abdominal aorta and its branches (21-60%). In order to manage this type of complication, splenectomy may be required, but conservative treatment by any means with the aim of acquiring proper haemostasis should be employed at any chance. More than 40% of splenectomies are performed for splenic injuries that occur during surgery for other abdominal organs. Splenectomy can lead to long term complications, such as thrombocytosis, blood clots and higher risk of infections, especially with encapsulated bacteria (Streptococcus pneumoniae, Neisseria meningitidis and Haemophilus influenzae).

Material and methods. We present three clinical cases which consisted of different splenic injuries during laparoscopic procedures, which were managed conservatively, without needing to perform a splenectomy. First case consisted of a splenic effraction in a cirrhotic patient during a laparoscopic rectosigmoidectomy. The second patient suffered a bleeding by splenic decapsulation during a routine laparoscopic hiatal hernia repair. Last but not least, in the third case we have encountered a splenic injury when inserting the trocars for a laparoscopic right adrenalectomy in a patient with morbid obesity.

The case series presented are very illustrative of a non-resectional treatment performed laparoscopically for a proper management of splenic iatrogenic injuries. Hemostasis was established by a combination of applied pressure with a mesh, electrosurgery and hemostatic materials or substances.

Conclusion. In summary, we consider that conservative management of splenic bleedings which may occur during laparoscopic intervention should be mastered by any general surgeon and preferably performed laparoscopically.

Metabolomic profiling of obese patients who underwent bariatric surgery

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Introduction. Energy metabolism and adaptation mechanisms for energy storage and consumption are highly relevant in obesity physiopathology. Considering that until now there is no clear cause of obesity, metabolic fingerprinting might be an effective way to better understand the changes that occur after different therapies, such as bariatric surgery.

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This study aimed to investigate the changes induced to energy metabolism and nutrient consumption by bariatric surgery, together with better understanding the adaptation of energy metabolism after the intervention.

Material and methods. Plasma samples collected from 31 obese patients (BMI>25 kg/m2) before gastric sleeve surgery, of which 15 were sampled a second time after 3 months after bariatric intervention. The study design also included 23 healthy patients (BMI<25 kg/m2) as control group. Metabolomic analysis included the measurement of more than 100 metabolites (amino acids and acylcarnitines) and metabolism indicators by LC-MS/MS.

Results. Comparative statistical analysis between the three groups revealed several significantly modified metabolites and metabolism indicators. Compared to healthy controls, obese patients are characterized by increased glutamine, valine and carnitine, together with decreased short and medium chain acylcarnitines, and decrease of several hydroxylated acylcarnitines. Gastric sleeve surgery induced a significant decrease in tyrosine, phenylalanine, valine, free carnitine, C5-OH-carnitine (hydroxyisovalerylcarnitine), and an increase in serine, glycine, medium and long chain acilcarntines.

Conclusion. Metabolomic profiling revealed several alterations in energy metabolism, generally characterized by decreased levels of various acylcarnitines. Following bariatric surgery (3 months after intervention), significant modifications occurred in several amino acids and acylcarnitines associated with increased β-oxidation and amino acid degradation.

Isolated sphenoid disease - a retrospective study

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Introduction. Isolated sphenoid sinus disease is a relatively rare pathology secondary to various aetiologies, including inflammation, fungal diseases, and tumours. Because it is located close to vital structures, it can potentially cause severe complications if not properly diagnosed and treated.

Material and methods. Our study aimed to evaluate all patients who presented with an isolated sphenoid sinus opacification visible on CT or MRI and were managed in our clinic between 2015 and 2022. Patients with multiple paranasal sinus involvement, isolated sphenoid cysts, pituitary and skull base tumours with direct sphenoid sinus invasion, and prior skull base or transnasal pituitary surgery were excluded from the study.

Recorded data included patient demographics, co-morbidities, presenting symptoms and signs, imagistic and intraoperative findings, histopathological results and follow-up details.

Results. Twenty-five patients were included in the study. There were 14 females (56%) and 11 males (44%). Age ranged from 30 to 65 years, with a mean age of 47.08 and a standard deviation of 10.112.

The most frequently presenting symptoms were headaches in 17 patients (68%) and sinonasal symptoms in 8 (32%). One patient (4%) had visual disturbances, and three patients (12%) were completely asymptomatic.

The underlying pathologies were classified as mucoceles in 8 patients (32%), fungal sinusitis in 6 patients (24%), chronic rhinosinusitis without nasal polyps(CRSsNP) in 4 patients (16%), choanal polyps in 4 patients (16%), fibrous dysplasia in 1 patient

(4%), desmoplastic fibroma in 1 patient (4%) and inverted papilloma in 1 patient (4%).

Endoscopic sinus surgery was performed in 22 patients (88%) for diagnostic or therapeutic purposes.

Conclusions. Isolated sphenoid sinus disease is an infrequent entity. Most cases have benign etiologies, but there is a propensity for local severe complications secondary to the involvement of vital adjacent structures. Endoscopic sinus surgery is recommended for both diagnostic and therapeutic reasons in all patients with isolated sphenoid sinus opacities.

Automatic characterization of prostate lesions on mpMRI acquisitions, using radiomic features and machine-learning algorithms

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Introduction. Prostate cancer (PCa) is the most frequent neoplasia in the male population. According to the International Society of Urological Pathology (ISUP), PCa can be divided into 2 major groups, based on their prognosis and treatment options. Multiparametric magnetic resonance imaging (mpMRI) holds a central role in PCa assessment, however, it does not have a one-to-one correspondence with the histopathological grading of tumors. Recently, artificial intelligence (AI)-based algorithms and textural analysis, a subdivision of radiomics, have shown potential in bridging this gap, having the potential of sparing patients of repeated invasive procedures such as prostate biopsies. We aimed to develop a machine-learning algorithm, which predicts the ISUP grade of selected prostate nodules on T2 weighted images, classifying them into clinically significand and indolent ones.

Material and methods. The study cohort was comprised of 55 patients and 76 lesions. All patients were examined on the same 1.5 Tesla mpMRI scanner. Each nodule was manually segmented using the open-source 3D Slicer platform. Textural features were extracted using the PyRadiomics library. The software was based on machine-learning classifiers. The accuracy was calculated based on the precision, recall and F1 scores.

Results. Median age of the study group was 64 years (IQR 61 – 68) and the mean PSA value was 11.14 ng/mL. 85.52% of the nodules were graded PI-RADS 4 or higher. Overall, the algorithm classified indolent and clinically significant PCa with an accuracy of 89.3%. Further, when trained to differentiate each ISUP group, the accuracy was 80.3%.

Conclusions. We developed an AI-based decision support system that accurately differentiates between the 2 PCa prognostic groups using only T2 MRI acquisitions, by employing radiomics with a robust, machine-learning architecture.

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PHARMACY
Fundamental Research

Potential of bilberry bioactive compounds to modulate gene expression in mycotoxin-exposed differentiated Caco-2 cells: an *in vitro* study

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Introduction. Mycotoxin presence in grains and grain-based products continues to be a major issue for food safety. Utilizing food ingredients rich in antioxidants, such as bilberries (Vaccinium myrtillus L. species, VM), may offer a strategy to mitigate their adverse effects. Therefore, the aim of this study was to analyze changes in mitochondrial gene expression using an in vitro cell model (differentiated Caco-2 cells) at the intestinal level, after exposure to mycotoxins and bilberries.

Material and methods. In the present study, the potential of bilberry to modulate gene expression was investigated starting by using an in vitro digestion model. Four types of bread samples were prepared: control (C), bread with ochratoxin A (OTA), bread with bilberries (VM), and bread with both OTA and VM (OTA-VM). Differentiated Caco-2 cells were exposed to the digests for 24 h. Total RNA was then extracted, and gene expression was evaluated using quantitative PCR (qPCR) analysis. Ten mitochondrial related genes — MT-ND2, MT-ND4, CLAU-2, OCCLUDIN, MT-CO1, MT-ATP8, MT-RNR2, SRXN1, SLC7A11, and ZO-2 — were analyzed with S18 as the reference gene.

Results. Results showed that gene expression in cells treated with VM-containing digests closely resembled control samples, indicating a stabilizing effect of bilberry compounds on gene expression. For cells exposed to OTA, several genes displayed downregulation, reflecting OTA's adverse impact. Although no significant differences were observed between the OTA and OTA-VM digests, favorable fold-change increases were noted in OTA-VM for the genes MT-ND4, MT-ND2, SLC7A11, ATP-8, and SRXN1. This suggests that bilberries might exert a subtle mitigating influence on OTA's effects, with slight fold increases in gene expression compared to OTA alone.

Conclusion. This study highlights bilberries' potential in supporting cellular homeostasis under mycotoxin exposure. Future research should further explore these bioactive compounds to clarify their role in modulating specific gene expression changes induced by mycotoxins.

Competitive cDNA-Fc/MXene modified aptasensor targeting *Staphylococcus aureus*

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Introduction. Antimicrobial resistance (AMR) represents the cornerstone of the modern healthcare systems and is foreseen to be one of the leading death causes in the next 50 years. Staphylococcus aureus is one of the species that continuously evolved to more resistant variants. The early and specific diagnostic, hence detection of the pathogen, could improve the targeted antibiotherapy and represents an efficient

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tool on the fight against AMR. The objective of this study was the development of an electrochemical competitive aptasensor for the rapid detection of S. aureus' surface protein A (PrA) from spiked and real samples.

Material and methods. The biosensor was elaborated on gold screen-printed electrodes (AuSPE), modified with an aptamer for the specific recognition of PrA, ferrocene-labeled complementary DNA sequences (cDNA-Fc) to improve the selectivity and titanium carbide nanosheets (MXene) to enhance the electrochemical signal. The protocol for the immobilization of the aptamer and the cDNA-Fc/MXene probe was optimized in terms of procedure. Surface plasmon resonance (SPR) was used to study the binding interactions between the aptamer, the cDNA sequences and the target molecule. PrA was detected by cyclic voltammetry using the Fc electrochemical signal as an indirect indicator for the protein binding. The sensor was incubated with real hemoculture samples confirmed with S.aureus.

Results. The suitable configuration for the aptasensor was established using the SPR analysis. A wide range of concentrations of PrA were incubated on the surface of the sensor, being tested in both standard solutions and real samples.

Conclusion. A biosensor using an aptamer and cDNA/MXene was developed for the fast detection of S.aureus specific marker (PrA) from both enriched samples and hemoculture samples.

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Nanoflowers doped with manganese for magnetic hyperthermia application

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Introduction. Magnetic nanoplatforms (MNPs), either internalized into cancerous cells or adhered to malignant tissue, under an alternating magnetic field (AMF), can generate thermal energy to kill or inhibit the growth of diseased cells. This is the principle of magnetic hyperthermia (MH), one of the alternative approaches to anticancer therapy. Increasing the utility of MH by using MNPs with enhanced thermal properties is necessary to induce apoptosis of cancerous cells. Due to their outstanding heating performance, resulting from their multi-core magnetic structure, magnetic nano-flowers (MNFs) are being noticed. This study aimed to synthesize a series of MNFs with variable Mn/Fe molar ratios via a modified polyol method and to evaluate their potential for MH therapy.

Material and methods. A series of four MNFs were synthesized and were further characterized by TEM, XRD, VSM, and hyperthermia measurements. The cytocompatibility of MNFs was evaluated in cancerous cells by Alamar Blue assay. The cellular uptake studies were performed for the three most promising MNFs. Based on the magnetic and biological properties, the ability of one type of MNFs to induce cellular death under an AMF was evaluated.

Results. MNFs with the highest Mn content displayed increased cytotoxicity and were not used in further studies. For the other 3 types of MNFs, a relatively high biocompatibility was observed. Besides a dose-dependent internalization, higher cell internalization was observed for MNFs doped with moderate quantities of manganese as a result of their size and colloidal stability. Regarding the MH therapy, an increased efficiency dependent on the dose of MNFs and the field intensity was observed.

Conclusion. The results obtained indicate that MNFs could represent promising candidates for MH therapy.

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Aptamer selection for serum protein Golgi-73 overexpressed in hepatocellular carcinoma

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Introduction. According to GLOBOCAN's 2022 report, hepatocellular carcinoma (HCC) is the 8th most diagnosed cancer and the 3rd leading cause of cancer-related deaths worldwide, with global deaths projected to reach 1.26 million by 2045. Recent diagnostic approaches have focused on serum monitoring of specific HCC biomarkers, such as Golgi protein-73 (GP-73), providing higher diagnostic performance and sensitivity in early stages compared to alpha-fetoprotein. Aptamers are short single-stranded nucleic acid sequences that can specifically bind to target molecules with high affinity, being selected using an iterative process called SELEX. This study focuses on selecting and characterizing an aptamer for GP-73 to support the development of analytical methods for early HCC detection.

Material and methods. The immobilization of GP-73 on magnetic beads (MBs) was optimized using two types of functionalized MBs. For the optimization studies and negative selection, bovine serum albumin was used. The selected DNA sequences were amplified using PCR, and the amplification yield and quality of the sequences were assessed through fluorescence analysis and gel electrophoresis.

Results. The quantitative analysis using the Bradford method revealed binding percentages of 77.63% for carboxyl-functionalized MBs and 99.62% for tosyl-functionalized MBs. Four rounds of selection were conducted according to the selection strategy.

Conclusion. The subsequent steps include continuing the selection process, cloning, and sequencing the selected single-stranded DNA sequences, as well as assessing their affinity. The ultimate goal of the study is to develop an electrochemical aptasensor for early-stage diagnosis, which could reduce mortality rates and healthcare costs.

Present-day Romanian perspective on antibiotic resistance and opportunities for action

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Introduction. The discovery of antibiotics revolutionized the management of infectious diseases, but their irrational use, frequently unjustifiably prescribed and sometimes in an erroneously manner, contributed significantly to the emergence and continuous worsening of cases concerning the resistant germs towards the antibiotics` efficacy. At the international level, by formulating the Global Action Plan aimed at bacterial resistance to antibiotics, the World Health Organization identified the need to impose effective measures to reduce the impact of bacterial resistance to antibiotics. The aim is to highlight the present-day Romanian perspective on the matter, within the European framework and initiate discussions towards opportunities for action.

Material and methods. A literature review had facilitated the analysis of multiple factors involved in the propagation of antibiotic resistance. Together with comparing the monitoring reports' available data, it had been possible to outline the progress achieved by certain member states of the European Union, considering the proposed objectives in limiting antibiotic resistance, by 2030.

Results. As for the year 2022, the total antibiotic consumption in Romania was far above the European mean. More to that, 58% of the Romanian responders, mistakenly agreed that antibiotics treat viral infections, according to the Special Eurobarometer 522. Intriguingly, the findings equally indicate that about 19% of the outpatients admitted to have procured the antibiotics without a prescription. Recurrence of infections with difficult-to-manage pathogens, such as Escherichia coli, due to superficial treatment of the initial infection, poor hygiene measures or lack of ready-to-use tools for correct diagnosis, could have a severe impact on the patient's quality of life and therefore on the society in which they operate. This fact translates into low productivity, generating economic losses and high costs for the health system.

Conclusion. Strengthening the legislation and actively educate the public, become mandatory, in Romania. Furthermore, the development and optimization of novel devices such as portable (bio)sensors, useful in testing biological samples, could facilitate the identification of the antibiotic of choice, effectively contributing to combating the spread of antibiotic resistance.

Synthesis of a novel cationic covalent organic framework with potential biomedical applications

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Introduction. Covalent organic frameworks (COFs) are a class of crystalline, porous organic polymers known for their permanent porosity and highly ordered structures. COFs are promising candidates for biomedical applications, particularly as antimicrobial agents and in molecular recognition. Chloramphenicol (CAP) is

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important for its broad-spectrum antibacterial properties, especially in treating serious infections when other antibiotics may be less effective. In this study, we have developed an electrochemical method for the detection of CAP in various human-use medical formulations. This approach utilizes carbon screen-printed electrodes (C-SPE) in conjunction with COFs to enhance analytical sensitivity and specificity.

Material and methods. The cationic COF was obtained by imine exchange, under solvothermal conditions by the reaction between 2-((5-(trimethylammonium)pentyl) oxy)benzene-1,4-diammonium hydrochloride and benzene-1,3,5-tricaboxaldehyde. C-SPE electrodes were modified with a suspension of chitosan, cationic COF, and ethanol. CAP was then preconcentrated on the modified surface. Detection of CAP was performed using cyclic voltammetry (CV) in Britton-Robinson buffer at pH 6. The antimicrobial activity of cationic COFs was tested against 7 pathogenic bacteria.

Results. The developed sensor demonstrated a broad detection range, a low limit of detection, high specificity, and effective results in detecting CAP from medical products intended for human use.

Conclusions. The easy synthesis of cationic COFs, straightforward modification of the C-SPE, and their high sensitivity and specificity for CAP make this electrochemical sensor a significant advancement toward integrating COFs in biomedical applications.

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Nanostructured electrochemical sensor for direct detection of kynurenic acid in biological samples

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Introduction. Kynurenic acid (KA) is a compound involved in cerebral neurophysiological and pathological processes with neuroactive properties. It is a metabolite of the amino acid L-tryptophan, produced via kynurenine pathway, and is present in various biological fluids. This degradation pathway is disrupted in most neurodegenerative diseases, making KA a biomarker for diagnosis and monitoring. The main objective was to develop an electrochemical sensor based on a nanostructured platform for the direct and sensitive detection of KA in biological samples.

Material and methods. The sensor was developed using carbon electrodes functionalized with a nanostructured polymeric film embedded with gold nanoparticles and reduced graphene oxide. Direct detection was performed via differential pulse voltammetry (DPV), using solutions of KA at various concentrations, with phosphate buffer, Britton-Robinson buffer across a wide pH range, and synthetic and real samples used to verify the medical applications.

Results. The electrochemical behavior of the biomarker was studied on the developed platforms, with maximum DPV signal intensity recorded in the presence of the analyte. Platform optimization was achieved through several methods: adjusting the

suspension composition used for electrode modification, adjusting functionalization parameters, and evaluating the influence of testing parameters on the electrochemical signal. The interference of KA with other metabolites in the kynurenine pathway was assessed in phosphate buffer, while testing in complex matrices was conducted using human saliva.

Conclusions. The developed electrochemical sensor enables the direct and sensitive detection of KA, representing a starting point for creating a wearable sensor for salivary detection of this biomarker, with potential biomedical applications.

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Antimicrobial effectiveness of *Ribes nigrum L.* leaf extracts prepared in natural deep eutectic solvents (NaDES)

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Introduction. The antimicrobial potential of extracts rich in bioactive compounds obtained from black currant *(Ribes nigrum L.)* leaves, prepared in natural deep eutectic deep solvents (NaDES), was investigated.

Material and methods. Extraction of polyphenols from R. nigrum leaves in NaDES was optimized based on experimental designs using two hydrogen bond acceptors (HBA) and three hydrogen bond donors (HBD). Several variables were investigated such as: molar ratio HBA:HBD, water percentage, extraction technique (ultrasound-assisted extraction (UAE) and ultra-turrax extraction (UTE)) and extraction time. Total polyphenol content (TPC), total flavonoid content (TFC) and phytochemical composition using liquid chromatography-mass spectrometry (LC-MS) were determined for all extracts prepared according to the experimental design. Antioxidant activity was also evaluated by DPPH assay and antimicrobial activity was assessed on four Gram-positive and three Gram-negative bacterial species as well as on Candida albicans.

Results. Extracts obtained by UAE showed higher concentrations of polyphenols and increased antioxidant potential. LC-MS analysis revealed the predominant presence of chlorogenic acid. The extracts showed significant activity against Gram-positive bacteria and Candida albicans strains.

Conclusion. The study highlights the antioxidant and antimicrobial potential of black currant leaf extracts prepared in NaDES. The use of NaDES opens perspectives for new therapeutic formulations based on polyphenol-rich plant extracts with antimicrobial efficacy.

A “three-in-one” ultra-sensitive device for electrochemical detection of tetracyclines in dairy, fish and polluted water, without prior sample clean-up

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Introduction. Tetracyclines (TCN)s and derivatives, are among the classes of antibiotics mostly abused by farmers, as growth promoter for animal production. The menace is becoming a public health issue, with increasing environmental contaminations, toxicity and anti-bacterial cross-resistance, fast spreading across communities. Strict legislations have been passed by several governments, including the European union (EU). Yet, exist an implementation gap, due to lack of handy tool, for easy detection and effective monitoring. Here, we developed a three-in-one ultra-sensitive electrochemical device that can detect TCN, without the multi-step, time-consuming tasks, involved in sample-preparation.

Materials and methods. Fe (III) citrate ligand (FCL) was used as solid-phase microextraction, having an excellent selectivity for TCNs. The FCL was immobilized on the surface of graphene oxide (GO) working electrode (WE), for capturing, pre-concentrating and sample clean-up; and overall boosting of electrochemical sensitivity. Protocol: 5 uL test sample was incubated in situ on the surface of FCL pre-coated GO for 30 min at room temp., before washing it off with excess water to eliminate the unbound impurities. A differential pulse voltammetry (DPV) was applied: Voltage (V) 0.0 -1.1(V); Step P: 0.005V; Mode A: 0.1(V); Mode T: 0.025 (s) and Interval: 0.5 (s).

Results. The sensor shows a linear range of 500 μM–1 μM in 0.1 M citrate buffer (pH 13.0), and LOD of 5nM, better than most conventional TCN sensors. The platform exhibits higher output-efficiency than the control (in multiple folds) under same condition, but without FCL or washing step.

Conclusion. The platform, provides the anchor for selective capture of TCN molecules, with improved conductance and sensitivity, required for excellent electrochemical testing. Also, the opportunity for on-site/point-of-care monitoring of TCN contamination, by field control agents, food supply chain marketers and home users.

Nature-inspired nano-system for synergetic anticancer therapy, sensing and modulation of tumor-microenvironment

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Introduction. The transforming growth factor (TGF-β) is a well-known driver of anti-angiogenic resistance, cancer metastasis, and immune evasion. Also, a key inducer of epithelial-mesenchymal transition (EMT), fibrosis, and immune-suppressive tendencies in the tumor microenvironment (TME). Recent research suggests that saponins may counteract tumors and abnormal extracellular matrix (ECM) production. Notably, the ginsenoside Rg1 from Panax ginseng has shown anti-cancer properties by

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inhibiting TGF-β1/Smad signaling pathway, which contributes to excessive collagen synthesis, interstitial fibrosis, and EMT. Therefore, to leverage these benefits, a natural saponin extract from ginseng was used as a coating material for a nanoparticle (NP) designed to co-deliver and enhance the efficacy of sorafenib (SOR).

Materials and methods. Nanoparticles (NPs) were synthesized from MnO_2 and SOR using a chemical precipitation method. Coating was achieved by exposing the NPs to colloidal saponin Rg1, making them responsive to low pH. The final product was characterized using relevant analytical tools.

Results. After coating, the zeta potential improved from -32.1 mV to 17.1 mV, and the average particle size increased from 167 nm to 364.6 nm. Sorafenib encapsulation efficiency was 61%, with a release profile showing higher drug release at pH 5.5, in phosphate buffer (PB) and at room temperature. Air bubbles were visible in the medium at pH 5.5, but absent in pH 7.4 (both with PB/ 0.1 mM H_2O_2). The emergence air bubbles confirm the oxygen release via MnO_2's catalase-like activity, suggesting that NP dissociation is feasible in the acidic TME.

Conclusion. This strategy therefore, holds a strong promise for targeting solid tumors; reducing hypoxia-driven immune escape and modifying the dense, fibrotic ECM, which potentially obstructs drug penetration and exacerbates SOR resistance.

PHARMACY
Pharmaceutical Specialties

Addressing pharmacovigilance in Romanian legislation on vaccination in the pharmacy

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Introduction. Pharmacy-based vaccination services have developed in many countries, particularly in the wake of the Covid-19 pandemic, becoming increasingly regulated by authorities and supported by international pharmacists' organisations. The pharmacovigilance tasks of vaccinating pharmacists are particularly important for monitoring vaccine safety and increasing population confidence in vaccination, as a tool to protect public health. The aim of this paper was to analyse the provisions addressing pharmacovigilance in the Romanian legislation that applies to vaccination in pharmacy, to assess their suitability to this context.

Material and methods. We used as materials the texts of the relevant normative acts, and as methods documentary research, thematic analysis and a pluralist method of legal interpretation.

Results. The Romanian legislation includes detailed provisions on the authorisation and organisation of influenza vaccination in community pharmacy under a pilot program, theoretical and practical training and evaluation of vaccinating pharmacists, including in pharmacovigilance of influenza vaccines, for patient monitoring and reporting adverse reactions to the competent authorities.

Conclusion. Simplifying the reporting, by harmonising the forms and procedures used by the national immunization authority and the national pharmacovigilance authority, could stimulate the involvement of pharmacies in vaccination and in monitoring the safety of vaccines on the Romanian market.

Kinetic modelling of olanzapine interactions with ciprofloxacin and norfloxacin in adult male Wistar rats: the mechanism of drug-drug interaction

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Introduction. This study aimed to investigate the kinetic modelling of drug-drug interactions between olanzapine (OLZ) and the antibiotics fluoroquinolone, ciprofloxacin and norfloxacin, using a three-step compartmental modelling approach. Olanzapine is metabolized mainly by CYP1A2, which is inhibited by both antibiotics, affecting its disposition in the body.

Material and methods. This three-period study included 14 male Wistar albino rats. During the reference period the rats received a single oral dose of 12 mg/kg body weight (b.w.) of OLZ. During the first and second test periods the rats received a 5 day oral pretreatment with 15 mg ciprofloxacin and 30 mg norfloxacin respectively, followed by a combination of ciprofloxacin/norfloxacin and OLZ, in the previously mentioned doses, on the 6th day. Venous blood samples for plasma LC-MS analysis of OLZ and its metabolite, N-desmethyl olanzapine, were collected. A three-tiered modelling approach

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was implemented to manage the large number of variable. In the first step, the primary focus was on establishing an optimal model for the parent compound.

Results. In the second step an optimal model for both the parent and the metabolite was developed. In the third step the focus was to explore the kinetic interactions of OLZ with ciprofloxacin and norfloxacin, and their effects on the disposition of OLZ and its metabolite. A 1st order, bicompartmental model with presystemic metabolism, no other elimination routes for OLZ and different relative bioavailability for OLZ and its metabolyte proved to be the best option based on the AIC score.

Conclusion. Given the complexity of kinetic analysis and the multitude of variables involved, a large number of model variants could result. This rational, staged approach provides a detailed mechanistic understanding of the interactions between OLZ and the two fluoroquinolone antibiotics.

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Management of clozapine-induced sialorrhea using oromucosal trospium suspension: a case study report

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Introduction. Clozapine-induced sialorrhea (CIS) is a common adverse effect that jeopardizes the efficacy of clozapine in treatment refractory schizophrenia. It can decrease the treatment adherence and irritate the patients. Currently, there is no authorized treatment for CIS, except for small studies with limited evidence. Xanomeline/trospium is a novel combination for the treatment of schizophrenia, which uses trospium as peripheral anticholinergic against the cholinergic adverse effects of xanomeline, including sialorrhea. Herein, we report the case of a patient with CIS treated by using an extemporaneously compounded oromucosal suspension of trospium in borax glycerin.

Material and methods. A 53-year-old patient with paranoid schizophrenia complains of sialorrhea following the treatment with clozapine p.o. 350 mg. The oromucosal formulation was prepared by pulverizing trospium film-coated tablets in a mill, followed by suspension of the obtained powder in borax glycerin. The obtained formulation was administered each evening for seven days. The patient was assayed for the sialorrhea severity, using the Toronto Nocturnal Hypersalivation Rating Scale (TNHR) for nocturnal sialorrhea and the Drooling Severity and Frequency Scale (DSF) for daytime sialorrhea, before initiation and on the third and seventh days.

Results. Before initiation, the obtained scores were TNHR = 4 and DSF = 7, evidencing a severe sialorrhea that woke up the patient during the night. On the third day, the scores were TNHR = 1 and DSF = 6, underlining the patient was no longer woken up by sialorrhea during the nights. Finally, on the seventh day, the scores were TNHR = 0 and DSF = 3, meaning the patient was no longer drooling.

Conclusion. The oromucosal usage of trospium against CIS proved to be successful for this patient, with major improvement during the seven days of treatment. Therefore, we considered this extemporaneously compounded oromucosal formulation as a promising solution for CIS.

Quality by design approach in the development of gastroretentive floating sustained release printlets

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Introduction. An important concept in the development and manufacturing of drugs in the 21st century is Quality by Design (QbD), which involves establishing the Quality Target Product Profile (QTTP) for the final product and the Critical Quality Attributes (CQAs) of the intermediate/ final products. This is followed by a systematic approach to optimizing both the formulations and the manufacturing process. The aim of this experimental study was to develop a sustained-release oral solid drug, manufactured via 3D printing (3DP), consisting of two compartments: one for immediate release (IR) and one for prolonged release (PR), using a QbD approach.

Materials and methods. The filaments for the IR compartment were made from polyvinyl alcohol (PVA), with 15% active substance (AS) ± mannitol as a plasticizer. The filaments for prolonged release (PR) were made from hydroxypropyl methylcellulose (HPMC), with a range of AS between 25-45%, and mannitol. The QTTP of the final product: oral administration, sustained drug release (40-50% in 2 hours and 85% in 24 hours in 0.1N HCl solution), weight uniformity of ±5%, and content uniformity of ±10% per unit dose. CQA for filament: mechanical properties and printability score. CQA for IR compartment: weight uniformity, drug content uniformity, at least 80% release in 2 hours. CQA for PR compartment: weight uniformity, drug content uniformity, minimum 12 hours of flotation, maximum 25% release in 2 hours, and at least 90% in 24 hours.

Results. The optimal filaments chosen for the IR compartment contained 15% AS and 15% mannitol, which provided the necessary flexibility for optimal printing. The IR compartment geometry chosen was a honeycomb design, which ensured rapid AS release in 0.1N HCl within less than 2 hours. The optimal filaments for printing the PR compartment were based on HPMC, which ensured gradual AS release over 24 hours, and mannitol, which improved filament flexibility and lowered the processing temperature, reducing the risk of AS degradation. The optimized PR compartment featured a dome design with an internal air chamber, providing low density to ensure printlet buoyancy. The systems floated for an average of 12 to 18 hours. The bicompartmental system, subjected to in vitro dissolution tests, demonstrated effective control over drug release: the IR compartment dissolved and released its AS in approximately 180 minutes, while the PR compartment gradually released AS over 24 hours.

DSC analyses of the IR and PR filaments confirmed that regardless of the AS loading, the AS was amorphized, which explained the ease of dissolution during in vitro tests. Amorphization of the drug is especially important for the IR compartment, as it ensures faster AS release compared to its crystalline form.

Conclusions. The results demonstrate the potential of 3D printing technology for manufacturing personalized medications and show that by appropriately combining formulation and design factors, 3D-printed oral drugs with flotation times exceeding 18 hours and sustained drug release over 24 hours can be successfully produced.

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Evaluation of the compression behaviour of lyophilised zein-based nanostructures to establish processing conditions for pediatric use orodispersible tablets

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Introduction. Nanostructures are studied intensively as oral drug carriers, but their processability into tablets is a subject rarely tackled. This study intends to monitor the direct compression (DC) properties of loratadine-loaded zein nanoparticles processed into powders through freeze-drying, with the intention to include them in orally disintegrating tablets (ODTs) for paediatric use.

Materials and methods. Nanostructures were prepared through the antisolvent precipitation of an ethanolic zein/loratadine solution in aqueous media and lyophilised with mannitol or maltodextrin as cryoprotectants. The lyophilised powders on their own or mixed in a 1:2/2:1 ratio with three commercially available ODT excipients were subjected to dynamic compaction analysis under three different compression loads. The force/displacement curves recorded during the compression process, the tablet diameter and height, and its crushing strength were used to determine compression properties.

Results and discussion. ODTs with a 6 mm diameter, containing 2.5 mg (1:2 nanostructure powder/excipient ratio) or 5 mg (2:1 ratio) of loratadine were produced using all the co-processed excipients. The lyophilised powders on their own exhibited a high elastic recovery after compression, which was attenuated by the use of DC excipients. The ODTs exhibited tensile strengths between 1.2 and 5.6 MPa, which increased along with the compression load. The powders lyophilised with maltodextrin had better tabletability, leading to tablets with higher tensile strengths at lower compression pressures. However, these powders are harder to process because of their porosity, which impedes the quantitative filling of the die.

Conclusions. With the aid of directly compressible excipients that enhance the compression properties of powders, lyophilised nanostructures can be easily processed into ODTs. Further studies will establish the process parameters for the compression of tablets with an adequate quality profile.

The influence of multiple-dose oxcarbazepine on the metabolism of single-dose Aripiprazole – an *in vivo* experiment in rats

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Introduction. Antipsychotics and mood stabilizers are often administered together for psychiatric disorders. The latter are susceptible to polypharmacy and have a high risk of developing drug-drug interaction. Aripiprazole (ARI), a 3rd generation antipsychotic drug, is extensively metabolized by the CYP2D6 and CYP3A4 isoenzymes, while oxcarbazepine (OXC), an antiepileptic and mood stabilizer drug, analog of carbamazepine, is a mild-moderate inhibitor of the CYP3A4 isoenzyme.

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This study aimed to assess the possible presence of a pharmacokinetic interaction between ARI single-dose and OXC multiple-dose, as pretreatment, compared to ARI single-dose alone in rats.

Materials and methods. The in vivo experiment was carried out on two groups, consisting of 12 Wistar albino rats each. The control group was given a single oral dose of ARI 8 mg/kg body weight (b.w.), while the test group received oral OXC 80 mg/kg/day for 5 days followed by a single dose of ARI. An in-house developed and validated LC-MS/MS method was used to determine the plasma concentration of ARI and its active metabolite concomitantly and non-compartmental analysis was employed to determine their pharmacokinetic parameters.

Results. The body exposure to ARI did not change significantly after five-day OXC administration, but led to a decrease in its mean Cmax of 51.37% (239.67 ± 168.59 vs. 116.55 ± 70.33 ng/mL). The increase in the mean kel led to a significant decrease in the mean half-life of 1.51-fold for ARI, while for the metabolite, the mean total AUC increased by 44.66% and the mean apparent systemic clearance reduced by 61.84%.

Conclusion. OXC pretreatment determined some changes in the pharmacokinetics of ARI and its active metabolite in vivo. Clinical data should further establish the significance of this interaction in humans.

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Fused deposition modeling 3D-printing, a feasible solution in the manufacture of oral solid dosage forms for pediatric use

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Introduction. Pediatric patients need different doses compared to adults, and meeting these needs is a challenge. The purpose of the study was to investigate the feasibility of the three-dimensional (3D) printing technique of fused deposition modeling (FDM), for the preparation of solid oral dosage forms for children with adjustable doses and sizes.

Materials and methods. In this study, spironolactone was the model drug, mannitol, the plasticizer, and polyvinyl alcohol (PVA), the filament-forming polymer. For optimization, an experimental plan (DoE) was used with two factors (the percentage of mannitol and spironolactone) and three levels of variation. The filaments were prepared by thermoplastic extrusion and the printlets by using an FDM 3D printer. The mechanical properties of the filaments were assessed by the three-point bending test (3PBT) and the stiffness test (ST), and the printlets were pharmaceutically characterised.

Results. Following the mechanical characterization of the filaments, it was demonstrated that an increase in spironolactone concentration, from 5% to 25%, reduces the hardness of the filaments from 1800 to 200 g. The percentage of 5% spironolactone, without mannitol, gave the highest rigidity, 1800 N/mm. The N1

filaments (5% spironolactone, 95% PVA) and N8 (15% spironolactone, 15% mannitol, 70% PVA) had the highest printability score (score 4) and were uniform in appearance. They were selected for preparing printlets with diameters of 3.33 mm, 6.66 mm and 10 mm. Due to the possibility of miniaturisation, doses ranged from 0.5 mg to 8 mg for N1 and from 0.75 mg to 20 mg spironolactone for N8. In vitro dissolution tests showed that 3.33 mm printlets dissolved most rapidly. For N1, over 30% of the substance was released in the first 30 minutes, and for N8, over 40% in 15 minutes.

Conclusion. The results demonstrate the ease of dose adjustment through 3D printing.

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Development and characterization of self-adhesive polymeric films with antiallergic effect

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Introduction. Films for cutaneous applications are emerging dosage forms with high clinical potential. They are highly flexible, easily applied on the skin having an esthetic aspect due to their transparency. A drug delivery system providing sustained release of the active pharmaceutical ingredient (API) to the skin would be more advantageous than traditional dosage forms used in the local treatment of allergies. The aim of the present work was to design and characterize self-adhesive cutaneous films with antiallergic effect, using the experimental design (DoE).

Materials and methods. Diphenhydramine hydrochloride (DPH) was used as API, while Eudragit NM 30D, polyvinyl alcohol (PVA), polyacrylic acid (PAA), and polyethylene glycol (PEG), either 400 or 4000, were the polymers of choice. A full factorial experimental design with 3 factors and 2 levels was created. The factors were the PVA ratio, the PAA ratio and the type of plasticizer. The responses were: fracturability, first fracture deformation, adhesive force, and in vitro DPH release profile. 11 formulations were generated, prepared in 2 steps via solvent casting method, and characterized in terms of mechanical and adhesive properties, and in vitro DPH release profile.

Results. The first fracture deformation decreased by increasing PVA ratio and increased by increasing PAA ratio. The adhesive force was positively influenced by increasing the PAA ratio and by the presence of PEG 4000. On the contrary, PEG 400 decreased the adhesive force. No significant impact of the factors was observed on fracturability. The in vitro DPH release was strongly enhanced by increasing the ratio of PVA and by the presence of PEG 400. PEG 4000 negatively impacted the drug release. Cumulative DPH releases at 18 h ranged from 38.3% to 93.2% and best fitted the Peppas kinetics.

Conclusion. PVA ratio impacted the responses the most, followed by PEG 400 and PEG 4000. Further studies regarding formulation optimization will be conducted.

Characterization of some *Escherichia coli* strains from three wastewater treatment plants in Romania

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Introduction. Antimicrobial resistance (AMR) is a global public health threat, with the environment acting as a reservoir and transmission vector. Wastewater treatment plants (WWTPs) play a crucial role in filtering pollutants but also in reducing the spread of resistant bacteria. This study investigates the prevalence and resistance profiles of Escherichia coli from three WWTPs in Romania, highlighting the importance of monitoring these systems to prevent AMR dissemination.

Materials and methods. Samples were collected from influents and effluents of WWTPs A, B, and C in the central-western region of Romania in April and August 2023. Isolation and identification of E. coli were performed using standardised microbiological methods, and antimicrobial susceptibility was assessed by minimum inhibitory concentration (MIC) testing. Resistance genes were detected via multiplex PCR, targeting blaTEM, blaCTX, tetA, tetB, and sul1 genes.

Results. The analysis revealed a 50% prevalence of E. coli in wastewater samples, with a high proportion (83.34%) of isolates showing multidrug resistance. The highest resistance was observed for ampicillin (66.66%) and ticarcillin/clavulanate (50%). Resistance genes were frequently detected, with 50% prevalence for tetA, tetB, and sul1, associated with resistance to tetracycline and sulfonamides. The findings emphasize the role of WWTPs as accumulation and dissemination points for AMR in the environment. Compared to clinical resistance rates in Romania, the high AMR prevalence in WWTPs suggests a potential risk for spreading resistance genes to the population, highlighting the need for urgent monitoring measures and a One Health approach.

Conclusions. This study provides preliminary data on the antibiotic resistance profiles of E. coli from WWTPs in Romania, demonstrating the need for integrated monitoring systems across public health and environmental sectors to mitigate the effects of AMR.

Therapeutic drug monitoring implementation led by clinical pharmacist in intensive care and the observed benefits

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Introduction. Determining the blood concentrations of antibiotics with the aim of Therapeutic Drug Monitoring (TDM) should represent a standard of care in Intensive Care Units (ICU). Globally, TDM is recommended for aminoglycosides, beta-lactams, linezolid, teicoplanin and vancomycin in critically ill patient. This tool has a role in maximizing therapeutic response, decreasing the risk of adverse reactions, decreasing mortality, but also prolonging the life of antibiotics by decreasing bacterial resistance (1,2). The objective of the present study was to evaluate the impact of TDM program implementation for vancomycin in patients admitted in ICU.

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Material and method. Following the positive response from the hospital management and the medical analysis laboratory to the request to start the TDM program, the clinical pharmacist together with ICU doctors identified the patients that were prescribed intravenous vancomycin and the minimum, respectively minimum and maximum serum concentration were dosed. Area Under the Concentration-time curve (AUC) and the subsequent doses of the antibiotic were calculated. Retrospectively, we assessed how the initial doses required adjustment and percentage of patients who suffered a deterioration in kidney function. In addition, we compared the incidence of kidney function decline in patients enrolled in the TDM program with the incidence of kidney function decline in patients not enrolled in the TDM program during the study period.

Result. Between January 2023 - May 2023, 27 vancomycin serum determinations were performed in 10 patients, all after reaching steady-state concentration. This led to dose changes in most cases (60%), 46.66% in the sense of decreasing the dose, respectively 13.33% in the sense of increasing it. In the same period, we identified 23 patients with prescribed intravenous vancomycin that were not included in the TDM program. Kidney function alteration was observed in 20% of the TDM patients, compared to 57% of the patients that were not included in the TDM program.

Conclusions. TDM represents a tool in avoiding underdosing and overdosing, having a role in establishing the optimal dose of vancomycin and avoiding the occurrence of nephrotoxicity, respectively increasing the chance of therapeutic success in patients hospitalized in the ICU.

Effect of walnut (*Juglans regia L.*) consumption on cardiometabolic and anthropometric parameters in a healthy middle-aged caucasian population with metabolic syndrome risk: a randomized controlled trial

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Introduction. Cardiometabolic risk factors (CMRs), including obesity, dyslipidemia, dysglycemia, and hypertension, significantly contribute to cardiovascular disease, the primary cause of mortality worldwide. Recent research has shown that walnut (Juglans regia L.) consumption may exert a positive impact on cardiometabolic (CM) parameters. However, clinical data regarding the effects of walnuts on CMRs in healthy middle-aged people are still inconclusive. The aim was to evaluate the impact of walnut consumption on CM and anthropometric parameters in middle-aged individuals with metabolic syndrome (MetS) risk.

Material and method. The effects of walnut consumption on lipid profile, glucose metabolism, blood pressure, and anthropometric parameters were assessed in 22 individuals (± 48.81 years, 47.62% women) with MetS risk. There were two 28-day intervention sessions, separated by a one-month washout period in between. Participants were randomly assigned to receive either 45 g walnuts/day or control (no walnut). During all intervention periods, participants were advised to consume a weight maintaining diet.

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Results. 21 participants completed the intervention. The walnut intake showed improvements in several CM and anthropometric parameters compared to control, with clear decreasing trends in triglycerides, total cholesterol, low-density lipoprotein cholesterol, as well as waist and hip circumferences, but without statistically significant differences ($p < 0.05$) between groups.

Conclusion. Daily consumption of walnuts may be beneficial to middle-aged Caucasian adults at risk of MS, but daily consumption over a longer period of time is necessary for significant reduction in CMRs.

Comparative evaluation of two sample preparation methods for label-free qualitative profiling of human salivary proteome

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Introduction. Salivary biomarkers are increasingly being recognized as a non-invasive and convenient alternative for diagnosing and monitoring various diseases, especially in the study of neurodegenerative diseases. Regardless of the collection method, the quality of saliva sample preparation is crucial for reliable protein identification. Various sample preparation methods have been proposed, but no evaluation comparing commonly used techniques has been conducted so far. The aim of this study was to compare the in-solution procedure with the recent solid-phase enhanced sample preparation (SP3) technology and evaluate how various sample preparation factors influence the salivary proteome.

Material and methods. Unstimulated saliva was collected and pooled from 10 healthy adult volunteers. For each protocol, two different proteome isolation methods were tested: precipitation by methanol-chloroform (MeOH-Chl) procedure and incubation with trichloroacetic acid for 60 minutes (TCA60). The protein pellet was resuspended in 100µL Rapigest® 0.1% prepared in ammonium bicarbonate 50mM (R) or 8M urea/ 2M thiourea (UT). Protein concentration was determined by Bradford Assay prior to in-solution and on-bead digestion using trypsin. Samples were subjected to nanoLC-MS analysis and processed within dedicated MS platforms. Column loading, proteome coverage and digestion efficiency was further evaluated.

Results. Protein content relied on the isolation method rather than the buffer used, TCA60 isolation method being the most effective. Data processing showed that 400 ng protein on column using 45 min gradient in HDMSE gave the highest number of protein identifications. In-solution protocol identified the highest number of proteins (288) across all tested conditions compared to Sp3 (243), and the use of

TCA60R resulted in the highest number of proteins with a good protein digestion efficiency (full cleavage of ≈80.6%).

Conclusion. In the analysis of human saliva, the in-solution protocol employing TCA60R produced the greatest quantity of statistically significant proteins within the saliva pool, surpassing the results obtained with SP3.

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DENTAL MEDICINE

Dental implant infectious pathologies and maxillary sinusitis: review of literature

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Introduction. In our times, dental implants are increasingly used as a method of oral rehabilitation in edentulous areas due to their functionality, aesthetics and similarity with natural teeth. There are many situations in which residual alveolar bone is deficient and sinus augmentation techniques are used to improve bone quantity of the alveolar bone ridge in order to insert dental implants. Sinus augmentation techniques use different materials such as autografts, allografts, and xenografts placed into the sinus cavity. Numerous difficulties arise following sinus elevation procedures and implant insertion in these regions, even with well-established surgical treatment guidelines and case analyses: membrane perforation and the formation of an oro-antral fistula, acute and chronic rhinosinusitis, and facial congestion. Another issue that arose during the sinus lift augmentation procedure and implant insertion was the spread of the infection from a periimplantitis-affected implant to the grafted area into the maxillary sinus. Infectious conditions affecting the tissue around a functional dental implant include mucositis and peri-implantitis. Bacterial biofilm that forms around the intraoral components of dental implants is the cause of both illnesses. The purpose of this review study was to determine the relationship between sinusitis and peri-implantitis in order to increase awareness of the significance of surgical procedure protocol.

Material and methods. We answered the following question in this review article: What are the correlations between peri-implantar infectious diseases and maxillary sinusitis? Two independent co-authors conducted a systematic examination of the literature in five databases—PubMed, Embase, Web of Science, Scopus, and SpringerLink —to determine the answer to this issue. The search strategy involved different combinations of MeSH key words: “peri-implantitis”, “peri-mucositis”, “peri-implant mucositis”, “sinusitis”, “maxillary sinusitis”, (peri-implantitis) and (sinusitis), (peri-implantitis) and (maxillary sinusitis), (peri-mucositis) and (sinusitis), (peri-mucositis) and (maxillary sinusitis), (peri-implant mucositis) and (sinusitis), (peri-implant mucositis) and (maxillary sinusitis). The following filters have been applied: Article, Case reports, Classical Article, Clinical Study, Clinical Trial, Randomized Controlled Trial, English, French. The authors reproduced the same search strategy previously described for each of the 5 databases. After applying the inclusion and exclusion criteria and eliminating duplicates, we chose 12 articles from the 250 that were found.

Results. All the included studies, according to our analysis, showed a positive connection between peri-implant infectious illnesses and maxillary sinusitis. Other pathologies, such as abscesses, oro-antral communications, or foreign body reactions brought on by the migration of implant or bone graft materials, have also been documented, with peri-implant infectious diseases as their initial cause.

Conclusion. This comprehensive review brought to light the connections between sinus pathology and peri-implant illnesses as well as the significance of preventing infectious peri-implant diseases in order to prevent the development of these complications.

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Effects of acupuncture and related techniques in temporomandibular disorders (TMD): a systematic review

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Introduction. Acupuncture has shown promise as a therapeutic option in temporomandibular disorders (TMD). Benefits include pain relief, reduction of muscle tension and improvement of jaw function. Alternative approaches, including dry needling and laser acupuncture, are also reported to improve TMD symptoms. This review aimed to summarise the most recent studies available on alternative therapies for TMD.

Materials and methods. An electronic literature search was conducted in 3 databases (PubMed, Web of Science, and Scopus) in order to identify articles on acupuncture, dry needling, or laser acupuncture. Search development, process, and two-step article selection were conducted by independent researchers. Data was extracted regarding study characteristics, population characteristics, acupuncture techniques used, and diagnosis and effects assessment methods, and was synthetized in tables. Risk of bias assessment was conducted using the ROBINS-I tool.

Results. Out of 431 identified results, 20 were included. We identified 11 studies on acupuncture, 3 studies on laser acupuncture and 6 studies on dry needling. A number of 5 studies presented low risk of bias, 7 studies presented moderate risk and 8 studies high risk. Most studies showed improvement of TMD symptoms post-intervention, evaluated by pain assessment scales and maximum mouth opening. Short-term pain reduction was observed in all groups that received acupuncture therapy. Laser acupuncture significantly relieved pain in all studies, while dry needling showed immediate and long-term pain relief, improvement in jaw function and reduction in muscle tenderness, when compared to controls.

Conclusion. Acupuncture is promising as an alternative, minimally invasive treatment method for TMD. When compared to controls or placebo, acupuncture and related techniques result in significant relief of TMD symptoms.

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Characterization of newly synthesized nanobiomaterials for the treatment of early enamel lesions

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Introduction. White spot lesions represent a demineralization of the enamel with various etiologies, carious or non-carious. These lesions can be compensated minimally invasively by remineralization processes or by using an infiltrating resin, such as ICON, a commercial material with advantages and limitations. Modern dentistry strongly emphasizes minimally invasive treatments. Therefore, research for a material that can overcome the limitations of existing possibilities and offer the best results is continuous. This study

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aimed to characterize four novel nanobiomaterials by testing their biocompatibility and physicochemical properties compared with the commercial material ICON.

Material and methods. For this study, four recipes of nanobiomaterials were obtained: NB 3, NB 6, NB 3F, and NB6F. These recipes are composed of varying proportions of TEGMA, UDMA, HEMA, Bis-GMA, and HAF-BaF2 Glass. We assessed the following physicochemical characteristics: the flexural strength, using the three-point test; the water absorption and solubility; the number of fluoride ions released; the polymerization conversion and residual monomers by HPLC. For the biocompatibility assay, the viability (with the CCK8 viability kit) and apoptosis (Annexin V-FITC Cell Apoptosis Detection Kit and FACS analysis) were tested.

Results. The study results demonstrated that adding UDMA modifies the properties of the synthesized materials by increasing the strength and elasticity of NB3 compared to NB6. Additionally, NB3 showed the lowest water absorption and solubility due to its hydrophobic nature. Among the samples with fluoride additives (NB3F and NB6F), the highest amount of fluoride was released on day 7 by the material without UDMA, while the NB3F sample containing UDMA released the least amount of fluoride on day 7. In terms of polymerization, NB6 and NB6F showed the best polymerization potential. Quantitatively, NB3 and NB6F had the fewest residual monomers, while NB6 had the most. For the biocompatibility analysis, NB 3 and NB 6 demonstrated significantly higher cell viability compared to the commercial material ICON.

Conclusion. These findings suggest that NB 3 and NB 6 may offer better biocompatibility and less cytotoxicity than ICON. Depending on the composition of the material and the proportion of its components, the mechanical properties can be influenced, and based on the targeted clinical application, all these variations should be considered to achieve optimal results.

Comparative approach to dental occlusion by conventional and computerized methods

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Introduction. An accurate clinical assessment of the dental occlusion is essential in prosthodontic treatment. The methods used to record occlusal contacts have improved in recent years, most notably with the introduction of computerized technology into clinical practice. The study aimed to investigate the occlusal condition by determining the contacts between the teeth of both dental arches, by using conventional and computerized methods for analyzing static and dynamic occlusion.

Material and methods. Twenty-five subjects with a mean age of 35 years participated in the study. Subjects were divided into groups: group 1 (n=10) with natural dentition, occlusal relationships of class I Angle on canines and molars, absence of anterior orthodontic treatment and group 2 (n=10) with tooth-supported fixed protheses. Five subjects with untreated partial edentulous spaces and signs and symptoms of temporomandibular dysfunction were excluded. Subjects were investigated by conventional method A and computerized method B. The occlusal contacts were recorded in method A, by 40 and 200 μm articulating paper, whereas in method B, they were captured using T-Scan technology at the maximum intercuspation, propulsion and lateral movements.

Results. The most contacts were found in both group 1 and group 2 when marking the occlusal contacts with articulating paper in the maximal intercuspation position compared to those recorded with T-scan. In eccentric movements of the mandible, active and passive occlusal interferences and premature contacts were identified with both articulating paper and T-scan, with no statistically significant differences detected between the two methods.

Conclusion. The conventional method is an accessible method, available to every practitioner, while the computerized method can be used in dental offices endowed with superior technology. The conventional method provides qualitative information, while the computerized method enables the quantitative information, as such a balanced occlusal scheme can be ensured, thus preserving the longevity of fixed prosthetic restorations.

Integrating periodontal treatment into cardiac patients rehabilitation

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Introduction. Periodontitis is a chronic infectious and inflammatory condition affecting over half of the global population. It can lead to severe local issues, such as alveolar bone loss and tooth loss, and has systemic impacts due to large subgingival bacterial loads and inflammatory elements. Links have been identified between periodontitis and conditions like coronary heart disease and cerebrovascular diseases. However, the latest studies on the impact of periodontal treatment on cardiovascular health found inconclusive evidence on whether standard periodontal therapies can prevent cardiovascular diseases or reduce their severe outcomes in those with periodontitis. This study focused specifically on atherosclerotic cardiovascular diseases within the broader category of cardiovascular conditions. Its objective was to examine the overall impact of nonsurgical periodontitis treatment in patients diagnosed with both cardio vascular disease and periodontitis.

Materials and methods. The study included 11 patients with both severe periodontitis and cardiovascular disease, which were addressed to the Periodontology Department of Iuliu Haţieganu University of Medicine and Pharmacy by cardiologists. All patients included in the study had a medical history of cardiovascular diseases and all included patients benefited from a full-mouth periodontal examination (baseline) and at two months after completing mechanical subgingival instrumentation, based on the recommendations of current guidelines. Subsequently, all patients continued with additional therapy approaches as necessitated by their individualized treatment plans, which included lifelong supportive periodontal care.

Results. Periodontal treatment including supragingival hygiene and subgingival instrumentation did not induce significant modifications of the mean attachment level, but for moderate pockets (probing depth = 5 mm), there was a significant decrease in of their median values at two months follow-up moment. A significant amelioration of the oral hygiene and gingival bleeding scores was recorded at two months follow-up.

Conclusion. Nonsurgical periodontal treatment enhanced the condition of superficial periodontal tissues, leading to a reduction in local erythema, gingival swelling, and bleeding on probing.

Primary xanthoma of the mandible

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Bone xanthomas represent rare pathological entities typically associated with endocrine or metabolic disorders, particularly dyslipidemias. In the absence of systemic disease, these lesions are classified as primary xanthomas. Primary mandibular xanthomas are particularly infrequent occurrences. This report seeks to elucidate the clinical presentation and radiographic features of a primary mandibular xanthoma, while also exploring its epidemiological profile, potential pathophysiological mechanisms, and differential diagnostic considerations.

From tradition to innovation: how digital tools and artificial intelligence (AI) transform occlusal contact point analysis

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Introduction. In the dynamic field of dentistry, technological advancements like digital tools and artificial intelligence (AI) are redefining traditional practices. Occlusal contact point analysis, historically done using articulating paper, now benefits from digital alternatives such as intraoral scanners. This study investigates the comparability of these modern tools, specifically CEREC®, MEDIT®, and 3-SHAPE® with conventional methods, aiming to assess their impact on diagnostic accuracy and clinical efficiency. Objective: to evaluate the effectiveness of digital intraoral scanners compared to the conventional articulating paper method in accurately capturing occlusal contact points.

Material and methods. An observational study was conducted on ten participants, where occlusal contact points were analyzed using both digital and traditional methods. Data collection adhered strictly to protocols ensuring maximum intercuspidation, and each participant's occlusal contacts were assessed with both techniques to provide a thorough comparison.

Results. Our findings indicate no significant difference in accuracy between the digital intraoral scanners and the traditional articulating paper method. This outcome challenges the perceived superiority of conventional practices, suggesting that advanced digital tools are equally reliable.

Conclusion. The study highlights the potential of digital scanners and AI to enhance clinical efficiency and improve patient outcomes without sacrificing accuracy. These findings support the integration of digital innovations alongside traditional methods, paving the way for a more precise and patient-centered approach in occlusal analysis.

Nanotehnology - its applicability in the regeneration therapy of soft and bone tissues of the oral cavity

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Introduction. Nanotechnology is the science of developing, testing, and using nanoscale structures and molecules. What makes it valuable in medical sciences is the development of materials and instruments with high specificity that interact directly at the subcellular level. At the cellular or tissue level, these materials and instruments with high specificity could be transformed into targeted clinical applications with the greatest possible therapeutic benefits and the fewest possible side effects. The aime of this study was to review the literature and to provide a more detailed picture of recent advances of nanostructured materials in the process of regeneration of soft and hard tissues of oral cavity.

Materials and methods. Electronic search of the most relevant articles published in English between January 2018 and May 2023 was done in several databases, such as: PubMed, Embase and Web of Science. A total of 183 articles were discovered and examined, and only 22 articles met the inclusion criteria for this review.

Results. The findings of this study demonstrate that using nanoparticles can improve the mechanical properties, biocompatibility and osteoinductivity of biomaterials. The oro-dental sector is one of the many therapeutic contexts in which nanostructured materials are employed. In addition to provide structural support that is more like real tissue and permits the insertion of different substances, they can be utilized as carriers or deliverers of medications with targeted or delayed release. Additionally, they can be used in the treatment of periodontal disorders, tissue engineering, and the regeneration of soft tissues and bones.

Conclusion. The design and manufacturing of bone graft substitutes have advanced significantly in recent years due to advances in tissue engineering and nanotechnology, which also show great promise for treating bone problems. For many applications and treatments, the development of intelligent nanostructured materials is crucial because it enables the long-term, accurate administration of drug, which improves outcomes.

Assessment of the reproducibility of three digital intraoral scanners

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Introduction. This study aimed to examine the precision of three different intraoral scanners when registering a complete dental arch.

Material and methods. One examiner with more than five years of experience in dental clinical practice scanned the intraoral cavity of one patient (both upper and lower arches and occlusion) with three different scanners (3Shape-Trios 3, Sirona-PrimeScan, and PANDA smart). For each device, the recording has been performed five times. Reproducibility was evaluated by superimposing the five scans using a dedicated

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software (Geomagic Qualify). The total errors across the model's measurement sites have been recorded. The following measurements were generated: mean deviation, standard deviation, maximum and minimum deviation, and root mean square (RMS). The data were analyzed statistically using the Levene test, Kruskal-Wallis, and Anova.

Results. The results of the ANOVA test revealed that the variability between groups is greater than the variability within each group, having an F value of 5.12 and p = 0.048. This suggests the existence of statistically significant differences between the performances of the scanners. The p-value was <0.05, below the significance threshold. The Panda P5 demonstrated excellent reproducibility, delivering consistent and reliable measurements for both upper and lower arches, with an RMS (Root Mean Square) of 57.2 for upper scans and 73 for lower scans. TRIOS 3 (Sirona) demonstrated good reproducibility, particularly for upper impressions having an RMS error of 83.84 μm, lower than that for upper impressions, which was 97.06 μm. The mean error of Trios 3 was 52.18 μm for upper impressions and 64.13 μm for lower impressions. CEREC Primescan (Dentsply Sirona) showed a balanced performance, comparable to Trios 3, with an RMS error of 106.94 μm for the upper arch and 120.33 μm for the lower arch.

Conclusion. Panda P5 excelled in terms of reproducibility, offering consistent and reliable measurements for both the upper and lower arches. TRIOS 3 (3Shape) also demonstrated good reproducibility, with minimal variability, yielding results comparable to Primescan (Dentsply Sirona).

Occurrence of endodontic complications following caries in pits and fissures versus smooth surfaces on temporary teeth

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Introduction. Dental caries, a progressive and prevalent disease affecting deciduous teeth, poses a significant risk for endodontic complications, particularly influencing the development and eruption of permanent dentition. The location of caries, either in pits and fissures or on smooth surfaces, may impact the rate and likelihood of complications, necessitating a clearer understanding to improve treatment prioritization. This study explores how caries location influences the incidence of endodontic issues, aiming to provide insights that could optimize preventive care and intervention strategies in pediatric dentistry. The primary aim is to determine whether caries in pits and fissures lead to more frequent and rapid endodontic complications compared to smooth surfaces. By understanding this relationship, the study seeks to enhance clinical prioritization in treating caries, thereby minimizing the likelihood of complications and supporting effective dental care for children.

Materials and methods. This research was conducted on a cohort from "George Cosbuc" Elementary and Secondary School, representing the northern Transylvanian population of Cluj-Napoca, Romania. Data from 97 students aged 6 to 19, collected over five years, were analyzed for caries incidence across dental surfaces and correlated with demographic factors like gender and linguistic background. Caries incidence was documented per appointment, with data digitized and analyzed to track trends by surface location (occlusal versus smooth) and potential complications. Inclusion criteria involved student consent, parental approval, and consistent attendance, with information safeguarded

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for confidentiality.

Results. Findings indicated that caries on occlusal surfaces were more frequent and showed a higher tendency toward endodontic complications than those on smooth surfaces. The average incidence was 48.25 caries per occlusal surface compared to 2.05 per smooth surface, with occlusal caries leading to complications, such as remaining roots, more frequently. Demographic analysis revealed that females had slightly higher caries rates than males, and learned German speakers experienced higher caries incidences than native speakers, suggesting potential differences in dental care priorities or access. The study supports a marked susceptibility of pits and fissures to caries and subsequent complications. Increased appointment frequency correlated with reduced caries incidence, emphasizing the role of regular dental visits in caries prevention. Differences in caries incidence across gender and linguistic groups may reflect social or behavioral factors influencing dental health. The higher rate among non-native German speakers suggests a potential link between bilingualism and increased appreciation for dental care, meriting further investigation.

Conclusion. The research demonstrates that caries on occlusal surfaces of temporary teeth are more likely to lead to endodontic complications than those on smooth surfaces. These findings underscore the need for location-based prioritization in caries treatment, especially in pediatric dentistry, to mitigate the risk of complications. While valuable for the studied population, future research should expand sample size and scope to enhance generalizability and inform broader dental care practices.

Regenerative endodontic treatment methods for immature permanent teeth - systematic review

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Introduction. Pulp pathology in immature permanent teeth is increasingly concerning because traditional treatments like apexification help with healing but often result in short roots and poor crown-root ratios. Regenerative endodontic techniques (RET) offer a promising alternative, supporting normal root development and even pulp tissue regeneration.

Materials and methods. This systematic review was designed and conducted in accordance with PRISMA guidelines. A bibliographic search was performed in the PubMed database using specific keywords. Studies were selected based on inclusion and exclusion criteria guided by the PICO model. Data were verified and extracted with Microsoft Office Excel, then standardized and organized.

Results. A total of 627 articles were initially collected. Based on the inclusion and exclusion criteria, 30 relevant articles were chosen. After individually reviewing each article, 10 articles were included in this systematic review: 8 were conducted on human models with a total of 322 subjects (334 teeth), while 3 studies used animal models involving rodents (n=12), pigs (n=3), and dogs (n=6). This review highlights that RET shows greater clinical success than traditional apexification, with the ability to promote root maturation. Most studies favor blood clot-induced regeneration, supported by mesenchymal stem cells from the apical papilla. Recent research has focused on biomaterials like autologous membranes, growth factors, scaffolds, and stem cells. While primarily tested on animal

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models, these studies suggest that stem cells hold strong potential for regenerating pulp tissue.

Conclusion. Regenerative endodontics is an innovative treatment that could transform root canal therapy by stimulating the body's self-healing to promote root system regeneration with minimal invasiveness. While scientific challenges remain, ongoing advancements are bringing regenerative endodontics closer to practical clinical use.

Apatite-forming ability of an experimental bioceramic endodontic sealer in simulated body fluid

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Introduction. The materials used for root canal obturation play an important role in ensuring the long term success of the endodontic treatment. Biological properties of endodontic sealers are important, and bioceramic sealers demonstrate superior biocompatibility and bioactivity compared to traditional ones. In their interaction with radicular dentine a mineral layer, comprised of calcium phosphate or even apatite, has been observed at the dentine-sealer interface. This layer, referred to as the "mineral infiltration zone", positively influences the adhesion of bioceramic material to radicular dentine. The aim of this study was to evaluate the apatite-forming ability of a bioceramic experimental endodontic sealer based on calcium silicates.

Material and methods. Freshly prepared material was placed into six plastic molds and allowed to set for 3 days at room temperature, in a moist environment. After setting four samples were immersed in simulated body fluid (SBF) and incubated at 37o C and 100% relative humidity; two of these samples were kept for 7 days, and the remaining two for 14 days. For comparative purposes, two samples were not immersed in SBF. The apatite-forming ability of the experimental bioceramic endodontic sealer was evaluated using XRPD, SEM and EDS analysis.

Results. XRPD analysis identified apatite crystals on material's surface after both 7 and 14 days of immersion in SBF. SEM images displayed the specific microstructure for bioceramic materials alongside with the presence of apatite crystals on their surface, while EDS analysis confirmed the presence of calcium and phosphorus.

Conclusion. The interaction between the experimental bioceramic endodontic sealer and SBF successfully promoted apatite precipitation on its surface, highlighting its potential for biomineralization.

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Effects of occlusal splint and manual therapy on condylar remodeling and skeletal changes in temporomandibular disorders

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Introduction. Temporomandibular disorders (TMD) can involve degenerative changes in the temporomandibular joint (TMJ), such as condylar erosion and subchondral cysts. Occlusal splints and cranio-mandibular manual therapy, either alone or in combination, are conservative treatments aimed at reducing pain and symptoms in TMD. This study evaluates condylar and skeletal changes after occlusal splint and cranio-mandibular manual therapy in TMD patients using cone beam computed tomography (CBCT).

Material and methods. A retrospective cohort study analyzed 24 TMD patients who received combined therapy until symptoms subsided. Pre- and post-treatment CBCT scans assessed osseous changes in condyles. Key skeletal measurements, including Sella-Nasion-A point (SNA), Sella-Nasion-B point (SNB), A point-Nasion-B point (ANB), Condylar angle, and anterior/posterior facial heights (AFH, PFH), were taken from CBCT-generated cephalograms. Statistical analysis was conducted using paired t-tests, Wilcoxon rank-sum tests, and McNemar and Stuart-Maxwell tests.

Results. Combined therapy lasted 7.42 ± 3.27 months, with 63.6% (21 of 33) of TMJs with degenerative changes showing significant remodeling ($p < 0.05$). Post-therapy, SNB decreased significantly from 75.61° to 74.82° ($p = 0.02$), ANB increased from 4.05° to 4.8° ($p < 0.001$), AFH increased from 112.85 mm to 115.3 mm ($p < 0.001$), PFH/AFH ratio decreased from 64.17 to 63 ($p = 0.012$), and condylar angle increased from 140.84° to 144.42° ($p = 0.007$).

Conclusion. Combined therapy facilitated significant condylar remodeling in degenerative TMJ, alongside skeletal adaptations such as mandibular retrognatism and increased facial height. Condylar remodeling should be a consideration in TMD treatment planning, and skeletal/dental parameters should be assessed before initiating occlusal splint therapy.

The influence of layering techniques and the use of dental operative microscope on the quality of direct restorations of proximal walls

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Introduction. The purpose of this study is to determine whether magnification and specific layering techniques result in superior restoration quality in terms of marginal adaptation, morphology, and overall integrity.

Material and methods. Eighty typodont molars were divided into two groups:

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direct vision and magnification. Each group was further divided into four subgroups based on layering techniques (Single Layer + Co-polymerized flowable, Single Layer + Prepolymerized flowable, Oblique + Co-polymerized flowable, Oblique + Prepolymerized flowable). Four independent observers assessed the restorations using a quantitative scoring system based on four criteria: proximal wall anatomy, mesial ridge anatomy, marginal sealing and surface texture.

Results. Under direct vision, significant differences in restoration quality were observed between groups, with the single-layer technique combined with prepolymerized flowable yielding the highest score (3.42±0.4). Conversely, no significant differences were found among the layering techniques under magnification, indicating a reduction in technique sensitivity. Additionally, there was no notable difference in restoration quality between direct vision and magnification conditions.

Conclusion. The results suggest that while layering techniques significantly impact restoration quality under direct vision, magnification may help standardize outcomes across different techniques. Future research should further explore these techniques and the role of magnification in clinical settings to enhance restorative outcomes.

Necrotizing sialometaplasia - the mimicker of malignancy

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Introduction. Necrotizing sialometaplasia (NS) is a benign inflammatory disease of the salivary glands, capable of mimicking malignancy. It is usually found in the palate, but can be found in any salivary gland, including the parotid gland. Several cases were reported in the literature, affirming its close resemblance to squamous cell carcinoma and mucoepidermoid carcinoma. Starting from a histopathological misdiagnosis, unnecessary or inappropriate therapy could be conducted by the clinicians.

Material and methods. A 23-year-old female was referred to our department for a second opinion after a primary surgery for a squamous cell carcinoma located in the left parotid gland. The patient was scheduled for radiotherapy in the following week. The patient noticed the lesion 6 months ago, as a ½ cm lump in the left parotid gland, with progressive growth to approximately 1.5 cm in 2 months. The firm parotid tumor was painful on palpation.

Two months later, after the initial oral and maxillo-facial exam, the CT and MRI imaging revealed a left parotid gland tumor of 20/18/25 mm with a mixed, parenchymal and cystic component, with diffusion restriction and inhomogeneous contrast uptake at the level of the solid component.

An open biopsy of the parotid gland tumor confirmed the diagnosis of squamous cell carcinoma of the parotid gland. One month later, the PET-CT showed FDG - avidity within the primary tumor and a few cervical lymph nodes, supporting an ongoing oncologic process. The patient underwent superficial parotidectomy and selective neck dissection (level II and III). The histopathological report showed a well differentiated squamous cell carcinoma measuring 20/15 mm (ap/cc), diffusely positive imunohistochemic staining (p63, CK 5/6, CK7), and 30 lymph nodes without metastatic spread. The patient was referred for oncologic treatment.

Results. Given the rare occurrence of primary squamous cell carcinoma in the parotid gland, and following a detailed clinical and imaging assessment, a second

histopathological review was advised by our surgical team. This re-evaluation, prompted by our awareness of the tumor's rarity and clinical findings, ultimately concluded that the lesion was not squamous cell carcinoma but necrotizing sialometaplasia.

While initial imaging studies (ultrasound, CT, MRI) often raise suspicion of malignancy due to the tumor-like appearance of NS lesions, these modalities also help localize the lesion, delineate its extent, and evaluate surrounding structures. Specific imaging features, such as areas of necrosis, surrounding inflammation, and potential lack of aggressive characteristics, can offer clues pointing towards NS. While gallium scintigraphy might suggest a non-malignant etiology, the definitive diagnosis of NS often relies heavily on histopathological assessment. Nevertheless, careful interpretation of imaging findings is a valuable tool to guide diagnostic workup and support an accurate diagnosis, potentially reducing the need for invasive biopsies or unnecessary surgical interventions.

Conclusion. Necrotizing sialometaplasia (NS), though self-limiting, can be easily mistaken for a malignant tumor. Careful examination of preoperative MRI findings is crucial for identifying potential NS features and preventing unnecessary treatment. If the parotid gland lesion appears more consistent with NS, a conservative „wait and see" approach may be appropriate, given its potential for spontaneous resolution within 3-12 weeks. If surgery is required, a thorough histological assessment using established guidelines will confirm the NS diagnosis.

Exploration of the prosaic atmosphere of the University Clinics Complex in Cluj-Napoca

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Introduction. More than a century after their establishment, in the late 1800s, the university clinics continue to shape the landscape of the Claudiopolis citadel. Characterized by a pavilion-style architecture inspired by Vienna, they serve as a reference point in the Romanian medical landscape. Aspects such as the impressive variety of specialized museum collections and the beautifully paradisiacal green spaces associated with the clinics create an environment for medical and educational activities that competes against the most select metropolis in the world. This study aims to promote and conserve the material, scientific, and cultural heritage of the region within the context of European universality.

Material and methods. In this study, the following resources were consulted and analyzed: specialized literature, period images, and accounts from personalities related to this field. The research is focused on the particularities and rationale behind the construction of the complex in order to identify its correlation with the needs of the population over time.

Results. The research findings indicate that giving meticulous attention to heritage represents an additional asset in terms of promoting and enhancing the visibility of this invaluable legacy.

Conclusion. An analysis of the past outlines useful conclusions by identifying issues and gaps in the implementation of cultural and public health policies. Only in this way can we ensure the conditions necessary to overcome these obstacles, thereby improving performance in the sectors referenced in this study. Lastly, it is worth noting that the tradition of Western countries in researching medical-pharmaceutical history serves as a genuine lesson from which the entire Romanian society should draw in order to ensure its

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own spiritual and material advancement.

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X ray interaction with the oral cavity by means of SERS analysis of saliva

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Introduction. In this study, Surface Enhanced Raman Spectroscopy (SERS) has been employed for the analysis of the salivary composition modifications before and after patient exposure to X rays. This technique has enormous benefits, offering the possibility to compare samples from the same donor. Therefore, some relevant salivary biomarkers and their diagnostic potential were investigated. A broader perspective on biological effects of X-rays could be obtained by evaluating the actual differences between the two imaging techniques under discussion. It is widely known that in the case of Cone Beam Computed Tomography (CBCT) the irradiation dose is lower compared to Computed Tomography (CT).

Material and methods. A total of 15 patients underwent a CT investigation, respectively 15 patients underwent a CBCT imaging investigation. From each patient, a 2 mL saliva sample was collected before exposure and a 2 mL sample after performing the CT or CBCT imaging technique. The samples were processed and stored until the time of SERS analysis.

Results. Overall, there is a significant increase in all vibrational bands present in the spectra of the samples measured post-irradiation as compared to pre-irradiation ones. Given that these bands have been assigned to the presence of specific biomolecules that have the potential to be considered salivary biomarkers (thiocyanate, opiorphin) for a broad range of pathologies, the intensity of these band has been analyzed and compared for each single sample.

Conclusion. The present study proves that SERS can be successfully used in the detection of molecular changes in saliva as a consequence of direct interaction between X-rays and the oral cavity.

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The relation between self-perceived dental aesthetics and self-esteem

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Introduction. This study evaluated the relationship between self-perceived dental aesthetics, self-esteem, and dental habits in a dental student sample from the Faculty of Dental Medicine.

Material and methods. A cross-sectional survey involving a sample comprising 172 1st and 2nd-year dental students from the programs taught in English and French languages within the Faculty of Dental Medicine of Cluj-Napoca, Romania has been conducted. The mean age of the subjects was 20.43, and the gender distribution was 41.3% male and 58.7% female. The Psychosocial Impact of Dental Aesthetics Questionnaire (PIDAQ), the Rosenberg Self-Esteem Scale (RSES), together with dental habits assessment questions and socio-demographic information in both English and French versions, were applied to the two samples, in pencil and paper self-completing format. Informed consent was obtained from each participant beforehand. Subscale and overall questionnaire scores were computed and used for statistical procedures (Pearson's correlations and t-test), investigating correlations between self-perceived dental aesthetics and self-esteem and differences between the concepts concerning the study year and gender.

Results. The overall mean PIDAQ score was 16.56 (n=172), while the overall mean RSES score was 32.71 (n=172). For both study lines, the Dental Self-Confidence PIDAQ subscale registered the highest score, indicating the highest perceived impact at this level. Statistically significant small correlations were identified between the RSES overall score and the Social Impact (r=-0.219, p=0.04), Psychological Impact (r=-0.175, p=0.22), Aesthetic Concern (r=-0.228, p=0.03) PIDAQ subscale scores, as well as the PIDAQ overall score (r=-0.208, p=0.06). The t-test revealed statistically significant differences for the Social Impact PIDAQ subscale scores t (165.16)=-2.083, p=0.39, with respect to the year of study; furthermore, statistically significant RSES overall score differences, regarding the variables gender t (170)=1.998, p=0.47 (M>F) and year of study t (170)=-2.429, p=0.16 (2^{nd}>1^{st}), were registered.

Conclusion. The current study highlighted a statistically significant relation between students' self-perceived dental aesthetics and self-esteem and statistically significant differences between these concepts concerning gender and year of study.

Comparison of the marginal adaptation between CAD/CAM and printing-pressed lithium disilicate crowns

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Introduction. The purpose of this study was to compare the marginal adaptation of printing-pressed lithium disilicate crowns with that of computer-aided design/computer-aided manufacturing (CAD/CAM) lithium disilicate crowns.

Material and methods. The study included 20 healthy premolars extracted for orthodontic purpose. The teeth were prepared for the monolithic crowns; they were scanned and divided into 2 groups. In group 1, the crowns were printed with a resin, and then they were pressed whereas in group 2, the crowns were fabricated by means of the milling technique. The crowns from both groups were cemented on the abutment teeth. Measurements of the marginal adaptation under SEM microscopy followed.

Results. The statistical analysis shows that the best values of the marginal adaptation were obtained for the buccal and oral tooth surfaces, being between 90% (printing-presses) and 95% (milling).

Conclusion. Lithium disilicate crowns fabricated by CAD/CAM provided a better marginal adaptation than those fabricated by printing-pressed, but both fabrication methods provided crowns with a clinically acceptable marginal adaptation.

NURSING AND HEALTH SCIENCES

Renal tubular acidosis - management strategies

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Renal tubular acidosis (RTA) occurs when the kidneys are unable to maintain normal acid-base homeostasis because of tubular defects in acid excretion or bicarbonate ion reabsorption. Using an illustrative clinical case, we aim to describe the main types of RTA observed in clinical practice and to provide an overview of their diagnosis and treatment. The three major forms of RTA are distal RTA (type 1; characterized by impaired acid excretion), proximal RTA (type 2; caused by defects in reabsorption of filtered bicarbonate), and hyperkalemic RTA (type 4; caused by abnormal excretion of acid and potassium in the collecting duct). Type 3 RTA is a rare form of the disease with features of both distal and proximal RTA. Accurate diagnosis of RTA plays an important role in optimal patient management. The diagnosis of distal versus proximal RTA involves assessment of urinary acid and bicarbonate secretion, while in hyperkalemic RTA, selective aldosterone deficiency or resistance to its effects is confirmed after exclusion of other causes of hyperkalemia. Treatment options include alkali therapy in patients with distal or proximal RTA and lowering of serum potassium concentrations through dietary modification and potential new pharmacotherapies in patients with hyperkalemic RTA including newer potassium binders.

Integrating kinetic rehabilitation techniques to optimize early recovery in Intensive Care Unit patients

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Introduction. ICU-acquired weakness (ICU-AW) is a prevalent condition among critically ill patients, affecting over 40% of ICU cases. ICU-AW encompasses critical illness myopathy, critical illness polyneuropathy, or a combination of both. This condition typically arises from factors such as multiple organ failure, sepsis, prolonged sedation, and extended mechanical ventilation. Clinically, ICU-AW is characterized by generalized muscle weakness, predominantly affecting the limb and respiratory muscles while sparing the facial and ocular muscles. This muscle weakness, often linked to prolonged mechanical ventilation, results in decreased functionality and a reduced contractile capacity of muscle fibers. Early mobilization, ideally within the first 72 hours following ICU admission, is recommended to prevent muscle degradation and improve patient outcomes. This study seeks to identify and evaluate kinetic interventions for early mobilization, grounded in current medical guidelines, to optimize rehabilitation strategies in ICU settings.

Material and methods. An electronic search of the PubMed database was conducted to identify studies published between 2021 and 2024. The search strategy employed keywords such as "intensive care unit," "early mobilization," "early ambulation," and "early rehabilitation." Of the initial 603 articles retrieved, 52 met the inclusion criteria following the application of filters and removal of duplicates. From these, 9 articles were selected for qualitative analysis.

Results. Early mobilization through various physical rehabilitation methods, including specific positioning techniques such as verticalization therapy, supine positioning, passive and active mobilization, supine cycling, bedside sitting, and active transfers to a chair, has been demonstrated to improve outcomes in heterogeneous populations of ICU patients. These interventions are implemented to maintain joint mobility, enhance muscle tone in both upper and lower extremities as well as the respiratory musculature, improve balance and postural stability, promote early gait reeducation, and increase the patient's functional endurance capacity. Before initiating early mobilization sessions, a thorough assessment of patient safety is crucial, particularly focusing on respiratory parameters (such as the presence of an endotracheal or tracheostomy tube, SpO2, FiO2, and PEEP) and cardiovascular stability. These precautions ensure that mobilization interventions are both safe and beneficial within the critical care environment.

Conclusions. Early mobilization, involving both active and passive approaches is essential for reducing the prevalence of intensive care unit (ICU)-acquired weakness and delirium, as well as for improving patient functional outcomes. Evidence indicates that initiating mobilization within the first 24 to 72 hours of ICU admission is associated with optimal therapeutic benefits. The choice of specific kinetic interventions is carefully tailored to the patient's clinical condition and is governed by principles of progressive adaptation and strict adherence to medical guidelines and recommendations.

RESEARCH CENTERS

Combined quantum chemistry and ultrasensitive vibrational spectroscopy analysis of nanoscale interactions established between CB[7] and atenolol enantiomers

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Introduction. In this study we have employed quantum chemistry calculations combined with Surface-Enhanced Raman Spectroscopy (SERS) analysis of the host-guest complexes in order to investigate the nanoscale interactions between CB[7] macrocycle and R/S-Atenolol enantiomers.

Material and methods. Molecular geometry optimizations and Raman spectra calculations have been performed using the Gaussian 16, revision C.01 software package engaging density functional theory (DFT) with the wB97XD exchange functional. The supramolecular systems were prepared at 1:1 stoichiometry ratio by mixing equivalent volumes of CB[7] solution with each atenolol enantiomer solution. For SERS analysis these mixtures were incubated with fresh prepared silver nanoparticles.

Results. According to DFT simulations, stable complexes with similar energies of interaction were formed. SERS spectra reflect that Raman signal is more amplified for 1 mM concentration as compared to 0.1 mM. Moreover, the shape of the 1 mM spectrum of macromolecular complexes resembles the CB[7] spectrum. R-atenolol@CB[7] system presents a slightly increased amplification of vibrational bands intensities as compared to S-atenolol@CB[7].

Conclusion. RUA@CB[7] conformers resulted to have an increased stability due to the four H-bonds established between R-Atenolol and CB[7] as compared to S-enantiomer. SERS measurements were able to experimentally prove this very slight affinity of CB[7] macrocycle for R-Atenolol. Furthermore, concentration plays a major role in this regard. We believe that understanding nanoscale molecular interactions analysis can support chiral discrimination applications.

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Liposome internalization mechanisms in non-adherent cells for enhanced targeted drug delivery – a preliminary study

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Introduction. Liposomes are widely used in clinical drug delivery due to their biocompatibility, drug encapsulation capacity, and potential for functionalization to target specific cells. Understanding the internalization pathways is crucial to optimize targeted therapies. Visualizing liposome uptake and internalization mechanisms supports their development for delivering cytotoxic compounds, with promising implications for targeted treatments in hematologic cancers and other suspension cell-related diseases.

Material and methods. This study involved a solvent evaporation synthesis method of liposomes, followed by a rigorous purification involving both filtration and dialysis. The lipidic nanoparticles were characterized by DLS/Zeta potential analysis, TEM, Raman and confocal microscopy. Liposomes internalization in non-adherent cells was assessed in the presence or absence of endocytosis inhibitor dynasore hydrate.

Results. The results of this study show the successful synthesis of 100-200 nm liposomes. Moreover, a method to visualize the internalization of these nanoparticles in non-adherent cells via confocal microscopy was optimized. We highlighted an active liposome internalization mechanism that was mostly blocked when cells were incubated with an endocytosis inhibitor. This provides important information on the interaction between these liposomes and non-adherent cells showing the potential of liposomes as effective carriers of cytotoxic compounds

Conclusion. This study provides important insights on the interaction between the liposomes and non-adherent cells, focusing on their uptake. The preliminary data provide a valuable foundation for further studies using cytotoxic compounds-loaded liposomes, advancing potential clinical applications in targeted therapies for cancers with suspension cell types.

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Real-life demographic landscape of congenital hemophilia in Romania

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Introduction. Hemophilia Type A is a genetic disorder characterized by the inability of blood to clot properly, leading to excessive bleeding. Acquired hemophilia (AH) is a rare disorder characterized by bleeding in patients with no personal or family history of coagulation/clotting-related diseases. Hemophilia A is the most common type of

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hemophilia, affecting about 1 in 5,000 males globally. Inv 22 is detected in approximately 50% of individuals with severe Hemophilia A, while inv 1 in less than 5%. This research will provide valuable insights into the mutation spectrum of Hemophilia A.

Material and methods. RNA seq - Small RNA Seq libraries were generated using the 'TrueQuant smallRNA-Seq Kit' for ultra-low input material by GenXPro GmbH in Frankfurt, Germany. LDPCR for Inv 22 –100 ng of gDNA was further used for LDPCR reaction using specific primers and using Expand Long Range dNTP Pack with 7-dazsa dGTP nucleotides. Inv 1 detection: The DreamTaq MasterMix 2x (Thermo) was used for amplification with a specific mix of three primers.

Results. Our study identified HBA1-201 as a common modified protein in patients with Acquired Hemophilia, distinguishing it from both severe and mild Hemophilia A, suggesting a potential biomarker for this acquired condition. Additionally, we detected 13 positive cases of inv 22 and 1 case of inv 1 in male patients with Hemophilia A. These findings highlight the importance of genetic testing in diagnosing Hemophilia A and acquired hemophilia.

Conclusion. Future studies should also explore the role of other genetic variants and their clinical implications, as well as expanding the analysis to a larger cohort for a more comprehensive understanding of hemophilia genetics in the Romanian population.

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Markers of senescence detected in mesenchymal stromal cells as a result of the bone marrow microenvironment alteration induced by myelodisplastic cells

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Introduction. Mesenchymal stromal cells (MSCs) possess the potential to differentiate into osteogenic and adipogenic lineages. However, senescent MSCs present altered differentiation patterns, favoring adipogenesis. The age-related shift toward adipogenic differentiation within the bone marrow not only compromises the physiology of the microenvironment and disrupts local homeostasis but also disturbs hematopoiesis, resulting in a myeloid bias. Given the potential impact of frequent age-associated mutations on the fitness of the bone marrow niche cells, the aging of MSCs may promote inflammation by enhancement of hematopoietic support (upregulation of prosurvival/proinflammatory signals), clonal hematopoiesis and myeloid skewing, potentially contributing to the development of myeloid cancers.

Material and methods. Primary bone marrow-derived MSCs and the BJ stromal cell line (100 k) were cultured in 6-well plates with or without the MDS-L (myelodysplastic syndrome-L) cell line (100 k) and subsequently treated by radiation (XRT), doxorubicin (DOXO) or DOXO + azacytidine (AZA) in different concentrations 0.10 μM / 0.25 μM to induce senescence. In total, 10 senescence markers were analyzed: CDKN1A, CDKN1B, IL1A, IL1B, IL6, IL8, TGF-β, FGF7, MMP1, MMP3 and a housekeeping gene (GAPDH).

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Results. We depicted senescence by morphologic analysis using SA-beta-Gal staining, colony forming unit assays (CFU-F), cell cycle analysis, and increased expression of p21/p16. Primary MSCs entered senescence in a more visible manner than the immortalized BJ cell line. Analyzing a panel of cytokines related to a senescence-associated secretory phenotype, we can conclude that MDS cells slightly induced senescence of MSCs.

Conclusion. More investigation at molecular level is needed to prove the impact of myelodysplastic cells on the bone marrow microenvironment, more precisely on primary MSCs from the hematopoietic niche.

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"Lazarus Response" when feto-maternal microchimerism kicks in: spontaneous remission in refractory primary mediastinal B cell lymphoma following twin pregnancy

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Introduction. Partial or complete reduction of a cancerous pathology in the absence or with insufficient treatment, known as spontaneous remission (SR), is a rare and poorly understood phenomenon. However, emerging scientific evidence suggests that immune modulations may be involved in this process. Feto-maternal microchimerism involves the transfer of fetal cells into maternal circulation during pregnancy, which influences the outcomes of cancer. This study aims to present a case of SR of refractory primary mediastinal large B-cell lymphoma (PMBCL) in a young woman during twin pregnancy and evaluate the potential role of feto-maternal microchimerism in the tumor remission.

Material and methods. Case report: the 27-year-old female subject was diagnosed with stage II PMBCL, refractory to two lines of chemoimmunotherapy. Following therapy failure, she became pregnant with twins and refused treatment termination. Genetic analysis: performed on blood samples collected during pregnancy and four years postpartum and PCR amplification was used to detect SRY gene, a feto-maternal microchimerism marker.

Results. The patient underwent full metabolic remission of lymphoma during pregnancy, sustained for 4 years. PCR revealed low-level feto-maternal microchimerism during pregnancy, indicated by the detection of SRY gene, and was absent in post-pregnant samples.

Conclusion. This case supports a plausible association of feto-maternal microchimerism and SR of malignancy. The observed remission during pregnancy suggests that fetal cells may have contributed to immune-mediated tumor control, warranting further investigation into the clinical applications of microchimerism in oncology.

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Changes in inflammatory status in patients with obesity who underwent gastric sleeve surgery

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Introduction. Obesity is a complex condition characterized by excessive body fat accumulation. This condition has reached epidemic proportions globally and it's associated with various molecular characteristics that contribute to its pathophysiology, among which chronic inflammation is widely recognized. Obesity is associated with numerous serious health complications, including type 2 diabetes, cardiovascular diseases and cancer. Thus, there is increasing focus in healthcare on methods of combating obesity, among which gastric sleeve surgery has shown significant efficiency in weight loss. The aim of the study was to investigate the molecular aspects of inflammation in individuals with obesity compared to those with a normal BMI, as well as to evaluate the inflammation status of a smaller subset of obese participants three months post-sleeve gastrectomy.

Material and methods. In the study were included individuals with normal BMI, patients with obesity who did not undergo gastric sleeve surgery and patients who underwent gastric sleeve surgery 3 months prior the study. The research utilized standard blood tests for overall comparison and plasma for measurements by ELISA of proinflammatory cytokines and proteins that are integral to immune and inflammatory regulation.

Results. The findings indicated a notable kinetic response following bariatric surgery, particularly in the levels of IL-18, MCP-1, and PD-L1. Both IL-18 ($p = 0.006$) and MCP-1 ($p = 0.035$) were significantly elevated in the obese cohort compared to the control group, while levels in the follow-up group were markedly lower. Moreover, there was a significant reduction in circulating PD-L1 levels in the obese group compared to controls ($p = 0.049$), with an increase observed after sleeve gastrectomy.

Conclusion. This research provides valuable insights into the interplay between inflammation, obesity and effect of sleeve gastrectomy, highlighting potential implications for the management of bariatric patients.

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Amino acids and acylcarnitines profiles in chronic kidney disease patients

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Introduction. Chronic kidney disease (CKD) significantly impacts global health, affecting almost 10% of the population and ranking as the third-fastest growing cause of death. High therapy costs make early detection of CKD a priority, considering that the current assessment methods are limited. This study aimed to examine alterations in plasma amino acids and acylcarnitines in CKD patients compared to healthy controls, to better understand their metabolic implications in this disease.

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Material and methods. Plasma specimens obtained from of 42 patients diagnosed with CKD at various stages, including individuals on hemodialysis, were analyzed and compared to 71 plasma specimens from healthy controls, with the aim to evaluate alterations in amino acids and acylcarnitines. To achieve this, a widely implemented sample preparation technique employing HCl-butanol as derivatizing agent was utilized. Following extraction and derivatization, the compounds were analyzed via FIA-MS/MS using an ACQUITY UPLC I-Class PLUS/Xevo TQ-XS IVD System.

Results. Out of 114 targeted metabolites, 94 have been statistically different between the two groups (p value <0.05, FDR) and a substantial number of 33 compounds being upregulated at least two times in CKD group than in control group. Remarkably, methylhistidine was found to be one of the amino acids with the highest statistical difference and fold change, along with short and medium-chain dicarboxyl-acylcarnitines, such as C3DC-carnitine, C5DC-carnitine, C6DC-cartine and C8DC-carnitine.

Conclusion. In conclusion, plasma levels of methylhistidine and dicarboxyl-acylcarnitines were identified as the most modified among the two groups. Further studies are required to gain a more comprehensive understanding of the broader implications of these findings in CKD patients.

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Comparative analysis of derivatized and underivatized mass spectrometry techniques in newborn screening

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Introduction. Worldwide, newborn screening laboratories use tandem mass spectrometry (MS/MS) to analyze amino acids (AA) and acylcarnitines (AC). While the derivatized sample preparation method [1] that chemically enhances analytes to improve detection is widely trusted, underivatized assays available in specialized commercial kits are gaining interest [2]. This study evaluates interlaboratory reproducibility between two laboratories using the butanol-HCl derivatized method, followed by a comparison of the derivatization method and the underivatized MassChrom® Kit across 1504 dried blood spot samples (DBS).

Material and methods. 276 DBS samples were analyzed by FIA-MS/MS using a derivatization method that requires butanolic-HCl extraction in two different laboratories (Romania and Iceland), within the same timeframe. Furthermore, AA and AC from 1504 DBS samples were extracted using a commercial kit provided by ChromSystems (MassChrom® underivatized) and the in-house method (derivatized). All samples underwent flow injection analysis with an ACQUITY UPLC I-Class PLUS/Xevo TQ-XS

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IVD System.

Results. The reproducibility of an in-house method was assessed by comparing results from 276 DBS samples across two labs, yielding consistent analyte values. Moreover, both the derivatized and underivatized methods successfully identified abnormal values, after comparing the results obtained from the 1504 DBS samples, using individual cut-off values for each method. Furthermore, a case of elevated 3-hydroxyisovalerylcarnitine (C5OH) was detected, highlighting the efficacy of the derivatization method in differentiating isobaric compounds such as methylmalonylcarnitine (C4DC) and C5OH.

Conclusion. While underivatized techniques offer a safer and potentially easier alternative to derivatization by avoiding harmful reagents and complex sample preparation in newborn screening, they also come with limitations, notably in differentiating isobaric acylcarnitines. Therefore, laboratories need to balance these methods within their screening practices, keeping in mind the comparability of the results obtained.

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Pilot study of newborn screening for inborn errors of metabolism using tandem mass spectrometry in Romania

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Introduction. Newborn screening (NBS) using tandem mass spectrometry (MS/MS) is an advanced tool that enables early diagnosis of nearly 50 inherited metabolic diseases from a single dried blood spot (DBS), allowing for prompt treatment initiation [1]. In Romania, newborn screening began in the late 1990s with the screening for phenylketonuria (PKU) using a fluorometric method. A few years later, it became part of the National Screening Program that currently screens for three genetic disorders: PKU, congenital hypothyroidism [2], and more recently, cystic fibrosis.

Material and methods. A total of 19,680 infants born in 11 counties between November 2023 and April 2024 were screened for amino acids, organic acids and fatty acid oxidation disorders. The DBS samples were provided by 3 out of 5 Regional Screening Laboratories and the compounds of interest were further extracted using a commercial kit provided by ChromSystems (MassChrom® underivatized). The samples underwent flow injection analysis with an ACQUITY UPLC I-Class coupled to a Xevo TQ-XS IVD System.

Results. Out of 57 cases with abnormal values, the most common findings were low free carnitine (10 cases), elevated propionyl-carnitine (7 cases), and elevated phenylalanine (5 cases). Two cases of PKU were confirmed, one being a false positive, and further testing with second-tier and molecular methods is required for the remaining 54 cases. Thirty-five percent of abnormal results were from premature infants, for whom a second sample could not be obtained, potentially leading to false positives.

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Conclusion. NBS using mass spectrometry enables specific and sensitive identification of metabolites related to various inborn errors of metabolism using a single DBS punch. This was the first extended NBS pilot project in Romania, but further steps are needed to confirm all positive cases and determine the incidence of the screened disorders.

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Volumetric absorptive microsampling for analysis of D-amino acids in hemodialyzed CKD patients

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Introduction. Over the last decade, along with sensitivity improvements of the analytical instruments, blood microsampling techniques have become increasingly prevalent due to their convenience and minimal invasiveness. Even though dried blood spot (DBS) collected on filter paper remains by far the most used microsampling approach, new devices such as Mitra® VAMS (Volumetric Absorbtive MicroSampling) emerged, making quantitative analysis possible. Contrary to DBS, VAMS can collect a precise amount of blood, regardless of hematocrit.

D-amino acids roles as biomarkers for chronic kidney disease was recently

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documented, therefore, in this study, the analysis of D-amino acids from dried blood specimens collected on VAMS was performed in order to evaluate the effect of hemodialysis on their levels.

Material and methods. Eleven patients have been sampled before and after hemodialysis. D-amino acids have been analyzed by LC-MS/MS after derivatization with (S)-NIFE, on an Agilent 1260 Infinity II coupled to Agilent 6495C instrument.

Results. The previously developed screening analytical method was successfully adapted for targeted analysis of D-Asn, D-Ser, D-Ala, D-Pro (using triple quadrupole instrument), being validated according to the latest bioanalytical validation guidelines. Using this approach, the levels of the four D-amino acids in whole blood collected from CKD patients were successfully measured, observing that in most cases the concentration of D-AAs decreased during hemodialysis. This result is in accordance with literature data regarding the effect of hemodialysis on L-amino acids. Nevertheless, D-AA levels remain higher than those which have previously been observed in healthy individuals.

Conclusion. The analytical method was successfully adapted for targeted analysis of D-amino acids. The subsequent analysis of patient samples revealed that even though hemodialysis affects D-AA blood concentrations, they remain relevant for diagnosis or monitoring purposes.

Characterizing heterogeneity in a Triple-Negative Breast Cancer cell panel using MS-based proteome profiling

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Introduction. Triple-negative breast cancer (TNBC) is marked by significant heterogeneity, as evidenced by clinical observations and various omics studies. Over the past thirty years, extensive research has focused on understanding the biological features and diversity of TNBC to develop effective treatment strategies3. Genomic and transcriptomic approaches have enhanced our understanding of TNBC by revealing the complex factors influencing its aggressive clinical presentations. However, their integration into clinical practice remains limited. To fully elucidate the metabolic adaptations associated with TNBC, insights from all omics levels are essential. Mass spectrometry-based proteomics is particularly valuable, as it allows for the accurate detection of low-abundance biomarkers across diverse protein concentrations, making it effective for studying metabolic changes in TNBC. Here, a label-free shotgun proteomics strategy was used to analyze proteomic profiles in three TNBC cell line models, aiming to clarify their intrinsic heterogeneity.

Material and methods. Proteins were extracted from the cell pellet and culture medium, then digested with trypsin. The resulting peptides were analyzed using Acquity M-Class® nano-LC with Synapt®G2-Si HDMS. Raw HDMSe data was processed using Progenesis®QIp, and differential analysis was conducted using MetaboAnalyst for differential expressed proteins (DEP) analysis and ClueGO for enrichment analysis, with network representations created in Cytoscape.

Results. Hierarchical clustering analysis revealed that the MDA-MB-231 and MDA-MB-468 cell lines are more similar, while the Hs 578T cell line exhibits a unique expression profile, confirmed by both proteome and secreted protein analyses. Intracellular

Proteome Profiling: A total of 1,462 proteins showed significant expression differences, with 264 having distinct patterns across all TNBC cells, linked to immune functions and extracellular matrix interactions. The Hs 578T line was characterized by proteins related to membrane trafficking and extracellular matrix organization. MDA-MB-231 exhibited distinct proteins associated with the TCA cycle and DNA synthesis, while MDA-MB-468 showed variations in amino acid metabolism, cholesterol biosynthesis, and RNA metabolism. Secreted Proteins Profiling: A total of 324 proteins exhibited significant differences, with 117 showing varying abundance across cell lines, linked to interleukin signaling, apoptosis pathways, and extracellular matrix organization. Hs 578T was differentiated by proteins involved in extracellular matrix organization and receptor signaling. MDA-MB-468 featured proteins related to protein metabolism and programmed cell death, while MDA-MB-231 was characterized by proteins associated with cofactor metabolism and membrane trafficking.

Conclusions. Using a mass spectrometry-based proteomics approach, we characterized the metabolic phenotypes of triple-negative breast cancer (TNBC) cell lines. This analysis revealed inherent variations in protein expression related to cancer hallmarks, as well as insights into signaling patterns and extracellular matrix interactions, all of which are crucial for understanding the complexity of TNBC and its metabolic characteristics.

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Novel serum biomarkers in intrahepatic cholangiocarcinoma: a pilot proteomic exploration

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Introduction. Cholangiocarcinoma (CCA) is a highly aggressive form of biliary tract cancer arising from the malignant transformation of cholangiocytes. A fundamental hurdle lies in comprehending the underlying biology of CCA tumorigenesis, as it holds significance for early detection and intervention. Monitoring alterations in protein abundance within serological proteomes throughout the course of disease progression can offer invaluable insights into the intricacies of CCA physiology and pathology. This study aimed to explore the serum proteome of patients with intrahepatic CCA (iCCA), hepatocellular carcinoma (HCC), liver cirrhosis (CIR), and primary sclerosing cholangitis (PSC) to identify new biomarker candidates along with possible pathways involved in the development of these complications.

Material and methods. Blood samples were collected from 60 patients (15 intrahepatic cholangiocarcinoma (iCCA), 15 hepatocellular carcinoma (HCC), 15 primary sclerosing cholangitis (PSC), and 15 liver cirrhosis (CIR)) and 15 healthy controls (HC) for the discovery cohort and from 45 patients (iCCA, HCC, PSC) and 15 HC for the validation cohort. After the depletion of six highly abundant proteins, serum samples were subjected to label-free ultra-high-performance nano-LC coupled with ultra-high-definition Q-TOF mass spectrometry (nano-LC-HDMSE) proteomics analysis. Raw data were acquired using MassLynx™ Software and data were processed by using ProgenesisQI for proteomics

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Results. By using high-throughput mass spectrometry proteomics analysis, significant differences were identified. Notably, serum amyloid A1 and A4 (SAA1, SAA4), along with vascular cell adhesion molecule 1 (VCAM-1) and angiopoietin-1 receptor (TEK), were found to have discriminatory power between iCCA and HCC. Heat shock protein 90 (HSP90), annexin A9 (ANXA9), alpha-1-antichymotrypsin (SERPINA3) and leucine-rich alpha-2-glycoprotein (LRG1) were highlighted for evidencing risk factors, such as CIR and PSC. This first pilot proteomic analysis underscores the reliability of identifying promising novel biomarker candidates for iCCA.

Conclusions. Our study provided a pioneering comparative analysis of the serum proteomes of iCCA, CIR, PSC, and HCC using high-throughput mass spectrometry. We identified distinct proteomic signatures, including proteins like SAA1, SAA4, VCAM1, and LRG1, as potential biomarkers for distinguishing iCCA from HCC and PSC. The results were validated by ELISA on an independent patient cohort. Validation in larger cohorts is essential to confirm these findings and integrate proteomics into clinical practice, reducing the need for invasive procedures like liver biopsies.

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Advancing *in vitro* findings toward *in vivo* efficacy in humanized mouse models for mantle cell lymphoma

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Background. ROR1 is a receptor for Wnt5a and other Wnt proteins, playing a critical role in cell migration, differentiation, and growth during embryonic development. While ROR1 expression is low or absent in normal adult tissues, it is significantly upregulated in various tumors, particularly Mantle Cell Lymphoma (MCL), an aggressive form of non-Hodgkin lymphoma.

Objective. This study is focused on developing a novel CAR T cell therapy targeting ROR1 and optimize its efficacy using in vitro MCL models as a precursor to in vivo studies in humanized mouse models.

Material and methods. CAR T cells were generated using a lentiviral vector and cultured in RPMI1640 media supplemented with IL-2 and Dynabeads for activation. The Z138 cell line was employed as the MCL model, with ROR1 expression confirmed by flow cytometry. Co-culture experiments were performed at various effector-to-target (E:T) ratios over different time points to assess CAR T cell efficacy. Cytokine release was measured via ELISA, and LDH activity was evaluated using a PicoProbe assay.

Results. Anti-ROR1 CAR T cells demonstrated a time-dependent inhibitory effect on Z138 cells, with significant increases in IL-6 and TNF-α release observed during co-culture. Elevated LDH activity was noted across all groups containing CAR T cells after

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24 hours.

Conclusions - Future directions. The next phase involves testing these ROR1-targeted CAR T therapies in humanized mouse models to evaluate their effectiveness in a more physiologically relevant tumor environment. This research seeks to improve targeted therapies for MCL patients and deepen our understanding of CAR T cell behavior *in vivo*.

The effect of biologically synthesized silver nanoparticles on mixed biofilms produced by bacteria and fungi

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Introduction. Silver nanoparticles (AgNPs) have become a subject of great interest due to their antimicrobial properties and are increasingly used to combat infections caused by microbial biofilms. Mixed biofilms, formed by communities of bacteria and fungi, exhibit extreme resistance to conventional antimicrobial treatments. This study analyzes the effect of biologically synthesized AgNPs, using Kombucha fermented tea, on mixed biofilms produced by Pseudomonas aeruginosa and Candida tropicalis.

Material and methods. AgNPs were synthesized using an extract of fermented Kombucha tea through the reduction of silver ions from $AgNO_3$. These nanoparticles were characterized by spectroscopic and microscopic methods to determine their size, shape, and stability. Antimicrobial tests were conducted on Pseudomonas aeruginosa and Candida tropicalis, both in separate cultures and in co-culture, to determine the minimum inhibitory concentration, minimum bactericidal/fungicidal concentration, and effects on biofilms observed by transmission electron microscopy.

Results. The tests showed a significant inhibition of Pseudomonas aeruginosa and Candida tropicalis growth, both individually and in co-cultures. The minimum inhibitory and bactericidal/fungicidal concentrations indicated a high efficacy of AgNPs against mixed biofilms, demonstrating stronger effects compared to Kombucha tea alone. Additionally, the AgNPs significantly impacted biofilm structure, reducing the microorganisms ability to adhere and form biofilms.

Conclusion. AgNPs synthesized biologically using Kombucha tea demonstrated a high potential in inhibiting and disrupting mixed biofilms produced by bacteria and fungi. Their antimicrobial efficacy suggests applicability in anti-infective treatments, especially in cases of biofilm-associated infections resistant to antibiotics.

Comparative identification of immune gene targets in lung cancer using cell line models and TCGA data

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Introduction. The high mortality rate of lung cancer is due to significant heterogeneity reflected also in complex immune evasion mechanisms, making it challenging to identify specific targets. In this study, we used microarray data from lung cancer cell lines from our lab and we compared the transcriptomic data with TCGA patient data to identify immune-related genes common to squamous cell lung carcinoma (LUSC) and lung adenocarcinoma (LUAD).

Material and methods. Microarray assessment was done using SureScan Microarray Scanner and cross-referenced the results with TCGA RNA-seq data for lung cancer patients (LUAD, n=574/ LUSC, n=553) and normal lung cell profiles using the GeneSpring GX v.13.0 software from Agilent Technologies for the analysis. Differential gene expression, immune pathway activity and mutation profiles were evaluated to identify genes that may serve as immune targets in lung cancer.

Results. Comparative analysis revealed common immune-related genes in LUSC, such as KRT6A, KRT5, DSG3, KRT17, KRT6C, KRT14, DSC3, MAGEA4, and PRAME, and LUAD - PRAME and STRA6. In particular, MAGE family genes such as MAGEA4 direct the expression of tumor antigens recognized by autologous cytolytic T lymphocytes, which form the basis for immunological targeting. PRAME, an antigen recognised in both cancer types, is associated with immune escape mechanisms. These shared transcripts highlight how cell line models can reveal key immune targets consistent across patient data despite inter-patient variability.

Conclusions. Despite patient heterogeneity, our approach showcases the advantages of a simplified cell line model to identify specific immune targets in both models and patient samples. While the cell line lacks the complexity of the tumor microenvironment, its simplified framework enables the efficient discovery of important immune regulatory genes such as MAGEA4 and PRAME, paving the way for further investigation of targeted immunotherapy in lung cancer treatment.

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The effect of smoking on miRNA pattern in female lung adenocarcinoma

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Introduction. Lung cancer is the most frequent malignant neoplasm in most countries and the main cancer-related cause of mortality worldwide, with significant sex differences and smoking status when it comes to risk, treatment response, and outcome. Smoking is the most commonly recognized risk factor that has mutagenic and carcinogenic activity, with an altering effect on transcription and genomic patterns. MicroRNAs (miRNAs) are small non-coding RNAs acting as post-transcriptional gene regulators. miRNAs proved to have an altered expression in pathological conditions, including lung cancer. In the current study, we have further characterized female-specific miRNA signatures in lung adenocarcinoma (F-LUAD).

Methods. This study is based on the analysis of smoking-associated miRNA expression in the TCGA (The Cancer Genome Atlas) LUAD group and the identification of novel female-specific (F-LUAD) smoking-associated miRNA biomarkers correlated with the mutation status of TP53, KRAS, and EGFR.

Results. The miRNA expression signature induced by smoking in F-LUAD is highly complex and influenced by a wide range of factors that impact patients' prognosis. We identified a miRNA expression signature associated with smoking in the F-LUAD group, which includes miRNAs involved in cancer-related signaling pathways. Smoking induces miRNA expression changes that are particular in F-LUAD, leading to specific miRNA-gene networks that regulate development and progression in F-LUAD cancer, correlated with mutational status.

Conclusions. The analysis of F-LUAD miRNAs provides a novel insight into the biological effects of smoking, thus promoting the exploration of specific susceptibility and therapy markers. This paper has highlighted the mixed findings in studies evaluating the gender paradox in lung cancer.

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Molecular architecture underlying angiogenesis in ccRCC

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Introduction. In 2022, renal cell carcinoma (RCC) was the most common type of renal cancer. About 75% of RCCs are clear cell RCC (ccRCC), with a 5-year survival rate of 12% if metastatic. We aim to explore the molecular architecture underlying angiogenesis in ccRCC patients and highlight potential biomarkers for early diagnosis, patient stratification, and targeted therapy.

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Material and methods. Fresh-frozen pairs of tumoral and adjacent non-tumoral tissues were collected from ccRCC patients (n=16;8T1/2;8T3/4). RNA isolation was done using the TriReagent Sigma-Aldrich protocol. cDNA synthesis was performed with the RT2 First Strand Kit from 500 ng of RNA. We used the PAHS-024Z PCR Array kit to investigate the alterations in the expression of angiogenesis genes. The results were analyzed at Qiagen's GeneGlobe Data Analysis Center. Molecular interactions were predicted with miRNet and Ingenuity Pathway Analysis.

Results. The gene expression analysis (all stages) revealed that ANGPT2, ANGPTL4, EFNB2, FLT1, PGF, S1PR1, and VEGFA were upregulated, while ANGPT1, CCN2, FGF1, FGFR3, PLAU, TGFB2, TIMP3 were downregulated. Stage analysis showed that overexpressed ANGPTL4 is a common trait, while overexpressed VEGFA is only associated with late stages. The underexpression of CCN2 was also common, while the underexpressed PLG was found only in early cases. MiR-124-3p, miR-181a-5p, miR-101-3p, miR-16-5p, miR-107, miR-155-5p, and miR-1-3p were predicted to be related to the angiogenesis genes. The lncRNAs MALAT1, TUG1, HOTAIR, H19, and LINC00963 may act as ceRNAs by sequestering these miRNAs, thus indirectly influencing angiogenic gene expression.

Conclusions. Angiogenesis is a crucial process in the oncogenesis and progression of ccRCC. Deciphering its genomic architecture highlights novel avenues for biomarker discovery. Our results pinpoint some of the most promising miRNAs and lncRNAs associated with angiogenesis in ccRCC. However, extensive validation on larger patient cohorts is required.

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Bacillus Calmette-Guerin exerts effects on trained immunity with potential implications for immunotherapy

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Introduction. Bacillus Calmette-Guerin (BCG) exerts effects that go beyond protection against tuberculosis. Much of its immunologic activity is attributed to obtaining trained immunity (TI), a capability of the innate immune system to recapitulate and mount potent counterattacks against recurring pathogenic threats distinct from those exerted by adaptive immunity. Stimulating TI could have potential clinical implications in immunotherapy.

Material and methods. We evaluated the effect of BCG vaccination on hematopoiesis and cytokine levels (TNF-α, Il-1α, IL-1β, and IL-6) by ELISA after immunostimulation with LPS after one versus two weeks from vaccination in a murine model. The results obtained after the treatment in each arm (BCG and control) were interpreted with the independent samples t-test using SPSS statistics version 23, with a p-value < 0.05 being considered statistically significant.

Results. The hemogram results showed that the changes induced by BCG vaccination on the trained immunity are not reflected in the absolute numbers of the cells

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of the three marrow lines—white, red, and platelets—in the peripheral blood. However, BCG vaccination influenced the levels of proinflammatory cytokines in the treated group.

Conclusions. Our results reflect those observed in the clinic after vaccination, where an increase in the absolute number of immune cells in the peripheral blood is not observed. However, the phenotypic changes appear due to the influence of BCG on the molecular profile, with changes in the expression of genes specific to the trained immunity. The evaluation of cytokine levels by the ELISA technique allowed us to appreciate the functional adaptation of the immune cells exposed to BCG *in vivo*.

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Are the antioxidants-loaded extracellular vesicles the future molecules for cancer follow-up in colon cancer signaling and regulation?

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Introduction. Colon cancer is still one of the most diagnosed cancers worldwide, with a high mortality rate, in contrast to the significant developments in its treatment. The primary therapy for advanced-stage colon cancer is still chemotherapy, with severe side effects. Some new treatment options include antioxidant bioactive compounds, which show anticancer activity and have no side effects. Extracellular vesicles (EV) help cells communicate and are involved in cell signaling/ regulation. This study aims to identify the possible role of antioxidants-loaded extracellular vesicles (ALEV) in the signaling and regulation of colon cancer.

Material and methods. Four colon cancer cell lines, HCT-116, RKO, HT-29 and CCL-229, were treated with Resveratrol(RE), Genistein(GE) and RE+GE at 50µM each for HT-29&CCL-229, and 60µM RE and 80µM GE for HCT-116 and RKO. The EVs were obtained 24h after treatment, followed by RNA extraction. EVs were comparatively evaluated using the microarray Agilent technology and analyzed with GeneSpring, IPA, and Venny 2.1.0.

Results. Obtained data showed 507 to 2445 altered genes in the cell lines' extracellular vesicles before and after treatment. The combined treatment generated the highest number of altered genes on most cell lines, except HT-29 cell line, where the highest number of altered genes was observed for the GE treatment. The top affected pathways were: CCL-229: Cellular Assembly and Organization, SUMOylation of transcription cofactors, HCT: Electron transport, ATP synthesis, and heat production by uncoupling proteins Vitamin D metabolism, Mitochondrial translation; HT-29: Reelin Signaling in Neurons Histone Modification Signaling Pathway Mitotic Prometaphase RKO: RHO GTPase cycle Assembly of collagen fibrils.

Conclusion. ALEVs are demonstrated to act in gene regulation and signaling. We identified specific altered genes linked to each cell line and observed distinct altered pathways that could be traced to the content of the isolated EVs.

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Modified plasma miRNA signatures for non-invasive detection of infection types: insights into immune pathway regulation

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Introduction. MicroRNAs (miRNAs) are small, non-coding RNAs that regulate gene expression and play essential roles in various cellular processes, including immune responses. Distinct patterns of microRNA expression have been associated with bacterial and viral infections, indicating their potential use as biomarkers of infection types. These miRNAs are stable in biofluids, non-invasively detectable and resistant during storage. Our study evaluate the clinical value of modified miRNA expression patterns in distinguishing between bacterial and viral infections by qRT-PCR.

Material and methods. Fifty-three infected subjects (16 with bacterial infection and 17 with viral infection) and 26 healthy controls provided plasma samples for this study. Total RNA was extracted and converted to hsa-miRNA for analysis of miRNAs (hsa-miR-21-5p, hsa-miR-29b-3p, hsa-miR-155-5p and hsa-miR-548a-3p) using TaqMan miRNA assays. The miRNet platform was used to analyze the interaction between miRNA targets and pathway enrichment and to identify potential molecular pathways regulated by these miRNAs. The DIANA-miRPath facilitated pathway analysis, confirming the role of miRNAs in immune-related pathways.

Results. Differential expression analysis revealed significant downregulation of three miRNAs in affected individuals compared to healthy individuals, with hsa-miR-21-5p ($p=0.0022$) and hsa-miR-29b-3p ($p=0.0051$) showing particularly substantial changes. The miRNet-based interaction network highlights the relationship between these miRNAs and immune response pathways, suggesting a role in infection-specific gene networks.

Conclusions. Modified miRNA expression profiles in blood plasma can be reliable as biomarkers for distinguishing bacterial and viral infections. The robust and noninvasive nature of miRNA detection in biofluids underscores its potential utility in clinical diagnosis. Further investigation of miRNA-regulated pathways may improve our understanding of host-pathogen interactions.

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The effect of Resveratrol and Genistein on colon cancer cell lines

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Introduction. Despite significant advancements in treatment, colon cancer remains one of the most diagnosed cancers worldwide, with a high mortality rate. Chemotherapy is still the primary treatment approach, though it is well-known for its severe side effects. New therapies have been developed to address this issue, including those utilizing antioxidant bioactive compounds, which have shown targeted anticancer effects with fewer side effects. This study aims to evaluate the impact of resveratrol and genistein treatment on colon cancer cell lines.

Material and methods. For this study, we used specific in vitro techniques for treatment evaluation, apoptosis, cellular morphology, scratch assay, colony assay, invasion assay, gene expression analysis using Agilent technology, GeneSpring, Venny 2.1.0 and IPA software. Four HCT-116, RKO, HT-29 and CCL-229, were treated with resveratrol(RE), genistein(GE) and RE+GE.

Results. Cells were treated with 50 μM of RE and GE for HT-29 and CCL-229 and 60 μM RE and 80 μM GE for HCT-116 and RKO. The treated cell lines present cell membrane asymmetry, cell shrinkage, and nucleus, fragmentation, inhibition of invasion capacity, with the more prominent effect in the case of the combined treatment. Also, treatments of colon cancer cell lines affect the cytoskeleton integrity and cause irregular nuclei. The microarray analysis identified 1 to 3509 common altered genes specific for colon cancer cell lines or treatment. They affect: Cell Cycle Checkpoints, RHO GTPase cycle, tRNA Charging, GTPase cycle, Neutrophil degranulation.

Conclusion. This study has shown that resveratrol and genistein inhibit the proliferation rate, reduce the invasion capacity and affect the cell's cytoskeleton of colon cancer cell lines, altering important cell signaling pathways. All of this could make these two antioxidant bioactive compounds promising treatments for colon cancer as a single therapy agent or as an adjuvant therapy together with chemotherapy.

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Common seeds microRNAs exert similar expression profile with different functionality in lung cancer male patients

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Introduction. Effective treatment of advanced non-squamous cell lung cancer (NSCLC), a type of lung cancer associated with high morbidity and mortality, remains challenging, highlighting the need to identify new biomarkers and therapeutic targets. This study aimed to elucidate the role of miR-28-5p and miR-708-5p in the development

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of late-stage NSCLC and investigate the relationship between these microRNAs, target coding genes, and related signaling pathways that promote tumour progression.

Material and methods. Based on internationally accepted diagnostic criteria, the study population consisted of 32 men diagnosed with stage III and IV NSCLC, for which informed consent was obtained. Paired samples of fresh-frozen tumor tissue (TT) and adjacent non-tumor tissue (TN) were obtained for analysis. The expression levels of miR-28-5p and miR-708-5p were determined by qRT-PCR. The comparative ΔΔCT method was used for data analysis, and expression levels were visualized graphically.

Results. In this group of men with advanced NSCLC, miR-28-5p and miR-708-5p were significantly overexpressed in tumor tissue compared to adjacent non-tumor tissue, suggesting a potential oncogenic role for these microRNAs in NSCLC. Further analysis reveals that these microRNAs affect essential signaling pathways, including extracellular matrix (ECM) and receptor interactions, adhesion junctions, and Hippocampal signaling pathways. These pathways are known to promote tumour growth, invasion, and metastasis, and may be important mediators of NSCLC progression, as determined by miR-28-5p and miR-708-5p activity.

Conclusion. The observed up-regulation of miR-28-5p and miR-708-5p in NSCLC tumor tissues supports their importance as potential biomarkers and therapeutic targets, especially in men with advanced disease. This study highlights the importance of further investigating the specific mechanisms by which miR-28-5p and miR-708-5p regulate target genes and signaling pathways in NSCLC.

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DOCTORAL SCHOOL

The burden of polyautoimmunity in an adolescent girl – a case report

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Introduction. It is well known that autoimmune diseases tend to coexist in a single patient. Autoimmune hepatitis (AIH) makes no exception in terms of associated pathologies, as about 30% of patients develop at least one separate autoimmunity. This phenomenon is of interest to clinicians, as it imposes treatment difficulties and influences patient prognosis.

Material and methods. We report the clinical, laboratory and ultrasound findings of a 13-year-old girl who was referred to our unit in order to investigate chronic hepatitis.

Results. Our patient had complained of fatigue, anorexia, and abdominal pain for several months. Upon examination, she was pale, and hepatosplenomegaly was noted. Laboratory studies showed elevated transaminases, cholestasis, and slight direct hyperbilirubinemia, with signs of altered liver synthesis. Immunoglobulin G titers were high, as well as antinuclear antibodies and anti-LC-1 antibodies, suggestive of type 2 AIH. Other potential causes, such as viral hepatitis and Wilson's disease, were excluded. The patient presented pancytopenia, while ultrasound and elastography findings were consistent with cirrhosis. Additional blood work showed high TSH and low fT4 levels in the setting of positive anti-thyroid peroxidase antibodies. Coombs test and IgG anti-erythrocyte antibodies were also found positive. As a result, we could interpret the case as type 2 AIH, autoimmune hemolytic anemia, and Hashimoto thyroiditis. She started high-dose prednisone and tacrolimus treatment, azathioprine being contraindicated due to hematological abnormalities. She had a good evolution of the liver disease, but with important corticosteroid toxicity.

Conclusion. AIH can present minor or no symptoms, so a high suspicion rate should be maintained in order to prevent the diagnosis only in the stage of cirrhosis. Moreover, polyautoimmunity should be actively searched in AIH patients due to its high incidence and implications in treatment decisions.

Somatic changes induced by maternal high-fat diet in the offspring. Possible deleterious effects of flavonoids?

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Introduction. The rapidly increasing rate of obesity has become an extremely important public health problem, particularly in developed countries. Obesity is associated with a range of health problems, often referred to as the metabolic syndrome. Adipose tissue is now regarded as an endocrine organ responsible for the hormonal secretion of adipokines, which are cytokines involved in various physiological processes. It has been established that adipokines play a key role in the regulation of many processes in the

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human body.

Material and methods. The aim of the current study was to use an animal model to investigate the possible influence of obesity and adipokines on the gestational period, on the development of offspring, and to assess whether these changes are influenced by the administration of antioxidant agents and flavonoids. The present study was performed using 5 groups of 7 female Wistar albino rats. Due to the limited number of studies investigating the existence of methods by which overweight as well as adipocytokine levels could be controlled during the gestational period, the possible effects of the administration of antioxidant or flavonoid compounds were investigated, and their effect on the resulting offspring was also followed. The study analyzed the effects of maternal obesity on offspring, as well as the existence of effects of the administered compounds on the weight of offspring, their brain weight, the existence of changes in the brain detected by electronic microscopy and anthropometric changes.

Results. The high-fat diet leads to increased weight gain in females and to the occurrence of increased size offspring compared to the control group, as it is already known that maternal obesity leads to the appearance of macrosomia. Obesity also produces changes in the offspring's cerebral tissue, which may have long-term consequences, but further studies on brain changes and their development are needed. The levels of molecules produced by adipose tissue (adipocytokines) increase in direct proportion to the degree of obesity and are involved in the development of pregnancy-related pathologies and the effects of obesity on offspring.

Conclusion. The results of this experimental study reinforce what is already known about the effects of obesity on the gestation period and offspring and at the same time, the current study highlights the existence of possible adverse effects of flavonoid compounds on the development of pregnancy and offspring, opening the way for future studies on the benefits and risks of using these compounds during gestational period.

Impact of genetic heterogeneity on clinical presentation in Noonan and Noonan-like syndromes

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Introduction. Noonan syndrome (NS) is a genetically heterogeneous disorder, primarily associated with mutations in the RAS-MAPK-signaling-pathway. This genetic diversity significantly impacts the clinical presentation, leading to a wide range of symptoms and complications, including cancer. Understanding this heterogeneity is important for accurate diagnosis and effective management.

Material and methods. This review synthesizes findings from the past 12 years, utilizing keywords such as ‚Noonan Syndrome,' ‚RASopathies,' ‚genetic mutations', and ‚RAS/MAPK pathway' to identify relevant literature. The analysis focuses on the relationship between genetic mutations and clinical features, highlighting variability in expressivity and overlapping phenotypes.

Results. The review reveals that approximately 75% of NS cases are linked to mutations in genes such as PTPN11, SOS1, KRAS, NRAS, and RAF1. The remaining 25% often lack identifiable genetic causes. Variability in clinical manifestations is obvious, with some patients exhibiting classic NS features while others present with milder or atypical symptoms. The findings also indicate that NS shares phenotypic similarities

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with related syndromes, which can complicate diagnosis. The clinical features of NS can change with age, complicating diagnosis. Recent studies have identified additional manifestations, such as renal and central nervous system abnormalities, suggesting a broader clinical spectrum than previously recognized. Advances in genetic testing (sequencing) have improved diagnostic accuracy and informed management strategies.

Conclusions. The genetic heterogeneity of Noonan syndrome profoundly influences its clinical presentation through variability in symptoms and overlapping characteristics with other syndromes. This complexity underscores the need for comprehensive genetic evaluation and heightened awareness among healthcare providers to ensure accurate diagnosis and effective management of affected individuals.

Risk factors and prognostic factors for patients with hepatic metastases of right vs. left colon cancer

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Introduction. Colorectal cancer is a leading cause of cancer associated deaths with liver metastasis developing in 25-30% of those affected. Literature suggests a survival difference between left and right sided liver metastasis of colonic cancer. The aim of this study is to describe a pattern of liver metastasis of left vs right sided colonic cancer and to identify possible risk and prognostic factors for the evolution of these patients.

Material and methods. We performed a retrospective study on a cohort of patients with a diagnosis of liver metastasis of colonic cancer admitted between 2021 and 2023. We separated the patients in 2 groups liver metastasis from left sided colonic cancer vs right sided. We excluded the patients with synchronic tumors on both sides of the colon and those with tumors located imprecisely.

Results. We identified 479 patients (118 in the right group, 361 in the left group). We compared the number of metastasis in both groups, most patients having multiple metastasis (over 5), 45.7% in the right group and 39.6% in the left group (p=0.5), the size of metastasis, most having tumors between 2-5 cm (62.9% in the right group, 52.3% in the left group), the number of liver segments involved, more than 3 segments being involved in 61% of the right group and 58.2% of the left group. We also compared the staging of cancer most patients being diagnosed in stage IV (71.2% for the right group and 64.7% for the left).

Conclusion. Although we found more patients with left sided colonic cancer having hepatic metastasis, no statistical difference in the evolution of the metastasis depending on the location of the primary tumor was observed.

A pilot study of multiplex ligation-dependent probe amplification evaluation of copy number variations in Romanian children with congenital heart defects

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Introduction. Congenital heart defects (CHDs) have had an increasing prevalence over the last decades, being one of the most common congenital defects. Their etiopathogenesis is multifactorial in origin. About 10–15% of all CHD can be attributed to copy number variations (CNVs), a type of submicroscopic structural genetic alterations. The aim of this study was to evaluate the involvement of CNVs in the development of congenital heart defects in a Romanian population.

Material and methods. We performed a cohort study investigating the presence of CNVs in the 22q11.2 region and GATA4, TBX5, NKX2-5, BMP4, and CRELD1 genes in patients with syndromic and isolated CHDs, using a multiplex ligation-dependent probe amplification (MLPA) based technique.

Results. A total of 56 patients were included in the study, half of them (28 subjects) being classified as syndromic. The most common heart defect in our study population was the ventricular septal defect (VSD), at 39.28%. There were no statistically significant differences between the two groups in terms of CHD-type distribution, demographical, and clinical features, with the exceptions of birth length, weight, and length at the time of blood sampling, that were significantly lower in the syndromic group. Through MLPA analysis, we found two heterozygous deletions in the 22q11.2 region, both in patients from the syndromic group. No CNVs involving GATA4, NKX2-5, TBX5, BMP4, and CRELD1 genes were identified in our study.

Conclusion. We conclude that the MLPA assay may be used as a first genetic test in patients with syndromic CHD and that the 22q11.2 region may be included in the panels used for screening these patients.

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Assessing the anti-inflammatory and antioxidant activity of Mangiferin in murine model for myocarditis: perspectives and challenges

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Introduction. Myocarditis, a leading cause of heart failure and death in younger populations, is commonly treated symptomatically. However, emerging treatments focus on reducing inflammation and fibrosis. Natural compounds, like flavonoids and phenolic

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acids, have shown promising anti-inflammatory and antioxidant benefits. Corticosteroids, commonly used in autoimmune myocarditis, appear to reduce mortality compared to conventional therapies for heart failure. This study investigates Mangiferin's effects on inflammation, nitro-oxidative stress, histopathology, and cardiac function in experimental myosin-induced autoimmune myocarditis. Effects of Mangiferin were compared to Prednisone, a reference anti-inflammatory, and Trolox, an antioxidant.

Material and methods. Thirty male Wistar–Bratislava rats were divided into five groups: negative control (C−), positive control with myocarditis (C+), and myocarditis groups treated with Mangiferin (M), Prednisone (P), or Trolox (T). Cardiac function was evaluated by echocardiography, with additional measures of nitro-oxidative stress, inflammation markers, and histopathology.

Results. Showed a trend toward reduced left ventricular ejection fraction in untreated myocarditis, with all treated groups showing improved LVEF and left ventricular fractional shortening. Mangiferin demonstrated the most significant improvement, including reduced left ventricular posterior wall thickness by day 21 compared to Trolox ($p < 0.001$). Early inflammation markers, IL-1β, IL-6, and TNF-α, were higher in the myosin group than in the control group, indicating inflammation. Mangiferin, Prednisone, and Trolox reduced IL-1β significantly ($p < 0.001$), with Mangiferin showing a greater reduction compared to both Prednisone ($p < 0.05$) and Trolox ($p < 0.05$). Mangiferin increased total antioxidant capacity ($p < 0.001$) and lowered nitric oxide levels ($p < 0.001$) compared to both the control and Prednisone groups. Additionally, Mangiferin reduced creatine kinase and aspartate aminotransferase levels significantly by day 7, with a continued effect by day 21 compared to untreated groups. Histopathological analysis showed myocarditis-consistent findings in untreated cases, while Mangiferin-treated rats exhibited only mild inflammatory infiltrates. Statistically significant differences in severity grades between study groups were noted ($p < 0.005$).

Conclusion. Mangiferin shows cardioprotective effects by reducing oxidative stress and inflammation, presenting a promising therapy for myocarditis; however, further studies are needed to fully assess its efficacy relative to Trolox and Prednisone.

Comparative analysis of factors and barriers intervening in research participation among Romanian and international medical graduates from one Romanian medical faculty across three generations

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Introduction. This study focused on the factors that encourage engagement in research activities, as well as the barriers that restrict medical students' involvement, until their final year of study at Iuliu Haţieganu University of Medicine and Pharmacy Cluj-Napoca, Faculty of Medicine. The main objectives of this study are to investigate potential disparities in research culture and student engagement in various research opportunities between Romanian and international medical graduates, as well as to conduct an examination of the observed patterns across various graduating years (2021–2023).

Material and methods. A cross-sectional investigation was conducted among

graduate students of the Faculty of Medicine at the Iuliu Haţieganu University of Medicine and Pharmacy in Cluj-Napoca, Romania. From 2021 to 2023, all graduate students from the Romanian and international programs of the faculty were asked to participate in the study by filling out an anonymous online questionnaire. The final sample included 572 participants, of whom 392 were students from the Romanian section and 180 were students from international programs.

Results. Motivation and personal interest drive research engagement, according to over half of graduates. For over one-third of graduates, institutional elements like financial support and education also play a major role, as does the desire to enhance their curriculum vitae. More than 25% of graduates value community influence, 70% of graduates attended medical congresses, 12–15% presented papers at medical conferences, 23% wrote medical articles, 10–15% published at least one scientific paper in medical journals, and 20% participated in medical school research projects. Comparative analysis between Romanian and international medical graduates showed that Romanian students start research earlier, attend more medical conferences, present posters, collect data for studies, and are more interested in publishing graduation thesis data in scientific journals. To encourage international students to participate in research, the study found that colleagues' examples were more important, and both time and funds were key barriers. The research also shows that 2022 and 2023 graduates will organize more scientific conferences. According to the study, 2022 graduates began their research earlier than others.

Conclusion. To increase student engagement in research activities, medical schools should prioritize the promotion of positive factors, minimize common barriers, offer customized support and resources, encourage collaborative research activities, and facilitate cross-cultural learning.

The effects of circulating vitamin D levels on pediatric ECG

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Introduction. Vitamin D deficiency is a widespread health issue within the pediatric population. In recent years, vitamin D deficiency has been linked to numerous cardiovascular diseases such as atherosclerosis, arterial hypertension, myocardial infarction, and heart failure. Furthermore, there are studies linking low vitamin D levels with electrocardiographic changes in both adult and pediatric populations. In the current retrospective study we sought to investigate whether circulating 25-OH-vitamin D levels can independently cause changes in ventricular repolarization, depolarization, and atrial conduction on ECG in the pediatric population.

Material and methods. Children were divided into 3 groups based on their 25-OH Vitamin D: the sufficient group had vitamin D levels greater than 30 ng/ml, the insufficient group had levels between 20-30ng/ml and the deficient group had levels lower than 20 ng/ml. QRS duration, QTc interval, Tpe interval, Tpe/QTc ratio, JTp interval, Tpe/JTp ratio, JTc interval, PR interval, P-wave duration, LAP interval and P-wave dispersion were evaluated from the ECG of the patients. We analyzed the association between vitamin D and the measured ECG parameters using one-way analysis of variance (ANOVA).

Results. A total of 66 patients aged 1 to 17 years were investigated. No statistically

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significant associations were found between vitamin D level and the ECG parameters assessed (p-values>0.05).

Conclusion. The present study does not support the hypothesis that vitamin D levels can independently cause changes in paediatric ECGs.

CT and MR imaging features of rare and atypical ovarian tumors: a pictorial review

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Introduction. Ovarian tumors include a wide spectrum of neoplasms with varying behavior and histopathological features that manifest by different imaging characteristics. Ovarian neoplasms can be divided into four main categories including epithelial cell tumors, germ cell tumors, sex cord-stromal tumors and metastases. Although epithelial cell neoplasms are the most frequently encountered, it is crucial to be familiar with the imaging features of the entire spectrum of ovarian tumors, including rare and atypical ovarian neoplasms. The aim of this pictorial review was to illustrate the CT and MRI characteristics of these less frequent ovarian tumors.

Material and methods. This is a retrospective analysis of cases of rare ovarian tumors from Cluj County Emergency Clinical Hospital. Images were selected from our institution's database and included CT and MRI studies. Only cases with histopathological confirmation were included. Imaging findings were reviewed by two radiologists (one with more than 10 years of experience in gynecological radiology and one radiologist in training).

Results. We presented a series of cases of rare ovarian tumors, including Sertoli-Leydig cell tumor and granulosa cell tumors. The focus was on tumor morphology and size, presence of solid and cystic components and enhancement patterns. Although the radiological findings were non-specific and may overlap, certain features may suggest a particular pathology.

Conclusion. Malignant conditions involving the ovary include a wide range of neoplasms with overlapping and nonspecific imaging characteristics. However, recognizing the imaging features of rare ovarian tumors can be helpful in the diagnostic approach and management.

The role of global longitudinal strain in the follow up of asymptomatic patients with chronic primary mitral regurgitation

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Introduction. The management of asymptomatic patients with primary mitral regurgitation (MR) remains controversial due to the subclinical, irreversible left ventricular (LV) dysfunction that occurs before a decline in left ventricular ejection fraction (LVEF), the parameter currently used by guidelines. Left ventricular global longitudinal strain (LVGLS), a measure of the longitudinal LV systolic function, has prognostic significance. Its role in the follow up of asymptomatic patients with MR is less well defined. The aim of this study was to assess the relative changes in LVGLS in a cohort of MR patients and to correlate these changes with the need for intervention during follow up.

Material and methods. We conducted a prospective study on a cohort of 218 patients, divided into three sub-groups according to MR severity (mild, moderate, severe). LVGLS was measured at baseline and every six months during a median follow-up of 30 months. The composite endpoint was the occurrence of heart failure symptoms, hospitalization for heart failure, a decrease in LVEF< 60%, an increase in left ventricular end-systolic diameter (LVEDD)>45 mm, new-onset atrial fibrillation, and cardiovascular death.

Results. Patients with moderate and severe MR had a significantly lower LVGLS at baseline than those with mild MR (19.5% and 19.1% versus 22.3%, p<0.01), despite a normal LVEF in all subgroups. The decrease in LVGLS was faster and more pronounced in patients with moderate and severe MR. Baseline LVGLS <18% and a relative decrease in LVGLS >10% were independent predictors of the composite outcome (HR=1.59, HR=1.74, p<0.01).

Conclusion. LVGLS can be used in the follow-up of asymptomatic MR patients, with a relative decrease > 10% in GLS being predictive of the need for valve intervention.

Biliary drainage for preoperative management of periampullary malignancies: a systematic review and meta-analysis

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Introduction. During the preoperative management of periampullary neoplasms, different drainage techniques have been developed to decompress the common bile duct in patients with obstructive cholangitis and severely affected liver function. We performed a systematic review and meta-analysis of resectable periampullary malignancies with the aim of establishing the safest and most effective preoperative biliary drainage method.

Material and methods. Our approach consisted of searching PubMed, BMC Medicine, and Scopus databases using keywords with a result of 1104 articles from 2010 to 2023. The remaining 26 articles that met our inclusion criteria were subjected to meta-

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analysis using R Commander 4.3.2.

Results. Endoscopic retrograde biliary drainage (ERBD) demonstrated a higher postprocedural pancreatitis rate (RR=3.05, p= 0.003) than percutaneous transhepatic biliary drainage (PTBD), and a higher rate of infectious complications (RR=3.08, p=0.003), intra-abdominal abscess (RR=1.85, p=0.002), postoperative pancreatic fistula (POPF) (RR= 1.52, p=0.001), and delayed gastric emptying (DGE) (RR=2.92, p= 0.015) than PTBD and/or endoscopic nasobiliary drainage (ENBD). Plastic stent (PS) had higher rates of catheter occlusion (RR=3.06, p= 0.04) and grade 2-3 POPF (RR=1.90, p= 0.004), while postprocedural pancreatitis (RR=0.33, p= 0.013), grade 1-2 complications (RR=0.79, p= 0.017) and wound infection rates (RR=0.63, p= 0.034) were lower than those of the self-expandable metallic stent (SEMS).

Conclusion. The choice of preoperative drainage method can influence postprocedural and postoperative complications rates. ERBD presents a higher procedure-related complication rate, prolonged hospital stay and more frequent postoperative complications than ENBD or PTBD.

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Comparison between infectious and other causes of acute pancreatitis in children

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Introduction. Acute pancreatitis (AP) is a rare disease, but the incidence is increasing in children. Etiology is highly variable and influences the long-term prognosis. We aimed to compare the infectious causes with the other etiologies of AP regarding the disease evolution.

Material and methods. We performed a retrospective study in which we included children diagnosed with AP during 2017-2023. We compared the demographic profiles, severity, duration of hospitalization, and evolution of AP of the infectious with the other causes.

Results. In our study, we included 30 children with 34 episodes of AP diagnosed based on the INSPPIRE definition. The leading cause of AP episodes was the infections (17.64%): 2.94% due to bacterial infection and 14.59% due to viral infection. The rest of the episodes had other causes (biliary lithiasis, toxic, metabolic diseases, systemic illness, pancreatic malformation) or remained of unknown etiology. The median age for the infectious group was lower than for the other cases (7.22±3.20 vs. 11.27±3.78 years, p=0.02). Regarding the severity, all patients from the infectious group had mild

forms, while the other group included moderate and severe episodes (50%). The mean hospitalization period was 5.66±2.42 days for the infectious causes and 9.35±6.58 days for the others (p=0.54). Fluid resuscitation, parenteral nutrition, and pain relief medication were the main therapeutic tools used in all patients. Exclusive parenteral nutrition was used in 50% of the infectious group and 67.85% of the rest of the cases. All patients had a favorable outcome.

Conclusions. Infections are a significant cause of AP in children. Our study identified a higher incidence of these cases than other studies, probably due to our small cohort. In our patients, the severity of infectious AP is milder compared with other etiologies.

The influence of exosomes isolated from mesenchymal stem cells on the regeneration of neurosensorial auditive cells affected by ototoxic treatments

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Introduction. The destruction of neurosensorial cells of the adult mammals' cochlea is irreversible, the actual treatments lacking efficiency. Mesenchymal stem cells (MSC) proved to favour tissue regeneration. The exosomes (nanometric extracellular vesicles) exert biological functions similar to the cells of origin. This study evaluates the effects of MSC- exosomes on the cochlear HEI-OC1 cells.

Material and methods. Mesenchymal stem cells were isolated from the bone marrow of CD1 mice, cultured and characterized regarding their stemness: differentiation towards bone and adipose tissues and the presence of specific markers by flow-cytometry and immunocytochemistry. The exosomes isolated by the precipitation method with the kit from Invitrogen and characterized at Nanosight were administered to HEI-OC1 cells and their effects were assessed: toxicity, the influence on cell proliferation and the potential protective effect on the cells affected by Cisplatin (viability tests- MTT and proliferation tests BrdU-ELISA).

Results. Mesenchymal stem cells showed positivity for: CD73 - 80.8%, CD105 – 97.55%; CD90- 91.2% while CD34 were 0.1%. MSC cultured in osteogenic differentiation medium were stained after three weeks with Alizarin Red showing ossification regions. In adipose differentiation medium the adipose cells were noticed after one week and were stained with Oil Red. The isolated exosomes were assessed at Nanosight having average dimensions of 132.7 nm and 1.37e + 007 particles/ml concentration. Exosomes showed no toxicity on HEI-OC1 cells after 24h and 48h incubation. When added before a toxic concentration of Cisplatin (IC50), the exosomes reduced significantly Cisplatin cytotoxicity ($p<0.5$ two-way ANOVA). The exosomes in the used concentrations could not enhance HEI-OC1 cells proliferation.

Conclusion. The exosomes isolated from CSM showed specific characteristics and could reduce the toxicity of Cisplatin on HEI-OC1 neurosensorial cochlear cells.

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The familiarity of Romanian psychiatrists with anti-n-methyl-d-aspartate receptor encephalitis: a web-based study

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Introduction. Psychiatrists are often the first to be consulted in patients with anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis. Thus, they need to be aware of clinical features, differential diagnoses, and treatment options for patients affected by this condition. In this study, we aimed to investigate the familiarity of Romanian psychiatrists with anti-NMDAR encephalitis.

Material and methods. We recruited psychiatrists from Romania and conducted a cross-sectional observational study by using a web-based survey.

Results. 111 psychiatrists completed the survey, of whom 47 (42.34%) were specialists, while 64 (57.66%) were trainees. The median length of training for specialists was ten years (IQR 9.5), while for trainees was 2.5 years (IQR 3). In total, 31 (27.93%) psychiatrists encountered a case of anti-NMDAR encephalitis, with no significant difference between specialists and trainees. 31 (27.93%) psychiatrists were either unaware of the disorder or only knew its name, while 77 (69.37%) had knowledge of an outline of it. Only 3 (2.7%) psychiatrists had comprehensive knowledge of the disorder. Respondents with a higher awareness level had undergone significantly longer training ($p=0.014$). Unsurprisingly, having encountered a case significantly influenced awareness levels ($p<0.001$). There were no significant differences between specialists and trainees regarding specific knowledge about anti-NMDAR encephalitis. However, higher awareness levels and having encountered a case significantly influenced answer accuracy for questions regarding psychiatric presentation and epidemiological features.

Conclusion. Our study indicates that Romanian psychiatrists have suboptimal knowledge of anti-NMDAR encephalitis, highlighting the need for improved awareness of this disorder.

Neural antibodies in first-episode psychosis patients with warning signs for autoimmune encephalitis

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Introduction. While autoimmune encephalitis (AE) remains an essential differential diagnosis in first-episode psychosis (FEP), testing all FEP patients for neural antibodies is not feasible in real-world clinical practice. Thus, some researchers suggest selective testing in patients with warning signs of AE. Moreover, criteria have been proposed for a category of so-called autoimmune psychosis (AP). Here, we aimed to determine the prevalence of AE in a cohort of patients with FEP.

Material and methods. To achieve our objective, we used a phenotype-driven algorithm. Initially, we screened patients for "yellow" and "red flags" indicating low or high pre-test probability warning signs for AE, respectively. We also evaluated patients

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for previously proposed warning signs and AP criteria. Next, patients with red flags underwent cerebrospinal fluid analysis (including neural antibodies), while patients with yellow flags underwent tests for serum neural antibodies, EEG, and brain MRI.

Results. We screened 78 patients with FEP and found that eight (10.3%) had at least one warning sign for AE: four (5.13%) patients had at least one red flag, while four (5.13%) had only yellow flags. Four (5.13%) patients met the criteria for possible AP. Two patients (2.56%) had anti-NMDAR encephalitis, while the remaining six (7.69%) received a primary psychiatric disorder diagnosis. The AP criteria failed to identify patients with definite AP due to a lack of paraclinical criteria.

Conclusion. Our study emphasizes the significance of including AE in the differential diagnosis of FEP.

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Circulating miR-18a and miR-532 levels in extrahepatic cholangiocarcinoma

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Introduction. Cholangiocarcinoma (CCA) is a highly aggressive cancer of the bile ducts with a poor prognosis and limited diagnostic markers. This study aims to investigate the potential of miR-18a and miR-532 as biomarkers for CCA by exploring their correlations with clinical parameters and traditional tumor markers such as CA19.9, CEA, and AFP.

Material and methods. This study involved a cohort of patients diagnosed with CCA. Serum levels of miR-18a and miR-532 were measured and analyzed in relation to various clinical parameters, including age, tumor markers, and histological features.

Results. Serum levels of miR-18a and miR-532 were upregulated in patients with extrahepatic cholangiocarcinoma (eCCA) compared to healthy controls ($p < 0.05$). MiR-18a and miR-532 levels were correlated with each other ($p = 0.011$, Spearman's rho = 0.482) but showed no significant correlation with age or traditional tumor markers (CA19.9, CEA, AFP). No significant differences in miR-18a and miR-532 levels were observed concerning tumor localization or histological grading. For predicting tumor resectability, miR-532 at a cut-off point of 2.12 showed a sensitivity of 72.73%, specificity of 81.25%, and an AUC of 71.3%, while miR-18a, at a cut-off of 1.83, had a sensitivity of 63.64%, specificity of 75%, and an AUC of 59.7%. ROC curve analysis suggested moderate diagnostic potential for miR-18a and miR-532, with AUC values of 0.64 and 0.689, respectively.

Conclusions. Although miR-18a and miR-532 showed significant upregulation in eCCA patients compared to healthy controls, they did not demonstrate significant associations with key clinical parameters, limiting their effectiveness as standalone diagnostic biomarkers. Further research involving larger, multi-center cohorts and additional molecular markers is necessary to validate these findings and explore the broader diagnostic potential of miRNAs in CCA.

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Exploring immunity: TREC and KREC levels in newborns with trisomy 21 and their link to telomere length

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Introduction. Trisomy 21, or Down syndrome, is associated with various immunological challenges, which may be linked to altered T-cell and B-cell development. T-cell receptor excision circles (TREC) and kappa-deleting recombination excision circles (KREC) serve as biomarkers for T- and B-cell lymphocyte production, respectively. This study aimed to evaluate the relationship of TREC and KREC levels with telomere length in newborns with Trisomy 21, providing insights into potential immune-deficiencies in this population.

Material and methods. We conducted a systematic review of eight representative articles published in the last five years that examined TREC and KREC levels in newborns with Trisomy 21. The selected studies were analyzed for their methodologies, sample sizes, and findings regarding TREC and KREC quantification, as well as telomere length measurements. Data were synthesized to identify correlations between these immunological markers.

Results. Newborns with Trisomy 21 consistently exhibited significantly lower levels of both TREC and KREC compared to healthy controls. Additionally, telomere length analysis indicated shorter telomeres in the Trisomy 21 cohort, suggesting a potential link between reduced lymphocyte production and accelerated cellular aging. The findings underscore the importance of monitoring immune function in this vulnerable population.

Conclusions. The decreased levels of TREC and KREC in newborns with Trisomy 21 may indicate an increased risk of immune-deficiencies, potentially exacerbated by shortened-telomeres. These results highlight the need for early-immunological-assessment and intervention strategies in this anomaly to improve health outcomes. Further research is warranted to explore the underlying mechanisms linking telomere length and immune function in this group.

Exploring the genetic basis of serotonin metabolism in antipsychotic treatments

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Introduction. Serotonin metabolism and serotonergic genes, particularly the serotonin transporter gene SLC6A4, are essential in modulating mood disorders and responses to antipsychotic therapies. The 5-HTTLPR polymorphisms within the promoter of this gene, characterized by short (S) and long (L) alleles, may influence the efficacy of selective serotonin reuptake inhibitors (SSRIs) in patients with depression or anxiety.

Material and methods. We searched the PubMed database for studies published in the last decade using keywords such as SERT, SSRIs, pharmacogenetics, and antipsychotic medication. Our focus was on SERT genotypes and their role in serotonin metabolism with implications for antipsychotic treatment, selecting ten relevant publications for analysis.

Results. The 5-HTTLPR polymorphism remains significant in evaluating SSRIs treatment, although the evidence is mixed. Many studies suggest that the short allele may affect treatment response and tolerability in major depressive disorder (MDD). Pharmacogenetic studies of SLC6A4 should include genotyping of rs25532 polymorphism, located within the promoter region, being involved in modulating serotonin transporter gene expression. Variability in antidepressant response based on drug class, ancestry, or gender highlights the complexity of pharmacogenetic influences. Short allele carriers exhibit reduced therapeutic response to escitalopram evaluated by the 21-item-Hamilton-Depression-Rating Scale. Some reports link the L allele to better SSRIs response, others show no association.

Conclusions. Meta-analyses indicate that the association between 5-HTTLPR and SSRIs efficacy may not be robust enough for standalone predictive use. Pharmacogenetic research offers valuable insights into antidepressant therapy outcomes, but should consider additional genetic and environmental factors. Continued investigation is essential for enhancing personalized psychiatric treatment strategies.

Polyarteritis nodosa - the great mimic

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Introduction. Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis which affects medium-sized vessels. Immunologic testing is negative and clinical manifestations are multisystemic. PAN can be triggered by infections, but most cases are idiopathic. This paper highlights the heterogeneity of the symptoms and somatic signs in PAN in the context of similar characteristic imaging findings.

Methods. We identified two patients with PAN in 2024 in the Rheumatology Department of the Railway Hospital Cluj-Napoca through the hospital electronic record system.

Results. The first patient (38 years old), with secondary hypertension,

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presented with dysphonia, wheezing, dry cough, dyspnea and fatigue since 2023. The thoracoabdominal CT scan detected celiac trunk occlusion and multiple aneurysms of the superior mesenteric artery, corroborated by CT angiography. To assess the patient's dysphonia, a neck CT scan was performed and revealed a 50% subglottic stenosis and osteitis of the cricoid cartilage. PAN and polychondritis with major organ involvement was the established diagnosis and the patient received treatment with Cyclophosphamide and Medrol. The second patient, a 68-year-old man, presented with sudden onset panniculitis on the limbs, associated with pain and fever. A skin biopsy was performed that showed medium-sized vasculitis. For the diagnosis of suspected PAN, a CT abdominal angiography was done, which revealed aneurysms of the right renal artery, confirming the diagnosis; treatment was initiated with Azathioprine and Medrol.

Conclusions. Manifestations of PAN are polymorphic and often mimic other conditions. For one patient, arterial hypertension and respiratory symptoms predominate, while for the other skin involvement and systemic manifestations are primarily noted. Alternative diagnoses were excluded for both patients. Imaging investigations are essential for the diagnosis, and the decision regarding treatment is guided by the severity of organ dysfunction.

Rare vascular involvement in IgG4-RD: what lies beyond periaortitis and aortitis?

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Introduction. Vascular involvement in IgG4-RD is mainly represented by aortitis and periaortitis. Medium and small-vessel vasculitis has rarely been described in IgG4-RD. Here we described two cases with IgG4-RD presenting with recurrent strokes.

Cases presentation. A 39-year-old male patient was referred to the rheumatology clinic with a history of 2 transient ischemic strokes and a cerebral infarction in the right middle cerebral artery (MCA) territory. He developed limb claudication, and CT angiography described vasculitis with severe stenosis of multiple upper and lower limb arteries. Sinusitis, atopy, sicca symptoms, thyroid disease, and bilateral proptosis were associated. MRI of the orbits showed extraocular muscle involvement. He had increased CRP and ESR levels, hypereosinophilia and markedly elevated IgG4 serum levels (1660 mg/dl). Other causes of vasculitis and vasculitis mimickers were ruled out and a diagnosis of IgG4-RD was made. He was started on glucocorticoids (GCs) and Azathioprine (AZA), then Mycophenolate (MMF). ENT symptoms and proptosis had remitted and no other ischemic stroke appeared. CRP and eosinophils levels normalized and IgG4 serum levels decreased (430 mg/dl). Another male patient has as experienced recurrent ischemic strokes in both middle cerebral artery (MCA) territories since the age of 29. MRI showed signs of vasculitis of common and internal carotid arteries. Sinusitis, lymphadenopathy, axonal neuropathy, and histologically proven chronic interstitial nephritis were present. He had markedly elevated IgG4 serum levels (3390 mg/dl), and kidney biopsy described changes consistent with IgG4-RD. Other causes of vasculitis were excluded and the case was interpreted as IgG4-RD. Induction treatment with GCs and Cyclophosphamide was started. The maintenance treatment used initially was AZA, then MMF. Due to a relapsing disease, Rituximab was introduced and his IgG4 serum levels significantly decreased (101 mg/dl).

Discussions. Both patients were referred with suspected primary systemic vasculitis. However, they also exhibited symptoms that extended beyond the classic profile of primary vasculitis, along with elevated IgG4 levels that normalized under treatment.

Conclusion. Vascular involvement in IgG4-RD is not limited to aortitis or periaortitis. In rare cases, it can affect medium and small-caliber vessels. IgG4-RD vasculitis should be considered in the differential diagnosis of recurrent stroke in young adults.

Research protocol: micro-ARNs in psychiatry, with focus on depression and gut dysbiosis

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Introduction. Micro-RNAs (miRNAs) are small, non-coding molecules that regulate gene expression post-transcriptionally. Studies suggest miRNAs impact neurobiological processes involved in psychiatric disorders, especially depression. This study will examine the expression profile of miRNAs in patients with depression and explore potential links with gut dysbiosis. Identifying these miRNAs as biomarkers could enhance diagnostic precision and foster the development of novel therapeutic approaches.

Material and methods. Blood samples from patients with depression and a control group of healthy subjects will be collected. miRNA levels will be analyzed via RNA sequencing to identify and quantify expression levels. Additionally, blood markers of gut permeability (zonulin, FABP2, LBP) will be gathered to assess dysbiosis. Bioinformatics methods will detect differences in miRNA expression between depressed patients and the control group, and explore correlations between miRNA profiles and gut permeability markers.

Expected results. We expect that specific miRNAs will show altered expression in depressed patients compared to controls. These changes may correlate with gut dysbiosis markers, suggesting a link between miRNA regulation and microbiome imbalances. Such findings could clarify inflammatory and neuroplasticity processes involved in depression.

Conclusion. This study aims to underscore the role of miRNAs in depression and their association with gut dysbiosis. Identifying miRNAs as biomarkers could aid in early diagnosis and continuous monitoring. Results may open avenues for personalized therapeutic strategies targeting miRNAs to help manage symptoms of depression.

Real life data on unprotected left main coronary artery revascularization from a tertiary center registry

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Introduction. Revascularization of left main (LM) lesions by percutaneous coronary angioplasty (PCI) or coronary artery bypass grafting (CABG) has been evaluated by multiple randomized trials and observational studies. However, there are no data on such patients in Romania to date.

Material and methods. Patients with significant LM stenoses investigated between January 2018 and April 2024 were extracted from the electronic system of SCJU Cluj. Patients who benefited from PCI or CABG were included in the analysis, excluding patients who benefited from conservative treatment, those who refused the intervention, as well as patients who died during the procedure, those with marked hemodynamic instability, as well as those with resuscitated cardiac arrest. Patient characteristics at admission were compared between the two groups, as well as their survival.

Results. A total of 186 patients with LM involvement were included in the analysis: 77 benefited from PCI and 109 benefited from CABG. Mean age was 68.8 years [95%CI: 66.6-71.0] vs. 67.5 years [95%CI: 65.8-69.3] ($p<0.001$). In the PCI group 9.1% (n=7) were elective examinations and 90.9% (n=70) were emergency examinations (n=13, unstable angina; n=30, NSTEMI, n=27, STEMI), while in the CABG group 38.5% (n=42) were elective examinations and 61.5% (n=67) were emergency (unstable angina (n=31), NSTEMI (n=34), STEMI (n=2)). Among patients treated by CABG, 32.1% (n=35) had diabetes vs. 13.0% (n=10), $p=0.003$; 44.0% (n=48) were hypertensive vs. 18.4% (n=14), $p<0.001$. There were no differences in terms of gender distribution (75.3% men (n=58) vs. 76.1% (n=83), $p=0.89$). Overall survival at 6 years was 80.7% (n=88) among patients with CABG vs. 63.6% (n=49) in the PCI group, $p<0.001$.

Conclusions. C artery bypass grafting was the predominant revascularization strategy in this real-world registry. While PCI patients were older and presented more often with acute coronary syndromes, CABG was associated with improved long-term survival.

Assessment of quality of life in patients diagnosed with polycythemia vera: a retrospective study

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Introduction. Polycythemia vera (PV) is a myeloproliferative neoplasm with clinical features including erythema of the face and extremities, pruritus, as well as a prothrombotic state which may lead to thromboembolic events. The aim of our study was to evaluate the quality of life of patients suffering from this disease by assessing the severity of their symptoms, while also establishing the efficacy of the treatment they are receiving.

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Material and methods. We included in our study patients diagnosed with PV who presented to the Hematology department of the Institute of Oncology Cluj-Napoca at least once between August 1st 2023 and July 31st 2024. To find out which symptoms were most severe, we used a modified version of the MPN SAF-TSS questionnaire, which required patients to evaluate seven possible symptoms on a scale of 1 to 10, where 10 corresponds to the highest possible perceived severity. Treatment efficacy was tested taking into account the number of presentations where a phlebotomy was deemed necessary to reduce the hematocrit while obtaining a specific treatment, such as hydroxycarbamide or ruxolitinib, compared to the total number of presentations.

Results. A total of 41 patients were eligible for our study. The symptoms most patients perceived as being highly severe were night sweats (according to 41% of patients), fatigability (31%) and abdominal discomfort (24%); on the other hand, symptoms deemed as least severe were fever (97%), weight loss (78%) and pruritus (73%). Out of the 35 patients treated with hydroxycarbamide, 21 required phlebotomies on less than 33% of presentations, while 6 patients needed venesections on more than 66% occasions. More than 90% of patients treated with ruxolitinib had a low requirement of phlebotomies.

Conclusion. Patients diagnosed with PV can face a myriad of symptoms, some of which may be of high severity. It is important to find out which symptoms can be most bothersome, as these may impose a need for a change of treatment.

The therapeutic potential of *Pinus Mugo* extracts

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Introduction. Over recent decades, medicinal plants have demonstrated significant potential as sources for drug development, primarily due to their rich reserves of bioactive compounds. Secondary metabolites within these plants are promising candidates for developing new herbal medicines with valuable pharmacological properties. The study aimed to identify the antioxidant effects of *Pinus mugo* extracts.

Material and methods. The *in vivo* effects were studied on an experimental model of acute inflammation. The extracts were administered by gavage administered in three different concentrations: 100%, 50%, 25%. The subjects were male Wistar Bratislava rats. To study the prophylactic effects, the extracts are administered from day 1 to day 7, on day 8 inflammation was induced. To study the therapeutic effects, inflammation was induced on the first day, then from day two to seven the extracts were administered. Oxidative stress parameters were total oxidative stress (TOS), total antioxidant Capacity (TAC), malon dialdehyde (MDA), oxid nitric (NO), advanced oxidation protein products (AOPP).

Results. The results obtained demonstrated that *Pinus mugo* extract administered as a pre-treatment and as a treatment lowered oxidative stress induced-inflammation by reducing the oxidants. Statistical analysis also demonstrated that *Pinus mugo* extract effects on oxidative stress were comparable to those of Diclofenac.

Conclusions. The results of the study underscore the potential of active compounds from *Pinus mugo* extracts for both prophylactic and therapeutic use. This versatility makes these extracts a promising candidate for further research and potential drug development.

The antioxidant and anti-inflammatory activities of polyphenols from red and white grape pomace in cardiac ischemia

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Introduction. Cardiac ischemia represents one of the leading causes of death worldwide. Therefore, there is interest in adjuvant therapies, such as polyphenols from grape pomace. The main objective of this study was to evaluate the anti-inflammatory and antioxidant effects of polyphenols from red and white grape pomace (GP) on isoproterenol (ISO)-induced cardiac ischemia.

Material and methods. Fifty male Wistar albino rats, randomly divided into 5 groups: I–reference, II–control; III–Ramipril, IV–white GP, V–red GP, were included in the experiment. On day 13, each rat in Groups II-V was induced with cardiac ischemia by intraperitoneal administration of 45 mg/kg ISO. The effects of the administered therapies were monitored by ECG on days 1 and 14, and by determining the values of IL-1, IL-6, and TNF-α in serum on days 7 and 14 and, respectively, in liver and cardiac homogenates on day 14 after animal sacrifice.

Results. No significant differences between the reference group (I) and the treated groups (III, IV, V) regarding the values of the three markers ($p>0.05$) were detected. However, these groups differed significantly from the control group (II) ($p<0.05$). Similar results were obtained for pro-inflammatory markers in the cardiac homogenates, but not in the liver one. ECG showed that ISO reduced the RR interval, while treatments did not prevent this effect. ISO also increased heart rate, an effect prevented only by ramipril. The amplitude of R waves was reduced, with all three treatments showing beneficial effects, but only red GP did not differ from the reference group. No differences were observed between groups regarding the PR segment, QRS, QT, and QTc intervals.

Conclusions. Grape pomace has the potential to protect the heart in ischemic diseases by reducing inflammation and regulating heart rate, where red GP was particularly effective in these regards. Grape pomace could be a promising candidate for developing new treatments for cardiovascular diseases.

Specific approaches to heart rhythm management in patients with atrial fibrillation and heart failure with preserved ejection fraction

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Introduction. There is limited knowledge on patients with heart failure (HF) with preserved ejection fraction (HFpEF) and AF. Often co-occurring, HF and AF can mutually reinforce each other and jointly contribute to a significantly poorer prognosis than either condition alone. This study aims to explore the specific methods of heart rhythm control in patients with AF and HFpEF, highlighting their unique clinical challenges.

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Materials and method. This study analyzed data from patients admitted to the Cardiology Department of the Clinical Rehabilitation Hospital in Cluj-Napoca, focusing on AF type, rhythm control methods, and echocardiographic parameters.

Results. One hundred thirteen patients with AF and HFpEF were included: 24 underwent radiofrequency ablation, 24 cryoablation, and 65 electrical cardioversion to sinus rhythm. Results indicated that patients with paroxysmal AF were significantly more likely to achieve rhythm control through cryoablation ($p < 0.01$), while those with persistent AF were more frequently managed with electrical cardioversion ($p < 0.01$). Echocardiographic assessments revealed that left atrial diameter was significantly larger in patients with persistent AF ($p < 0.01$).

Studies showed that catheter ablation demonstrated significant improvements in survival, freedom from AF recurrence, and quality of life compared to drug therapy. These benefits appear to be greater than those seen in patients without HF, suggesting that ablation may be particularly advantageous for patients whose symptoms and functional impairments are linked to both AF and HFpEF.

Conclusions. This study highlights the challenges in managing AF in patients with HFpEF. Rhythm control methods vary by AF type, emphasizing the need for tailored treatment strategies. Further research is essential to confirm these results and evaluate the long-term effects of rhythm control interventions in this population.

Gender-related particularities of comorbidities in patients with heart failure with preserved ejection fraction

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Introduction. Several studies suggest that comorbidities in HFpEF patients directly impact the syndrome's progression. They act through interconnected pathophysiological pathways: chronic inflammation, oxidative stress, endothelial dysfunction. This study aims to better characterize the comorbidities profile of HFpEF patients with a focus on gender-related particularities.

Material and methods. This study analyzed data from patients admitted to the Cardiology Department of the Clinical Rehabilitation Hospital in Cluj-Napoca. The analyzed comorbidities were: diabetes mellitus, obesity, chronic kidney disease, hyperuricemia, arterial hypertension, pulmonary arterial hypertension (PAH) and atrial fibrillation.

Results. A total of 62 patients were enrolled in the study, consisting of 28 men and 34 women. PAH was significantly more frequent in men compared to women ($p = 0.02$). For other comorbidities examined, no statistically significant differences were observed between genders, including diabetes ($p = 0.25$), obesity ($p = 0.43$), chronic kidney disease ($p = 0.54$), hyperuricemia ($p = 0.69$), arterial hypertension ($p = 0.51$), and atrial fibrillation ($p = 0.40$).

Although HFpEF and PAH have unique pathophysiological causes, they share notable similarities. Both originate at the vascular level with endothelial dysfunction, increased vascular rigidity, and collagen deposition. This is due to factors like reduced nitric oxide availability, heightened oxidative stress, and metabolic comorbidities. Given these overlaps, novel therapies and a clearer understanding of vascular dysfunction mechanisms may improve outcomes in both PAH and HFpEF.

Conclusion. Among HFpEF patients, comorbidities are generally distributed evenly across genders, with pulmonary hypertension potentially representing a more specific risk factor for men in the progression of this form of heart failure.

Association of glycemia and C-reactive protein values with acute kidney injury and mortality in patients with different types of pneumonia

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Introduction. The mortality rate from Community-acquired pneumonia (CAP) or coronavirus disease 19 (COVID-19) is high, especially in hospitalized patients. The aim of the present analysis was to investigate the disturbances of glucose and lipids metabolism along with inflammatory status regarding the short-term evolution for pneumonia patients of different etiologies.

Material and methods. This retrospective study comprised of 398 patients divided as follows: 155 with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia, 129 participants with viral CAP and 114 with bacterial pneumonia.

Results. Compared with a value <110 mg/dL for fasting plasma glucose (FPG) at admission, levels between 110-126 mg/dL are associated with mortality in both COVID-19 (OR=3.462, 95% CI: 1.275-9.398, p=0.015) and bacterial CAP participants (OR=0.254; 95%CI: 0.069-0.935, p=0.039), while a value ≥126 mg/dL was linked with mortality only in SARS-CoV-2 patients (OR=3.577, 95%CI: 1.166-10.976, p=0.026). Also, FPG at admission and glycemic variation during hospitalization was linked with acute kidney injury (AKI) in bacterial CAP. Regarding the inflammatory syndrome, the C-reactive protein is associated with mortality only in bacterial pneumonia patients-p<0.0001. No relation between lipid biomarkers and complications or in-hospital outcomes was observed in all three participant groups.

Conclusion. Finding biomarkers associated with in-hospital complication or mortality can bring an individualized therapeutic decision that may reduce the poor evolution and the mortality in pneumonia patients.

Cholangiocarcinoma in Romanian patients - a two-center retrospective research

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Introduction. Cholangiocarcinoma is a rare tumor of the biliary tract, characterized by its aggressive nature. It can be classified as intrahepatic or extrahepatic (perihilar or distal). Inflammation plays a key role in the pathophysiology of this disease. Data is scarce on the population of Romanian patients with this diagnosis; therefore, this study aimed to shed light on the topic whilst taking into consideration the variations caused by demographic factors.

Material and methods. Patients with a histopathological diagnosis of intrahepatic or extrahepatic cholangiocarcinoma from two Romanian hospitals were included during the time frame 01.01.2018-31.12.2022, however patients with insufficient data or with an uncertain diagnosis were excluded. Data regarding demographic characteristics and inflammatory markers was collected.

Results. From the 279 patients included 58.4% were males. The age at diagnosis did not display significant difference between males and females. The diagnostics of participants were: intrahepatic- 39.4%, perihilar- 29.4%, distal cholangiocarcinoma- 26.2% and the rest had an uncertain primary site. Systemic inflammatory index (SII) was significantly higher in patients with perihilar cholangiocarcinoma than in other localizations (Median=1040; interquartile range=1130; p=0.017). Neutrophil-to-lymphocyte ratio (NLR) was positively correlated with the age of diagnosis, tumor localization not being a decisive factor (ρ=0.168; p=0.006).

Conclusions. The distribution based on tumor location was slightly different from available data on other populations, with a predominance of intrahepatic localization. Males and females are affected as previously reported. Moreover, SII is higher in patients with perihilar cholangiocarcinoma compared to patients with other localizations. The positive correlation between NLR and the age at diagnosis could be explained by the increase of systemic inflammation as result of an increase in the number of comorbidities.

Analysis of comorbidities and guideline-directed treatment optimization in heart failure with atrial fibrillation: insights from a prospective observational single-center study

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Introduction. Heart failure (HF) and atrial fibrillation (AF) are interconnected pathologies that complicate patient management. Comorbidities and therapy choices play a critical role in prognosis. This paper examines the prevalence of comorbidities in HF and AF patients and in-hospital guideline-directed therapy optimization, aiming to improve clinical outcomes.

Material and Methods. We prospectively enrolled patients admitted to the

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Cardiology Department of the Clinical Rehabilitation Hospital in Cluj-Napoca from August to October 2024 with any form of AF and HF with reduced (HfrEF) or preserved ejection fraction (HfpEF), defined by the 2021 European Society of Cardiology HF Guidelines. Data collected included demographics, comorbidities, and treatments at admission and discharge. The use of outcome-impacting drugs indicated in HF was specifically documented, comparing them at admission versus discharge. We also made note of the reasons for which optimal therapy could not be implemented.

Results. The study included 65 patients: 45 with HFpEF and 20 with HFrEF. Hypertension and permanent AF were significantly more frequent in patients with HFpEF compared to HFrEF (84.4% vs 50% $p<0.01$, and 40% vs 15% $p = 0.047$). Among HFrEF patients, 20% were on all four guideline-directed therapies at admission, rising to 55% at discharge ($p = 0.039$, McNemar test). For HFpEF, SGLT2 inhibitor use increased from 20% at admission to 40% at discharge ($p < 0.01$). Major barriers in therapy implementation were symptomatic hypotension (for ARNI), advanced chronic kidney disease (for MRA, and SGLT2 inhibitors) and bradycardia (for beta-blockers).

Conclusion. This study underscores different comorbidity profiles in HF associated with AF and highlights improvements in guideline-directed therapies at discharge. However, certain barriers continue to limit optimal therapy. Addressing them is crucial to enhancing outcomes in this complex population, prompting future research in this direction.

Evaluation of candidates for major lung resection in identifying obstructive sleep apnea syndrome

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Introduction. Obstructive sleep apnea syndrome (OSAS) is a common respiratory condition, significantly impacting morbidity and mortality. Although the role of OSAS as a risk factor for perioperative complications has been well documented in other surgical specialties, its influence in thoracic surgery, particularly in major lung resections, remains inadequately explored. Given the high prevalence of OSAS among elderly patients, its preoperative evaluation in the context of lung resection surgery is essential for optimizing perioperative management and reducing the risk of postoperative complications.

Material and methods. Ninety-one patients scheduled for major lung resection were divided into two groups: Group 1, including patients diagnosed with OSAS, and Group 2, without it. Inclusion criteria were adult patients with lung cancer eligible for major lung resection, regardless of whether OSAS was treated or untreated. Evaluation methods included medical history and clinical examination, arterial blood gas analysis, biochemical panel, spirometry, transthoracic echocardiography, chest X-ray, ECG, and OSAS risk assessment questionnaires (STOP-BANG and the Epworth Sleepiness Scale). Patients with high scores on the sleepiness questionnaires underwent polygraphy to confirm the OSAS diagnosis.

Results. In the first stage, patients were evaluated and classified according to severity score, resulting in 48 patients with low risk, 29% with moderate risk, and 18% with high risk. Nocturnal polygraphy was performed on patients with moderate and high risk, revealing significant variability in OSAS severity.

Conclusion. This methodological approach emphasizes the importance of thorough evaluation of sleep apnea among patients undergoing lung resections, facilitating the implementation of appropriate therapeutic interventions in this vulnerable group.

The effect of heated tobacco product extracts on biofilm formation by respiratory pathogens

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Introduction. Heated Tobacco Products (HTPs) emit toxic compounds despite being marketed as "reduced-risk" alternatives. Exposure to conventional and electronic cigarette vapor enhances biofilm formation. Biofilms are resistant microbial colonies, encased within an extracellular matrix, linked to persistent respiratory infections. This study investigates the effects of HTP vapor on biofilm formation in respiratory pathogens.

Method. Cigarette smoke extract (CSE), IQOS™ and Glo™ extracts were prepared by bubbling the smoke/vapor through appropriate culture media (4 cig/50 mL), and filter sterilized. Marlboro Red™ cigarettes, Terea™ sticks with an IQOS ILUMA™ device and Glo™ neo™ sticks with a Glo™ HyperPro™ device were used. Included were standard strains of *Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumoniae, Streptococcus pneumoniae, Haemophilus influenzae* as well as a *Moraxella catarrhalis* clinical strain. Biofilms mixed with the extracts 1:1 were incubated in 96-well plates for 24 and 48h. After methylene blue staining, absorbance was measured at 620 nm.

Results. Statistically significant differences between the smoke/vapor extracts and the negative controls were observed predominantly at 48h, in the case of CSE exposed *H. influenzae* (p=0.004), *S. pneumoniae* (p=0.008), IQOS™ extract exposed *H. influenzae* (p=0.016), *K. pneumoniae* (p=0.027), *S. aureus* (p=0.006), *S. pneumoniae* (p=0.015), Glo™ extract exposed *K. pneumoniae* (p=0.025), *M. catarrhalis* (p=0.011), *S. pneumoniae* (p=0.02). The Glo™ extract was found to not differ significantly from CSE for *M. catarrhalis* (p=0.276), *S. aureus* (p=0.07).

Conclusion. These findings demonstrate that substances contained by HTP vapor increase bacterial biofilm formation by respiratory pathogens, suggesting an increase in virulence.

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Unmasking recurrence: how initial procedure efficiency parameters influence pulmonary vein reconnection during re-do atrial fibrillation ablation

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Introduction. Atrial fibrillation (AF) recurrence after initial radiofrequency (RF) catheter ablation often necessitates repeat ablation procedures. A key factor in recurrence is pulmonary vein (PV) reconnection. This study investigates the association between PV reconnection and specific parameters of the index ablation procedure.

Material and methods. We conducted a retrospective analysis of patients who underwent a repeat RF catheter ablation for AF recurrence. Data on PV reconnection, number of reconnected veins, and parameters from the initial ablation procedure—including duration, radiation dose, and radiation exposure time—were collected and analyzed. Statistical correlations were assessed to determine associations between these procedural factors and PV reconnection in repeat ablations.

Results. Pulmonary vein reconnection was detected in a substantial proportion of patients undergoing re-do ablation, with significant variations in the number of reconnected veins. Analyses demonstrated that longer initial procedure durations ($p=0.003$), higher radiation doses ($p=0.022$), and increased radiation exposure times ($p<0.001$) were positively correlated with PV reconnection and a higher number of reconnected veins.

Conclusions. The observed correlation between PV reconnection and initial procedure parameters—specifically, duration, radiation dose, and exposure time—suggests these factors play a role in the long-term success of RF catheter ablation for AF. Extended procedure durations and higher radiation doses may indicate technical challenges or complexities in achieving durable PV isolation during the initial procedure, which could result in incomplete lesions and subsequent reconnections. Addressing these factors in the index procedure may enhance procedural efficacy and reduce the risk of recurrence. Thus, optimizing initial ablation techniques could minimize the need for repeat interventions and improve patient outcomes in AF management.

Clinical progression and lung function in COVID-19-infected lung transplant recipients: the role of Remdesivir

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Introduction. COVID-19 has emerged as a prevalent infection among lung transplant recipients (LTR) posing significant risks for adverse outcomes. While initial outcomes during the pandemic were concerning, the impact of COVID-19 therapies is still unclear. Our study aims to assess how the treatment by Remdesivir in COVID-19

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LTR influences the clinical progression and lung function in a cohort of COVID-19 -LTR from France.

Material and methods. We conducted a retrospective cohort study, including 130 lung transplant recipients diagnosed with confirmed COVID-19 and hospitalized at ”Marie Lannelongue” Hospital from Paris, France in the period from January 2020 to December 2023. We compared clinical outcomes, details regarding hospitalization (duration, oxygen requirement, admission in intensive care unit), severity and and spirometry results before and 3 months after infection in patients treated with remdesivir (n=50, R group) versus control group, LTR-COVID19 infected without remdesivir treatment, (n=80, NR group).

Results. The two groups were homogenous in terms of vaccinations, and both groups presented similar rates of severe COVID19 disease. There was no significant difference in the hospitalization length, oxygen requirement and rate of ICU admission between the two groups. There was no significant decline in forced expiratory volume in 1 second of expiration (FEV1) at 3 months after infection in those treated with R versus those NR, but a significant decline in FEF25 - 75% was observed in NR group ($p<0.05$).

Conclusion. In our COVID-19 infection in LTR treated with R or NR results a clinically significant decline in lung function (FEF25-75%) at 3 months in those without remdesivir treatment.

Atypical COVID-19 deaths: histopathological insights

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Introduction. COVID-19, caused by the novel coronavirus SARS-CoV-2, rapidly escalated into a global pandemic characterized by diverse clinical manifestations. While the acute phase of the pandemic has subsided, SARS-CoV-2 continues to circulate. This study documented atypical histopathological findings in patients who died from severe COVID-19.

Material and methods. Tissue samples were harvested from the lungs, heart, liver, kidney, spleen, and brain during the autopsies performed at the Institute of Forensic Medicine in Cluj-Napoca between April 2020 and December 2020. All tissues were processed for microscopic examination, stained with hematoxylin and eosin, and pulmonary tissues were further stained with trichrome Masson and SARS-CoV-2 nucleocapsid immunohistochemistry. The study included only adults without microscopic evidence of COVID-19 lung damage.

Results. Ten cases were analyzed, with most being male (n = 9), and none exhibited typical lung pathology associated with COVID-19. Most of the patients (n = 6) were over the age of 70. Notable findings included: pulmonary microthrombi (n = 6), alveolar edema (n = 9), emphysema (n = 7), and interstitial fibrosis (n = 7). Additionally, myocarditis was observed in 4 cases, while diffuse cardiosclerosis was present in 8. Hepatitis was noted in 7 cases, along with acute tubular necrosis and chronic pyelonephritis, both affecting 5 of the patients. Splenic lymphocyte depletion occurred in 7 cases, and encephalitis was identified in 2 patients.

Conclusions. This study of atypical COVID-19 fatalities highlights the potential role of systemic inflammation and endothelial dysfunction in increasing mortality, even in the absence of typical pulmonary lesions. These findings underscore the importance of recognizing and addressing the systemic effects of SARS-CoV-2 infection, which can manifest as widespread inflammation and thrombotic events in various organs.

Effects of *Lavandula angustifolia* oil on diabetic rats with carrageenan-induced thrombosis

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Introduction. Previous research has evidenced the therapeutic properties of *Lavandula angustifolia* oil (LAO), relating to anxiolytic, antibacterial, and antifungal actions. The beneficial effects of LAO on inflammation in thrombosis has been previously demonstrated. This study aimed to investigate the effects of LAO on diabetic mellitus (DM) rats with induced experimentally thrombosis.

Material and methods. Wistar rats were randomly allocated into five groups, each consisting of ten rats. Group C, control group, received intraperitoneal saline (i.p.). Group D, was administered saline pretreatment and subsequently had DM. Group T, was administered saline pretreatment and subsequently had thrombosis. Group TD, designated as the DM and thrombosis group, was administered saline pretreatment. The fifth group TDL received pretreatment of LAO at a 200 mg/kg body weight dosage via i.p. and DM and thrombosis. Glycemic status and markers of oxidative stress and inflammatory chemokines were measured. Specific organs underwent histology examinations for each group.

Results. The findings demonstrate that rats pretreated with LAO exhibited significant improvements in glycemic control by lowering glycemia at half, reduced oxidative stress to normal value, and decreased inflammatory to biomarkers to normal value compared to the TD group ($p<0.0001$). Histopathological analysis showed improved morphological aspects in studied organs within the LAO-treated group.

Conclusion. Our outcomes showed that LAO exhibits antidiabetic effects on rats, potentially through mechanisms involving antioxidant and anti-inflammatory properties. Rats pretreated with LAO had no thrombosis in histological analysis, and necrosis was absent in pancreatic cells or Langerhans islets compared to the untreated group.

Novel catechol-thiazolyl-hydrazonoethyl-coumarin hybrid compounds with antioxidant activity

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Introduction. Oxidative stress is a major factor in the pathology of various diseases as the latest discoveries in this field have shown. This motivates the continuous development of both natural and synthetic antioxidants in hopes of establishing a new drug for human use. Herein, we present the synthesis and antioxidant activity of seven

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catechol-thiazolyl-hydrazonoethyl-coumarin hybrid compounds (1-7).

Material and methods. The compounds were obtained through a three-step reaction process. The structures were confirmed through IR, MS, 1H NMR, and 13C NMR spectral analysis. The antioxidant activity was in vitro assayed using both antiradical and electron transfer assays. The employed tests were ABTS and DPPH as antiradical assays, expressing the results as half-maximal inhibitory concentrations (IC50), and Total Antioxidant Capacity (TAC), Reducing Power (RP), Ferric Reducing Antioxidant Potential (FRAP), and Cupric Reducing Antioxidant Capacity (CUPRAC) as electron transfer assays, expressing the results as molar equivalents (Eq) of Trolox and/or ascorbic acid.

Results. The compounds were obtained in various yields between 42.25-99.50%. All seven compounds had lower IC50 values (IC50 = 7.06-33.49 μM) compared to ascorbic acid (IC50 = 50.17 μM) and Trolox (IC50 = 16.57 μM against ABTS and 36.69 μM against DPPH) in the antiradical assays. The number of molar Eq ascorbic acid varied between 1.33-2.20 in TAC and 0.84-2.02 in RP. The number of molar Eq Trolox ranged between 0.84-2.02 in RP, 1.14-1.45 in FRAP, and 2.27-3.63 in CUPRAC. The most active antioxidants were 6 and 7 due to their additional phenol group, although the other five compounds also had very good antioxidant activity.

Conclusion. Based on the obtained results, seven novel compounds with antioxidant activity were developed, which can be further investigated for different other biological activities.

Simultaneous electrochemical detection of inflammatory-associated cytokines in biological samples

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Introduction. Cytokines are signaling biomolecules that play crucial roles in various processes of the organism, including cell growth, inflammation, and cancer-related processes. Because of these roles, they serve as valuable biomarkers for diagnosing certain medical conditions and monitoring responses to pharmacologic therapy. The study aimed to design a customized platform for Interleukine-6 (IL-6) and Tumor necrosis factor (TNF-α) simultaneous electrochemical detection in biological fluids with prospects for biomedical applications.

Material and methods. Customized electrochemical cells were in-lab printed. The surface of the working electrodes was modified with Au and Pt nanoparticles to increase the detection sensitivity, and two specific aptamers labeled with two different redox labels were used to ensure the detection's specificity.

Results. The developed platform was characterized through electrochemical and morphological techniques and subsequently applied for the specific, simultaneous detection of IL-6 and TNF-α using cyclic voltammetry. Key analytical parameters, including the limit of detection, limit of quantification, and sensitivity for both IL-6 and TNF-α, were assessed, and the platform was tested on real samples.

Conclusion. The developed sensor enables the specific simultaneous electrochemical detection of IL-6 and TNF-α, highlighting its suitability for medical applications.

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Personalized medicine for antibiotics treatment: aptamer selection for point-of-care electrochemical assessment

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Introduction. In the field of precision medicine, aptamers have emerged as an innovative and versatile class of biorecognition elements for the development of miniaturized monitoring systems for various types of diseases. Vancomycin is used as first-line treatment for severe infections and has a narrow therapeutic window; therefore, therapeutic drug monitoring is required. This study presents the main strategy and results regarding the selection of a novel aptamer for vancomycin using SELEX technology and its use in the development of a portable electrochemical aptasensor.

Material and methods. The selection of the aptamers was realized using magnetic beads-based SELEX technology by alternating positive-, negative- and counter-selection rounds. The evolution of the selection was monitored by enrichment assays, fluorimetry and gel electrophoresis analyses. After cloning and sequencing, the affinity of the aptamers was evaluated by surface plasmon resonance (SPR). Docking analysis and molecular dynamics calculations were performed to characterize the aptamer-vancomycin complexes. For aptasensor development, gold screen-printed electrodes were used, and each step was optimized using electrochemical measurements.

Results. The highest bound percentage of sequences towards vancomycin was observed in round 7 out of a total of 9 selection rounds. After cloning and sequencing experiments, the most representative sequences were analyzed by SPR measurements, obtaining dissociation constants (Kd) as low as 260 nM. Several strategies were addressed and optimized to obtain the optimal sensing platform for vancomycin assessment.

Conclusions. The developed aptasensor will be further used for the quantification of vancomycin from clinical serum samples.

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Beta-glucan as an immune activator and its application in targeting tumor associated macrophages

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Introduction. β-glucans are polysaccharides formed from monomers of D-glucose linked by β-glycosidic bonds (1-3) or (1-4) and a β-branch (1-6), with a linear structure, helical or very branched. They are biologically active polymers found in the cell wall of bacteria, in fungi, algae, cereals, with immunomodulatory effects on the immune system. β-glucans extracted from yeast has immunomodulating activity, demonstrated by activating dendritic cells and macrophages, directly by binding to Dectin-1 receptors. This action leads to an increased antitumor activity and the initiation of the inflammatory

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response by simultaneously stimulating T cytotoxic cells and T helper cells triggering thus an intense activity to eliminate tumor cells.

Material and methods. Liposomes with β-glucan were obtained by the lipidic film hydration method. MDA-231 tumor cells resistant/sensible to doxorubicin were co-cultivated with β-glucan and monocytic THP-1 cells activated with LPS. Cytotoxicity tests-MTT and alamar blue were performed for evaluation of MDA-231 cells viability. Free liposomes labelled with PKH- staining kit were microscopically visualized as a method of cell internalization evaluation.

Results. The PKH staining allows the visualization of the internalization of liposomes in the target cells. IC50 value of Doxorubicin on tumoral MDA 231 cells was 61,87 μg/ml. Co-cultivation of THP-1 cells with MDA-231 and treatment with 50 μg/ml doxorubicin induced a decrease of tumor cells viability to 53%. Adding 200 μg/ml β-glucan to co-cultures induced a profound decrease of MDA 231 viable cells to 25%.

Conclusions. The viability of MDA-231 tumor cells sensible to doxorubicin after doxorubicin /doxorubicin with β-glucan treatment in co-culture is more decreased in comparison with MDA-231 resistant tumor cells. Treatment with doxorubicin and doxorubicin/β-glucan of tumor cells in monoculture induced marked cytotoxicity at the doses used, which was intensified by the combination of doxorubicin and doxorubicin with β-glucan.

An *in silico* model for the study of angiogenesis in ccRCC

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Introduction. Renal cell carcinoma (RCC) is the most common type of renal cancer, with about 434,840 annual cases and 155,953 deaths worldwide. The five-year survival rate is 70% but can drop to 12% in the metastatic clear cell RCC (ccRCC), the main subtype. Angiogenesis is responsible for the malignant transformation of ccRCC, especially due to the inactivation of the VHL gene, a common trait in ccRCC cases. Thus, exploring the regulatory mechanisms of angiogenesis in ccRCC could provide valuable biomarkers. Our study proposes an in silico model for the study of angiogenesis in ccRCC.

Material and methods. We interrogated starBase/ENCORI and TCGA repositories to identify candidate lncRNA and miRNA involved in regulating angiogenesis in ccRCC. In R 4.3.0, we used the TCGAbiolinks 2.30.0 package to retrieve gene and miRNA expression quantification. We added gene symbols to the raw expression files by mapping the ensemble IDs to gene symbols with the org.Hs.eg.db 3.18.0 library. Data annotation, TPM normalization, log transformation, scaling, PCA, neighborhood graph computation, and UMAP were conducted on the Panomics platform. Differential gene expression was done using DESeq2. We downloaded up/down-regulated genes and miRNAs from TCGA for angiogenesis-related analysis. Using the miRNA-Target database, we filtered interactions specific to the DE miRNAs. We focused on lncRNA pairs that included up-/down-regulated genes for RNA-RNA interactions, sorting results by alignment score.

Results. Angiogenesis-related genes, such as VEGFA and TIMP3, interact with key regulatory miRNAs identified from TCGA datasets, like miR-429 and miR-1269a. Moreover, lncRNAs such as NEAT1 and MALAT1 were predicted to sponge these

miRNAs, thus regulating angiogenesis.

Conclusion. This network highlights a complex regulatory axis that might facilitate the angiogenic process in ccRCC and can be further investigated for biomarker discovery.

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Bilberries phytochemical characterization and assessment as functional ingredient against ochratoxin A toxicity *in vitro*

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Introduction. Mycotoxin contamination in cereal-based foods represents a major health concern, particularly regarding ochratoxin A (OTA), a common mycotoxin with proved toxicity. Natural antioxidant sources, including bilberries (*Vaccinium myrtillus L.*, VM), are potential mitigating agents due to their rich phytochemical profile, which may counteract OTA's harmful effects.

Material and methods. In the present study, the first step was to evaluate the total phenolic content, antioxidant activity, and detailed phytochemical composition—including hydroxycinnamic acids, hydroxybenzoic acids, flavanols, flavonols, and anthocyanins—in lyophilized bilberries harvested from the spontaneous flora from Romania. Afterwards an in vitro digestion model simulated gastrointestinal conditions to assess OTA bioaccessibility and cytotoxicity effects in bread samples: Control, VM (2%) fortified, OTA-contaminated (15.89 ± 0.13 mg/kg), and OTA (16.79 ± 0.55 mg/kg) with VM (2%).

Results. Bilberries reduced OTA bioaccessibility by 15% at the intestinal level, demonstrating a significant inhibitory effect on toxin absorption. In Caco-2 cells, OTA-VM digests led to improved cell viability compared to OTA digests, with protective effects evident across various exposure times. In Jurkat cell assays, OTA digests increased cell death by 11%, while the addition of VM reduced this to 1%, suggesting a strong protective influence. Reactive oxygen species (ROS) analysis supported these findings, with OTA-VM digest producing significantly lower ROS levels—3.7 times less than OTA digest.

Conclusion. The Romanian bilberries show strong potential as a functional ingredient in mitigating OTA's cytotoxic effects, offering antioxidant benefits that reduce OTA bioaccessibility and oxidative stress in cellular models. These findings highlight the benefit of bilberry-enriched foods in protecting against mycotoxin contamination effects.

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Objective assessment of dental shade modification, OHRQoL and dental aesthetic self-perception, before and after prophylactic dental procedures in pediatric patients – a pilot study

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Introduction. The current study aims to investigate the changes in self-perceived oral health-related quality of life (OHRQoL) in relation to dental shade modifications assessed before and after professional prophylaxis procedures. Based on the study purpose, the following null hypothesis was formulated: the prophylactic treatment session has no effect on the patients' objective oral hygiene health status, self-perceived OHRQoL, and dentofacial aesthetics.

Material and methods. The current study was designed as a pilot study in which 40 pediatric patients were examined. The patients presented unaltered cognitive and communicational functions and underwent three sessions of examination or treatment performed by two medical examiners, as follows: i) Initial examination, including dental chart, generated through classical and instrumental methods (SOPRO intraoral camera in "Cario mode"); the oral hygiene index (OHI-S), obtained by classical and instrumental methods (SOPRO intraoral camera in "Perio mode"); Dental shade assessment, employing visual and instrumental methods (Vita Classical and Vita Easyshade V Spectrophotometer); Evaluation of oral health-related quality of life (COHIP-19); Measuring of the self-reported dental aesthetics (PIDAQ). Prophylactic procedures followed: scaling, airflow and professional brushing. ii) Two stages of evaluation (immediately after the prophylactic procedures) and after one-month follow-up comprising the same data described in the previous section. OHI-S and questionnaire subscale scores were computed, and the CIEDE2000 color difference and whiteness index for dentistry (WID) were calculated. A one-way repeated measures analysis of variance (ANOVA) was conducted to assess the change in the patients' objective oral hygiene health status, self-perceived OHRQOL, and dentofacial aesthetics before, immediately after, and one month after the prophylactic treatment session.

Results. The prophylactic procedures led to changes in dental color recorded both classically: two shades (9%), one shade (28%), no shade modification (63%), and instrumentally: one shade (33%), no shade modification (67%). The initial, pre-treatment classically investigated OHI-S mean score (1.3) strongly decreased within the immediate post-prophylactic treatment examination (0) and maintained a low value at the 1-month examination (0.6). The mean PIDAQ scores varied as follows: 25.82 before the treatment session, 11.12 immediately after the treatment session, and 11.65 one month after. The repeated-measures ANOVA indicated that the mean OHI-S scores statistically significantly differed across the three procedure sessions $F(1.54, 183.36)=370.02$, $p=0.001$. The post hoc pairwise comparison, using the Bonferroni correction, indicated statistically significant OHIS score differences between the pre-treatment and the immediate post-treatment evaluations ($p=0.001$); the immediate post-treatment and the 1-month follow-up evaluations ($p=0.001$); the pre-treatment and the 1-month follow-up evaluations ($p=0.001$). The repeated-measures ANOVA also indicated that the mean PIDAQ scores statistically significantly differed across the three procedure sessions $F(1.11, 132.97)=130.28$, $p=0.001$. Moreover, the CIEDE2000 color difference and Windex for dentistry values were situated above the acceptability threshold immediately after the prophylactic procedures. The following mean values were registered: for

CIEDE2000 color difference T0-T1 – 2.70; T0-T2 – 2.31; for ΔWindex T0-T1 – 5.28; and ΔWindex T0-T2 – 4.12.

Conclusions. The initial motivation session and the prophylactic procedures led to an improvement in dental color. They generated responsible behavior regarding oral hygiene, which led to decreased OHI-S index values recorded at the immediate post-treatment and 1-month follow-up examination. The prophylactic treatment session also led to immediate color difference values situated above the acceptability threshold.

Generative artificial intelligence-based program in summarizing scientific literature: a case study

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Introduction. Generative AI (Artificial Intelligence)-based programs found their usefulness in scientific writing, including summarizing the scientific literature. The study evaluated the accuracy of an AI tool for synthesis of scientific literature.

Material and methods. Thirty full papers reporting twinning tools (digital and virtual) in cancer were evaluated. The Coral AI generative AI-based program was used to summarize the articles. The Coral AI (©Pearl Labs) was interrogated on 23 September 2024 and was asked to "Make a summary from a scientific point of view regarding the practical applications of reported results. Please include references". The AIDetect (©XYZAI, Inc.) was used to test if a human-generated the text. The AIDetect retrieved three analytics, % of human writing style, readability score, and grade level. The references indicated in the text generated by Coral AI were summarized by the researcher and analyzed as previously described.

Results. The Coral AI provided a summary of 378 words: an introduction, a six-point summary, and an ending paragraph. For this summary, Coral AI provided 6 references, indicating the page from which the information was extracted (e.g., Defraeye et al., 2023, Page 13). Two of the listed references were not among the 30 articles provided. The sources of Coral AI summary were the Introduction, Results and Discussion, Conclusions, and References sections. The AIDetect identified an 8% human writing style in the text, a readability of 15%, and a grade level of 15th, indicating that the text could be understood by a person with advanced education, such as college level or higher. The expert summary comprised 378 words, identified by AIDetect as 100% human, with a readability score of 43% and a grade level of 10th.

Conclusion. The AI-generated summary is not able to capture multiple input sources or specific results and has information supported by secondary references rather than the scientific article itself as the source of data.

Student Section – Scientific START

Redefining breast surgery: comparing robotic-assisted and traditional reconstruction techniques – a literature review

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Introduction. Breast cancer is a rather consequential public health issue, with numerous cases diagnosed worldwide. One treatment option for this condition is the mastectomy, which can be very destructive. As a result, breast reconstruction is an essential part of patient care. The primary aim of this review is to determine whether the novel robotic technology used for flap harvesting can improve autologous breast reconstruction.

Material and methods. The database searched was PubMed, using the search algorithm: („Robotic Surgical Procedures"[Majr]) AND „Mammaplasty"[Majr]. The included studies were selected within the 2016 – 2024 time frame. The inclusion criteria limited the search to papers studying the female gender and human species. Any techniques other than robotic flap harvesting for autologous breast reconstruction were excluded from the selection. The quality of the studies was assessed via the CARE checklist.

Results. Analysis of the included papers revealed that, compared to the traditional technique, robotic-assisted reconstruction was more advantageous for patients and surgeons, the latter reporting reduced physiological tremor, fixed arm retraction, lowered physician strain, and decreased operation time. Facial incision reduction resulted in lower median hospital stay for patients undergoing robotic surgery. Additionally, the novel approach appears to increase perfusion reliability and decrease postoperative opioid requirement and abdominal wall morbidity, to the detriment of the traditional technique. However, robotic-assisted reconstruction might pose some impediments, such as a significantly higher surgery cost. Regarding complications, there were no statistically significant differences between the two groups.

Conclusion. Based on the evidence provided, robotic-assisted breast reconstruction seems to be the wiser choice for patients in need. However, more studies should be conducted to establish the explicit criteria for choosing to perform it.

Inhibition of FLT3 overcomes bone marrow microenvironment-mediated resistance to venetoclax in non-FTL3 mutated acute myeloid leukemia

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Introduction. Venetoclax, a potent small-molecule inhibitor of BCL-2, targets a critical pathway for leukemic cell survival by promoting apoptosis in AML cells, which frequently overexpress BCL-2 to evade cell death. Despite its efficacy, a significant limitation of venetoclax is the eventual development of resistance, especially in the

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bone marrow microenvironment, where AML cells interact closely with mesenchymal stromal cells. Our preliminary data have shown that bone marrow-derived stromal cells contribute to this resistance by secretion of soluble factors, resistance that is maintained even without direct cell-cell contact. This stroma-mediated resistance poses a significant challenge in AML treatment, as it can limit the durability of responses to venetoclax-based therapies. Therefore, our study aimed to conduct a high-throughput cytokine screening to identify specific cytokines whose inhibition might help overcome stromal cell-mediated resistance to venetoclax. Identifying these cytokines could uncover new therapeutic targets to enhance venetoclax efficacy and delay or prevent resistance in AML patients.

Material and methods. To identify bone marrow-derived cytokines contributing to stroma-mediated VEN resistance, we conducted a high-throughput siRNA screening on hBMSC to profile relevant cytokines produced by this niche. To establish a reliable AML cell line model that mimics venetoclax (VEN) resistance within the bone marrow microenvironment, twelve AML cell lines were cultured and treated with VEN. Each cytokine was individually knocked down in hBMSC using siRNA transfection, enabling a precise evaluation of the impact of each cytokine on VEN resistance. For data analysis, inhibitory concentration (IC) 50 values were calculated using CalcuSyn 1 software, while statistical assessments were performed using GraphPad Prism 9 (GraphPad Software). All experiments were conducted in triplicate to ensure reproducibility and reliability, unless otherwise indicated. Comparisons were made using a two-tailed unpaired Student's t-test, with significance defined as $P<0.05$.

Results. Following an initial screening the MOLM14 FLT3 mutated and the THP1 non-FLT3 mutated AML cell lines were chosen to carry out further experiments. For FLT3 non-mutated AML we identified CXCL10, CCL2 and FLT3-ligand as potential targets. These cytokines do not influence sensitivity to VEN in the presence of FLT3-mutations.

Conclusions. Our study introduces an innovative approach to modulate the bone marrow microenvironment by inhibition of FLT3 which can disrupt the protective niche and sensitize leukemic stem cells to treatment. By targeting stromal-cell-mediated resistance, our strategy aims to both extend the duration of MRD negativity and improve overall survival.

Risk factors in developing alcohol withdrawal syndrome complicated with delirium tremens

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Introduction. Alcohol withdrawal syndrome follows the reduction of heavy, prolonged alcohol use. Diagnosed by the ceasing or diminishing of alcohol intake after a long period of consumption of great amounts and two or more symptoms - increased heart rate, tremors, nausea, insomnia, hallucinations, anxiety, and convulsions, alcohol withdrawal syndrome typically appears within hours or days after cessation. The most severe complication, delirium tremens, is defined by sudden attention disturbances, altered consciousness, and cognitive dysfunction.

Materials and methods. We conducted a retrospective study including patients hospitalized in 2023 in the psychiatry wards of the County Emergency Hospital, divided

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in 2 cohorts: patients diagnosed with alcohol withdrawal syndrome complicated with delirium tremens and patients with alcohol withdrawal syndrome.

Results. Multiple risk factors for delirium tremens exist. Socio-demographic factors include age over 40, homelessness, and unemployment. Age augments risk due to the extended alcohol exposure and obtained tolerance. Alcohol intake, especially over 18 units/day and continuous drinking patterns—also elevate delirium tremens risk, with prior episodes of alcohol withdrawal syndrome or delirium tremens, seizures, or alcohol-induced psychosis serving as additional risk factors. Laboratory results aid risk assessment, abnormal liver tests, thrombocytopenia, and electrolyte imbalances are common among high-risk patients. However, hepatic cirrhosis or liver insufficiency may be protective due to endogenous benzodiazepine buildup. Predictive clinical signs include high heart rate, elevated blood pressure, and tachypnea.

Conclusion. Management relies on prompt benzodiazepine treatment, delays raising the risk of delirium tremens. Untreated alcohol withdrawal syndrome may progress rapidly to severe complications, as coma or death, emphasizing the need for immediate intervention to prevent critical patient decompensation.

An uncommon cause of recto-vaginal fistula due to extrapulmonary tuberculosis - case report and literature review

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Introduction. Anorectal tuberculosis (TB) is a rare form of extrapulmonary TB that may occur alongside pulmonary or abdominal TB, or independently. Diagnosing it is challenging due to its similarity to other anorectal conditions and the potential absence of caseation. A rectovaginal (RV) fistula is a pathological epithelialized tunnel through the RV septum.

Materials and methods. We present the case of a 41-year-old female patient, S.L., admitted in 2024 to the County Emergency Hospital's General Surgery 1 ward.

Results. S.L. had a history of pulmonary TB diagnosed a year prior, two cesarean deliveries, essential arterial hypertension, and a long-term smoking habit. In September 2023, she reported lumbar pain, narrow stools with occasional blood spots over 3-4 months, loss of appetite, and fecal discharge through the vagina. Initial management included a temporary lateral baguette sigmoid colostomy to prevent sepsis and promote healing, along with standard TB therapy. By May 2024, MRI revealed scar tissue in the lower rectum and stenosis, with no visible fistulous tracts. Histopathological examination confirmed a rectovaginal fistula complicated with complete lower rectal stenosis due to anorectal TB, showing caseous nodules in the RV septum that had ulcerated and epithelialized. In June 2024, S.L. underwent ultralow anterior resection of the rectum with a mechanical T-T colo-anal anastomosis due to complete fibrous stenosis and no options for dilation. Her recovery was favorable; she was discharged with normal bowel function and an intact surgical site, retaining a baguette colostomy in the left iliac fossa. Restoration of intestinal continuity is planned within 4-6 weeks after a control recto-sigmoidoscopy.

Conclusion. This case highlights the rarity of anorectal TB and its debilitating symptoms, emphasizing the need for increased awareness among surgeons and clinicians regarding uncommon diagnoses, particularly in patients with relevant history.

Adolescent borderline personality disorder and mixed anxiety-depressive disorder: the impact of peer suicidality on treatment compliance

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Introduction. Borderline personality disorder (BPD) is present in more than 70% of actively suicidal adolescents, posing a considerable socioeconomic burden. Given the frequent co-occurrence of BPD and mixed anxiety-depressive disorder (MADD), diligent monitoring and multimodal treatment are essential for ensuring positive outcomes.

Case report. A 16-year-old male patient presented in May 2023 with social withdrawal, poor academic performance and absenteeism causing him to fail 10th grade. A psychological examination revealed affective instability, social anxiety, unstable gender identity, suicidal ideation and insomnia, leading to the diagnosis of MADD and BPD. Treatment was initiated with psychotherapy and quetiapine 50 mg for sleep regulation. The patient's condition worsened over the next year due to low compliance. After two of his friends committed suicide in July and September 2024, adherence improved significantly. He is currently on sertraline 50 mg, quetiapine 100 mg, and valproate 600 mg with symptom remission.

Discussion. This case illustrates the challenges of addressing adolescent BPD and MADD. The first-line treatment in both cases is psychotherapy, but its success depends on patient compliance. Further, although it is recommended to limit pharmacological interventions to low-dose antipsychotics like quetiapine for mild sedation, nonadherence may lead to symptom aggravation. Remarkably, despite suicide risk factors like psychosocial stress and gender dysphoria, the patient's exposure to peer autolytic behavior resulted in him gaining insight and accepting treatment. Here, mood stabilization was achieved by increasing the antipsychotic dosage and adding an antiepileptic while depressive symptoms were targeted with sertraline.

Conclusion. In order to manage adolescent BPD and MADD effectively, clinician-family collaboration should focus on ensuring adherence in the context of peer influence, which can either hinder or support recovery.

Diagnosis of early caries using open source 3D software: methodology and results

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Introduction. This study explores the use of open-source 3D software, specifically Blender and MeshLab, for the diagnosis of early caries. They are mainly used in fields such as cinematography, architecture, and game development. We developed two distinct methodological approaches to optimize these tools for dental diagnostics.

Material and methods. The first method relies exclusively on MeshLab. Dental arch files, imported in .obj format, enable immediate 3D visualization of the dental structures in color. To highlight potentially carious areas, shading settings are

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adjusted to increase color contrast, enhancing the visibility of affected surfaces. This initial phase provides a quick and effective visual analysis of the dental arches, helping in the preliminary detection of lesions. The second method involves a more advanced transformation process, utilizing both Blender and MeshLab. First, the .obj file, imported into Blender without color, is modified in edit mode, where vertices are unwrapped. After configuring the export settings to retain UV coordinates, normals, colors, and modifications, the file is transferred to MeshLab. In MeshLab, a vertex-to-texture color transfer is applied, generating a final .jpeg file in 2D. This file provides layered views of the dental arches (maxillary, mandibular, and occlusal views) facilitating detailed color-coded observations.

Results. The intra- and inter-rater agreement for early-stage caries identification on 3D virtual models compared to clinical examination, was >0.8 and it was statistically significant ($p<0.05$), regardless of the examiner experience level.

Conclusion. This approach improves precision in visualizing dental arches, marking a significant step forward in the visual diagnosis of early carious lesions. Using these open-source tools in dentistry could lead to faster, cost-effective, and accessible diagnostics, ultimately enhancing clinical practice.

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Moral distress related to ethical dilemmas in dentistry - a literature review

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Introduction. Moral distress is a negative emotional response that occurs when we act in ways that are inconsistent with deeply held ethical values, principles, moral commitments or professionalism (Kherbache et al, 2021; Sasso et al. 2015). Dentists can feel the pressure related to patients' safety, valid consent, negative environment or personal behaviors that could lead to moral distress. The study's purpose was to identify, describe and summarize previous studies on moral distress experienced by dentists. The objectives were: 1) to establish how moral distress is perceived by dentists; 2) to identify factors that contribute to moral distress; 3) to emphasize the consequences of moral distress on dentists.

Material and methods. We used electronic databases (Medline/PubMed and Google Academics), and all eligible articles were hand-selected into a table with the title of the article, the origin of the study, the publication year and the type of study. The inclusion criteria: review studies, quantitative/qualitative studies and mixed methods studies, while excluding studies that did not deal with moral distress, dental students, or were published before 2008.

Results. After applying the search criteria (first search: "Moral Distress" AND "Dental Students"; second search: publishing timeline filter "2008-2023"), we found 502 articles on PubMed from which we included 3 and we found 19,100 articles on Google Academics from which we included 2. In total we found 5 articles that met the criteria, published between 2008 and 2022. The affiliations of authors were from Spain, Bangladesh, the United Kingdom and Saudi Arabia.

Conclusion. The relevance of identifying moral distress among dental students is to prevent ignorance and the lack of empathy among future practitioners. Students can be encouraged in their passion for dentistry by seeing healthy ethical behaviors in the academic environment.

Case presentation - ectopic hepatocellular carcinoma mimicking metastatic disease

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Introduction. Ectopic hepatocellular carcinoma (EHCC) is a rare form of carcinoma that arises from extrahepatic liver tissue and can be difficult to distinguish from metastatic hepatocellular carcinoma. This tissue has an elevated risk of neoplastic development due to impaired vascular supply and biliary drainage. This case is unique because we found only nine left subphrenic EHCC cases reported in the literature.

Case presentation. A 47-year-old male patient is admitted to our service after the discovery, during oncological follow-up, of a left subphrenic tumor mass without having any symptoms. The patient's medical history includes an endoscopically removed bladder tumor, a left radical nephrectomy, and systemic lupus erythematosus with lupus nephritis.

MRI shows a 48/14/66 mm space-occupying lesion between the liver, spleen, and diaphragm, with heterogeneous gadophilia, increased since the 2023 examination. Uro-CT reveals a well-defined, irregular tumor, isodense with the spleen, raising suspicion of post-operative splenosis. Other differential diagnoses considered were metastasis from hepatocellular carcinoma or from previous renal and bladder malignancies.

The patient underwent laparoscopic tumor excision, and had a favorable postoperative recovery with antibiotic treatment, thromboembolism prophylaxis and hydroelectrolytic rebalancing.

Histopathology revealed a lobulated, whitish tumor with variable-sized nodules. Microscopy found medium-sized epithelial cells with brown-yellow secretions. Immunohistochemistry showed: CK7 – few positive; CA19-9 – two positive ducts; Hepatocyte – positive; AFP – 80% positive. The tumor was encapsulated, without angiolymphatic invasion or necrosis, suggesting EHCC.

The patient has been monitored for a month now, without postoperative complications. The recurrence rate for EHCC following surgery is 25%.

Conclusion. Oncologic monitoring is crucial not only for detecting metastases but also for new primary tumors. Reporting more cases and understanding this carcinoma's aggressiveness is essential because preoperative MRI diagnosis of EHCC is challenging and early surgery can significantly improve outcomes for patients.

A tumor's unlikely path: rare urinary tract invasion by renal cell carcinoma – case presentation

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Introduction. Renal cell carcinomas are the most common type of urogenital cancer and include several subtypes, with clear cell renal cell carcinoma (ccRCC) accounting for approximately 70% of cases. Although ccRCC frequently invades the renal vein, it can rarely extend along the pelvicalyceal system, presenting as a tumoral thrombus, thus requiring differential diagnosis with upper tract urothelial carcinoma (UTUC).

Case presentation. We present the case of a 61-year-old man with a history of intermittent left lumbar pain and microscopic hematuria for 9 months. Additionally, 24 hours before the presentation, the patient had spontaneously passed a cylindrical tumor-like mass during voiding.

CT-urography revealed an incomplete duplex collecting system in the left kidney, along with enlargement and deformation of the upper pole. A heterogeneous-iodophillic mass with irregular contours was identified, showing partial extrarenal development. The observed invasion of both superior and inferior pelvicalyceal systems (PS) and ureters, alongside the dilatation and enhancement of the ureteral wall, mirrored typical features seen in UTUC. Another CT was later performed and revealed a small nodular mass in the left adrenal gland. 3D laparoscopic left nephroureterectomy and adrenalectomy were performed via a transperitoneal approach.

Histopathology revealed a yellow mass with necrosis, hemorrhage, and invasion of the PS and ureters, featuring cells with clear cytoplasm and prominent nucleoli at x400 magnification, consistent with ccRCC, Fuhrman grade 2. No angiolymphatic, capsular, or adipose tissue invasion was observed. The cylindrical mass passed during voiding showed necrotic ccRCC features. The left adrenal nodule had characteristics of an adrenal cortical adenoma. Three months after the surgery, a CT-TAP was performed, showing no local recurrence or distant metastases.

Conclusion. Urinary tract-invading ccRCC is rare and has an unpredictable prognosis. Despite significant therapeutical advances, early imaging detection, accurate staging, and differential diagnosis remain crucial for effective treatment.

Approaches for preventing early-onset psychosis in ADHD patients at risk: a case report

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Introduction. Pediatric attention deficit hyperactivity disorder (ADHD) is commonly complicated with behavioral issues, and is also significantly linked to early-onset psychosis. The latter affects about one-fifth of first-episode patients, highlighting the need for cautious management in susceptible populations.

Case report. An 11-year-old boy presented in March 2021 with hyperactivity and educational maladjustment for the past 8 years. The psychological evaluation led to a diagnosis of ADHD with predominantly hyperactive presentation. Initial treatment

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was atomoxetine and psychotherapy, reducing hyperactivity but not family conflict. By February 2022, persecutory confabulations and rationalization ensued alongside aggression, prompting the diagnosis of oppositional defiant disorder (ODD) and a switch to aripiprazole 2.5 mg. Social and academic improvements followed, but symptoms worsened after the patient's parents divorced in November 2023 due to the father's alcohol and gambling addictions. Family counseling led to emotional stabilization by March 2024, though academic difficulties persist.

Discussion. Parental alcohol and gambling disorders are important risk factors for primary psychosis in children, making the father's history relevant to case management. As psychostimulants may accelerate psychosis onset in predisposed ADHD patients, this drug class was avoided in favor of atomoxetine and subsequently a low-dose antipsychotic to address aggression. Still, the combined pharmacological and psychosocial interventions yielded mixed results, likely due to the patient's unstable family environment, which highlights the importance of clinical monitoring in the context of early signs of thought and imagination disorders.

Conclusions. In light of the fluctuating clinical evolution of child psychiatric disorders, special consideration must be given to the pharmacological and psychosocial management and follow-up of ADHD in pediatric patients at risk for psychosis.

Unlocking the mind-body connection: bruxism versus psychological factors

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Introduction. Bruxism, manifested through teeth grinding or clenching, is a condition with implications for the overall health of the body. Understanding and managing the mechanisms of bruxism are essential for preventing complications and improving patients' quality of life.

Aim and objectives. This study investigates the relationship between bruxism and various psychosocial factors, including stress, anxiety, depression, and personality traits. Using a questionnaire distributed to 41 participants, I collected data about the subjects' bruxism-related behaviors and associated levels of stress, anxiety, and depression.

These data were organized in a spreadsheet, with each variable in a separate column. Using statistical tests (Chi-Square) and graphs, I analyzed the association of bruxism with each variable.

Results. The results indicate that individuals with nocturnal or diurnal bruxism tend to have higher levels of stress, anxiety, and depression, as well as perfectionist tendencies in terms of personality traits. This association suggests that bruxism is not only a physical problem but also has a significant psychological component.

I conducted a comparison with existing specialized studies, and these comparisons show that my study is well-aligned with the literature, highlighting the complexity and multidimensional nature of bruxism and the importance of addressing both physical and psychological aspects.

Conclusion. My study suggests that bruxism is closely linked to psychosocial factors such as stress, anxiety, and certain personality traits like perfectionism. These relationships underscore the importance of a comprehensive approach to managing bruxism, which includes both physical and psychological interventions. Understanding these connections is crucial for developing effective prevention and treatment strategies, thereby improving the quality of life for those affected.

A frightening tale of Behçet disease: case report

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Introduction. Behçet disease (BD) is an idiopathic disease, primarily characterized by vasculitis involving vessels of any caliber. Ocular involvement is present in 70% of cases, mainly manifesting as uveitis.

Case report. A 28-year-old woman presented to the Ophthalmology Clinic with sudden onset reduced visual acuity in both eyes (OU) and pain with ocular movement. Patient history includes two episodes of blurry vision, photophobia and pain OU, which spontaneously remitted in 2 weeks. The best corrected visual acuity was 0.9 in her right eye (OD) and 0.7 in her left eye. Slit lamp examination revealed intermediate uveitis and optic disc edema OU. Blood tests (BT) were negative for infectious or immune diseases. A brain MRI revealed no abnormalities. The diagnosis of pars planitis and anterior inflammatory optic neuropathy OU was established. The patient was treated effectively with systemic corticosteroids. In the following 7 months, she had recurring episodes of uveitis, with severe vision loss OD. Meanwhile, extended autoimmunity and infectious BT returned negative. Following a vitrectomy, histopathology infirmed a potential diagnosis of lymphoma. Gradually, the patient developed panuveitis OU, with hypopyon OD, oral ulcers, epigastric pain and pseudofolliculitis, raising our suspicion of BD. Rheumatology started with cyclophosphamide and corticosteroids, with a favorable evolution. HLA-B51 testing was negative, but, given the clinical manifestation, the diagnosis of BD was established.

This is a case where the diagnosis became clear several months after the patient's initial presentation, due to the suggestive clinical signs appearing gradually. Despite its strong association with HLA-B51, only 38% of BD patients are positive.

Conclusion. BD can have many clinical presentations, and it should be suspected in young patients with panuveitis. A thorough patient history should always be performed, in order not to miss any manifestations of the disease.

Arsenic trioxide reprograms the bone marrow microenvironment and eliminates minimal residual disease in acute myeloid leukemia

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Introduction. The bone marrow microenvironment (BME) plays a critical role in the persistence of minimal residual disease (MRD) by driving different resistance mechanisms in acute myeloid leukemia (AML). Acute promyelocytic leukemia (APL), a subtype of AML, however, is effectively treated with all-trans retinoic acid (ATRA) and arsenic trioxide (ATO). We hypothesized that this combination works synergistically, with ATO modifying ATRA's pharmacokinetics (PKs) and potentially enhancing its action in the BME by increasing retinoid availability.

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Material and methods. We performed mass spectrometry to detect ATRA levels. Leukemia cell lines were cocultured with ATO-pretreated mesenchymal stromal cells and treated with ATRA +- ATO and gilteritinib, an FLT3-inhibitor. The combination was also tested in vivo, on xenograft models.

Results. Our data suggest that ATRA alone upregulates CYP26 expression, leading to lower ATRA concentrations. However, ATO suppresses this CYP26 upregulation, thereby enhancing ATRA PKs and increasing their availability in systemic and bone marrow environments. ATO's effects on stromal CYP26 activity also improve the differentiation of APL cells and sensitivity to FLT3 inhibitors in FLT3-mutant AML cells. ATO reverses stromal-mediated protection by downregulating CYP26, enhancing ATRA-induced differentiation in APL cells and restoring sensitivity to gilteritinib in FLT3-mutant AML cells co-cultured with MSCs. These findings were confirmed in mouse AML xenograft models, where the combination of gilteritinib and ATO extended survival by reducing the MRD burden post-treatment.

Conclusions. Our study demonstrates that ATO restores the sensitivity of FLT3-mutant AML cells to FLT3 inhibitors like gilteritinib by downregulating stromal CYP26, eventually leading to deeper remissions in preclinical models. This mechanism highlights the potential of targeting the BME to overcome MRD persistence, offering a new therapeutic approach.

The effectiveness of final irrigation in endodontic treatment

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Introduction. To compare the penetration depth of NaOCl into the dentinal tubules of extracted teeth using various activation methods.

Material and methods. The root canals of 30 extracted human teeth were prepared with a sequence of endodontic files. The root canals were randomly divided into two groups, and final irrigation was performed using sodium hypochlorite as follows: group I – conventional needle irrigation, Group II – laser-activated irrigation. Subsequently, methylene blue was inserted into the canals and activated according to groups I and II. Teeth were sectioned horizontally, and examined under a microscope, and dye penetrations were measured in three sections per tooth. Data were statistically analyzed.

Results. Using laser activation increases the penetration depth of the irrigant, thereby improving the efficiency of canal irrigation.

Conclusion. Greater penetration depths are anticipated for teeth irrigated and activated by laser compared to those activated manually.

By the pricking of my thumbs: a case of systemic sclerosis with digital necrosis

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Introduction. Systemic sclerosis (SSc – commonly known as scleroderma) is a rarely occurring autoimmune disease characterized by generalized fibrosis and vasculopathy. Almost all patients are female and present with skin thickening, Raynaud's phenomenon and esophageal reflux or dysmotility. The leading causes of death in scleroderma are interstitial lung disease and pulmonary arterial hypertension.

Case report. A 45-year-old chronic smoker patient with no previous medical history presents in the Rheumatology Service with bilateral distal phalangeal ulcerations with signs of progression towards gangrene. The only viable finger had small necrotic ulcerations ("rat-bite" ulcers). A capillaroscopy reveals mega-capillaries with areas of hemorrhage. The patient recalls multiple episodes of swelling and pain in both hands, alongside cutaneous induration, which have led to the current necrotic lesions. According to the patient's paperwork, he has been previously consulted by multiple health services and has been suspected of frostbite (later thought to be vasculitis). Considering the atypical presentation, an extended serology and immunology panel was requested. Bloodwork reveals the presence of anti-PL7 antibodies, ANA+ 1/1280 and anti-Scl70 antibodies in high levels. A native thoracic CT scan shows specific pulmonary involvement (ground-glass opacities). Six cycles of cyclophosphamide are administered and well tolerated. The patient is referred to the Surgery Department for necrectomy. After 4 months, the patient presents hyperpigmentation with a "salt and pepper" pattern and small ulcerative spots covering most of his backside, updating the diagnosis from limited systemic sclerosis to diffuse systemic sclerosis. The current evolution is favorable.

Systemic sclerosis proves to be a challenging diagnosis for many practitioners by itself. Nevertheless, atypical presentations with unusual debut symptoms make this diagnosis even more troublesome. Despite the fact that this pathology is known to be usually occurring in young female patients, clinicians should be aware that there are exceptions. The current case is misleading not only because of the patient's gender, but also because of his lifestyle (smoker of a pack of cigarettes per day) and because of work conditions (construction worker). Moreover, the necrotic ulcerations could have been wrongly identified as frostbite marks.

Conclusion. Atypical presentations of systemic sclerosis are a complex and challenging task. A quick diagnosis is mandatory in order to maintain the patient's life quality by preserving his hand motility and lung function. There are few and far between cases of this autoimmune disease in men and it is known that this leads to a worse long term prognosis than in women.

The impact of COMT genetic variants on cardiovascular and psychiatric disease risk: a comparative perspective

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Introduction. Catechol-O-methyltransferase (COMT) plays a crucial role in breakdown of catechol neurotransmitters influencing prefrontal cortex functioning and cardiovascular responses. Genetic variations, particularly the Val158Met polymorphism, influence COMT enzyme activity and have been linked to various neurological and psychiatric disorders, as well as cardiovascular issues. We characterize eight COMT single nucleotide polymorphisms (SNPs) rs4680 (Val158Met), rs737865, rs165599, rs2075507, rs4633, rs4818, rs6269, and rs165774, to evaluate their potential influence on disease susceptibility.

Material and methods. This review synthesizes findings from population-based studies, examining the correlation between COMT variants with psychiatric disorders and cardiovascular conditions such as hypertension, coronary artery disease, heart failure, and arrhythmias. A systematic search of the PubMed databases revealed 20 relevant articles with a particular emphasis on the impact of COMT variants.

Results. The Val158Met polymorphism shows a strong link to psychiatric susceptibility. Met allele associates with increased vulnerability to stress, anxiety, mood disorders, as well as increased cardiovascular risk due to enhanced sympathetic nervous system activation. Other variants, are associated with stress resilience, indicating COMT's significant role in influencing both mental and cardiovascular health. Notably, variations in the COMT gene have been found to influence the effectiveness of dopaminergic agents, antidepressants and antipsychotic medications.

Conclusions. COMT polymorphisms, particularly Val158Met, appear to significantly influence both psychiatric and cardiovascular disease susceptibility. Genetic testing, elucidating the complexities of the COMT gene, may help guide individualized therapy based on predicted responses to available medications, as part of personalized risk management in clinical practice.

Portal hypertension management of a patient with congenital thrombophilia: a case report

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Introduction. MTHFR C667T heterozygous mutation is extremely common, affecting around 15% of white individuals and interfering with the way their bodies process folate, causing among others thrombophilia and high blood pressure. PAI1 mutation, on the other hand, is a very rare genetic disorder which also affects blood clotting. We will be presenting the management of a patient presenting both mutations and the consequent congenital thrombophilia which have led to portal vein thrombosis at an early age and refractory portal hypertension since then.

Case presentation. The patient, a 39-year-old woman, presented to the gastroenterology ward for monitoring her condition, having a history of portal

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cavernoma with portal hypertension, grade 3 esophageal varicose veins and a Mallory-Weiss lesion. She has a family history of gastric cancer, which has affected all her grandparents and her father. Her condition debuted at 12 years old with significant splenomegaly caused by portal thrombosis, requiring a splenectomy and splenorenal shunt. After 15 years, the splenorenal shunt was thrombosed and the surgical attempt at permeabilization was unsuccessful. At this point, she had grade 4 esophageal varices, so it was decided to perform the hiatal dissection of the esophagus and the ligation of peri-esophageal veins and the left gastric vein to reduce pressure in the varicose veins.

This year, there have been 3 variceal binding prophylactic procedures. Her chronic treatment has remained unchanged for several years: Propranolol, Eliquis and folic acid. She is to take Clexane injections instead of Eliquis for the month following the latest procedure to reduce the risk of ligature ulceration bleeding. She is to be re-evaluated in 3 months. Other shunts to reduce portal hypertension have been discussed but are contraindicated.

Conclusion. Prognosis is guarded due to the chronic nature of portal hypertension and portal cavernoma which can lead to liver dysfunction, along with the challenge of preventing variceal bleeding.

How does Sirtuin 3 contribute to Parkinson's disease therapy

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Introduction. Sirtuin 3 (SIRT3) is a NAD+-dependent deacetylase predominantly located in mitochondria-rich tissues, such as the heart, brain, and liver. It plays a crucial role in regulating reactive oxygen species (ROS) levels and mitochondrial metabolism, making it a potential therapeutic target for neurodegenerative disorders, including Parkinson's disease (PD).

Material and methods. This study reviews findings from six relevant articles published in the last ten years, focusing on the relationship between SIRT3 and PD, particularly its effects on mitochondrial dysfunction and α-synuclein aggregation.

Results. Parkinson's disease affects 1-2% of the elderly population and is characterized by symptoms such as muscle rigidity, tremors, and postural instability due to the degeneration of dopaminergic neurons in the substantia nigra pars compacta. This degeneration is linked to mitochondrial dysfunction and subsequent apoptosis driven by ROS and α-synuclein accumulation. Research indicates that SIRT3 protects dopaminergic neurons by reducing ROS production, preventing α-synuclein aggregation, and enhancing cell viability. Specifically, SIRT3 deacetylates key mitochondrial proteins like superoxide dismutase 2 (SOD2) and ATP synthase β, promoting ATP generation and reducing oxidative stress.

Conclusion. In animal models of PD, activation of SIRT3 has been shown to decrease dopaminergic neuron degeneration. These findings underscore the need for further investigation into SIRT3 as a promising druggable target for PD treatment, potentially offering new avenues for therapeutic intervention in this debilitating disease.

The Impact of SIRT1-mTORC1 signaling on microglial activation following optic nerve injury

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Introduction. SIRT1 is a NAD+-dependent deacetylase that plays a vital role in DNA repair, oxidative stress response, mitochondrial function, inflammation, and immune responses. Recent studies have linked SIRT1 to the inhibition of the mTORC1 signaling pathway, which acts as a sensor for redox status, energy, and nutrients, influencing protein synthesis and immune responses. SIRT1 is also implicated in optic nerve injuries; following optic nerve crush, microglial cells secrete pro-inflammatory cytokines like TNFα, leading to neurodegeneration. This review explores the relationship between SIRT1-mTORC1 signaling and microglial activity in diseases associated with optic nerve injuries, aiming to identify strategies to mitigate axonal loss.

Material and methods. A literature review based on PubMed search selecting 10 relevant articles (from last 10 years) was conducted to gather insights on the SIRT1-mTORC1 pathway and its effects on microglial activity related to optic nerve injuries.

Results. The interaction between microglia and retinal ganglion cells (RGCs) is dynamic during injury. In early stages of optic nerve injury, microglial depletion may promote axonal recovery. TNFα regulates SIRT1 inactivation; thus, blocking TNFα could preserve active SIRT1 and suppress ocular autoimmune diseases. Additionally, mTORC1 serves as a substrate for SIRT1, highlighting its benefits.

Conclusions. Disruption of the mTORC1 pathway alleviates inflammation from optic nerve injury by altering microglial phenotype. Therefore, the SIRT1-mTORC1 signaling pathway is crucial for regulating microglial activation and RGC phagocytosis after optic nerve crush.

The long-term success of single-tooth crowns in relationship with marginal adaptation

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Introduction. Marginal adaptation is essential for the long-term success of single-tooth crowns, having a direct impact on periodontal health and the longevity of the restoration. This study compares marginal adaptation among various types of dental preparations, evaluating the advantages and disadvantages of each technique.

Aim and objectives. The aim of this study is to assess the marginal adaptation of single-tooth crowns based on the types of dental preparations used. The main objectives include identifying the technique that ensures the best marginal adaptation and analyzing the factors that may influence these outcomes.

Results. The results highlighted significant differences in marginal adaptation among the analyzed preparation types. Shoulder-less preparations demonstrated superior marginal adaptation, with better-defined margins and reduced plaque accumulation, suggesting an advantage in maintaining gingival health. In contrast, shoulder preparations exhibited less precise adaptation, being associated with a higher

incidence of gingival inflammation and secondary marginal caries. The study indicated that the operator's technique and the material used for the crown are essential factors influencing marginal adaptation. 3D digital imaging confirmed the superior margin adaptation of shoulder-less preparations.

Conclusion. The conclusions of the study emphasize the importance of correctly choosing the type of preparation for single-tooth crowns. Optimal marginal adaptation contributes to clinical success and the durability of restorations, suggesting a preference for shoulder-less preparations in certain clinical situations. This research highlights the necessity of considering both the preparation technique and the restorative material to prevent long-term complications.

Diagnosing splenosis: the impact of ultrasound on clinical thinking - case report

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Introduction. Splenosis is characterized by benign splenic tissue implanting in various sites, often following splenic trauma or surgery. This case report emphasizes the challenges of accurately diagnosing a pathology with nonspecific or absent symptoms.

Case report. A 27-year-old female patient presented with paroxysmal pain in the lower abdomen. Her medical history featured post-traumatic splenectomy in childhood. Physical examination revealed no significant findings. Laboratory tests showed microcytic hypochromic anemia.

The ultrasound depicted multiple hypoechoic nodules disseminated intraperitoneally and retroperitoneally with an almost spherical shape and predominantly peripheral vascularization. Elastography indicated intermediate-type rigidity. Contrast enhanced CT depicted multiple intraperitoneal and retroperitoneal nodules with tissue similar to lymphatic type but recommended a biopsy for clarification.

Linear endoscopic ultrasound (EUS) found several nodular lesions with regular, smooth contours in the near vicinity of the liver, stomach and pancreas. Contrast enhanced endoscopic ultrasound revealed early contrast uptake with rapid homogenization in the arterial phase, without wash-out in the venous phase suggesting a benign lesion. Fine-needle aspiration (EUS-FNA) from a retroperitoneal lesion was performed. The pathology confirmed neoformed splenic tissue.

The final diagnosis was splenosis, which does not require treatment in asymptomatic patients.

Differential diagnosis such as lymphoma, peritoneal carcinomatosis, endometriosis were considered. The association between EUS-FNA and the administration of contrast agents has facilitated detection and biopsy of splenic tissue, having a defining role in achieving the correct diagnosis.

Conclusions. Comprehension of the clinical context and combined ultrasound techniques allows for rapid, minimally invasive diagnosis of lesions, thus avoiding surgical intervention.

Unexpected effects of an iris cyst after cataract surgery

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Introduction. A cataract is the opacification of the lens, commonly associated with the patient's aging. The only effective treatment is surgery. Phacoemulsification uses ultrasound energy to break up the lens for easier removal. Potential postoperative complications to be aware of are corneal edema – due to intraoperative endothelial cell damage, and, rarely, the formation of iris cysts.

We report the case of a patient who underwent cataract surgery in both eyes and postoperatively developed corneal edema and subsequently an iris cyst in the left eye (OS). Despite its unexpected effect on the corneal edema, the cyst partly covered the pupil and had to be excised. The corneal edema eventually reappeared.

Case presentation. A 75-year-old female, with a medical history of astigmatism presents with blurry vision in both eyes. Testing revealed cortical and nuclear opacities in the right eye, nuclear opacities in the OS, and low visual acuity in both eyes. Both eyes underwent cataract surgery.

Iris incarceration occurred during the procedure. Postoperatively, the patient developed corneal edema in the OS for which a topical treatment with hyperosmotic glucose was instilled. An iris cyst also developed from epithelial downgrowth, which was later confirmed by pathology. This cyst covered the endothelial defect leading to corneal edema. Although it cleared the cornea, it had to be surgically removed because it affected the patient's vision. After 3 months, the edema reappeared.

Conclusion. Secondary iris cysts are rare after phacoemulsification surgery, with very few cases being described. This case displays a unique interplay between two cataract surgery complications. The cyst's effect on the corneal edema was unexpected, making this case even more particular and highlighting the complexity of cataract surgery and its postoperative complications.

Circulating tumor DNA: a potential key biomarker for prognostic assessment in breast cancer

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Introduction. Breast cancer is the tumor with one of the highest number of new yearly cases, one of the most important therapeutic challenges being its potential for recurrence, with up to 30% of cases recurring, revealing the need for more prognostic factors. Circulating tumor DNA, a component of a liquid biopsy, is a minimally invasive method to gather genetic information that is representative for the primary tumor and the metastatic sites. The role of this review is to evaluate the prognostic value of circulating tumor DNA in breast cancer patients.

Material and methods. This narrative review was conducted through searching the PubMed and Cochrane databases using the following key terms: "breast neoplasm",

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"circulating tumor DNA" and "prognostic" while accounting for synonyms and using Boolean operators. The automated filter for clinical trials was applied. The search resulted in 98 articles. After duplicate removal and screening based on title and abstract eligibility, 17 articles were included. Four reviewers performed extensive full-text reading of the included articles.

Results. Analysis of the reviewed studies identified the following common correlations of circulating tumor DNA: N stage, early detection of recurrence, aggressiveness, response to treatment. Several studies have shown that circulating tumor DNA can detect molecular relapse prior to imaging evaluation. The biomarker was repeatedly analyzed along other already established prognostic factors and was found to increase prognostic significance. One important finding for future research was identified to be circulating tumor DNA's heterogeneity, which has shown predictive value in assessing treatment response and identifying therapeutic resistance. For example, a direction worth exploring is represented by circulating tumor DNA mutations in the PIK3CA gene, as variations in prognosis related to treatment choice have been observed.

Conclusion. In this review circulating tumor DNA proves to be a promising minimally invasive biomarker for breast cancer prognosis, offering valuable insights on cancer progression and treatment response, thus representing a pivotal advancement in personalised medicine.

Cephalic duodenopancreatectomy and right hemicolectomy: one of the best treatments for pancreatic and duodenal tumors

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Introduction. This kind of procedure is considered to be a major abdominal procedure, with a 2% mortality on elective surgeries and up to 23-29% on the emergency cases. This is a reason why we have very few cases in the medical literature, but they are life-saving procedures on the complex pancreatic lesions, ulceration hemorrhage, tumor hemorrhage, duodenal fistulas and sepsis. This case report highlights a clinical case of a 62-year-old man, presenting at the emergency department with upper gastrointestinal tract hemorrhage of unknown origin, detailing the diagnosing protocol, the intervention, and the post-intervention treatment.

Case report. The patient presented at the emergency department with hemorrhagic shock of unknown origin, hemoglobin and hematocrit (H&H) very low (5.2 g/dl, 10.9%), WBC 20.000/µL, APTT 166,2 sec. He got blood transfusion and was transferred to the CT scan, where the D3 invading tumor, with active hemorrhage and invasion to the first 1/3 of the transverse colon was found. After that, the patient was taken to the operating room. Also, he received an upper gastrointestinal endoscopy, which revealed that the endoscopic hemostasis was impossible to be performed. So, the cephalic duodenopancreatectomy (Whipple) and right hemicolectomy procedure were chosen, the operation went well, and the patient was discharged 10 days later.

Conclusion. Duodenal cancer is a very dangerous condition, especially in patients with associated risk factors and diseases. This case highlights the importance of early diagnosis and intervention in those patients. Also, the multidisciplinary teams are a real help in the treatment process.

Urgent TIPS in cirrhosis: managing recurrent variceal bleeding and encephalopathy

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Introduction. Cirrhosis often leads to life-threatening complications, including variceal bleeding because of portal hypertension. This case report emphasizes that transjugular intrahepatic portosystemic shunt (TIPS) is a key intervention for lowering portal pressure and preventing recurrent bleeding.

Case report. A 59-year-old woman with hepatitis C-related cirrhosis, treated two years ago and classified as Child-Pugh B, presented with melena and altered general state. Examination showed pallor and large amounts of blood in the rectum. Laboratory results revealed anemia and mild hepatocytolysis. Imaging confirmed signs of portal hypertension with splenomegaly, gastric and esophageal collaterals, and mild ascites.

Endoscopy showed grade II/III esophageal varices with active bleeding, treated by band ligation. Recurrent bleeding in the following day necessitated urgent TIPS placement reducing the portal pressure gradient (PPG) from 20 mmHg to 9 mmHg.

Complications included mild encephalopathy episodes, in the context of infectious colitis and urinary tract infections. During follow-up, TIPS dysfunction was observed, leading to reintervention to restore the PPG.

Baveno VII guidelines support urgent TIPS placement for recurrent variceal bleeding when initial measures fail. This patient's Child-Pugh B, MELD 13 score, high hepatic venous-portal gradient which indicates a high rebleeding risk, aligned with unresponsiveness to primary measures made TIPS intervention within 72 hours crucial to reduce mortality and improve clinical outcomes.

Hepatic encephalopathy may develop as a consequence of infection, given that TIPS shunts blood away from the liver's detoxification process.

Conclusion. This case illustrates the importance of early TIPS in accordance with Baveno VII guidelines for the management of high-risk variceal bleeding.

Unveiling hidden cirrhosis: a case of acute gastrointestinal bleeding revealing advanced hepatocellular carcinoma

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Introduction. Cirrhosis is diagnosed histologically by the presence of regenerative nodules surrounded by fibrosis, disrupting liver architecture and increasing intrahepatic resistance to portal blood flow. Common causes include alcohol abuse, metabolic disorders, viral infections, autoimmune conditions, genetic disease and cryptogenic factors. Hepatocellular carcinoma (HCC) is a severe complication with a 2-5% annual incidence in viral cirrhosis cases.

Case report. A 55-year-old woman initially presented in the ophthalmology service for retinal detachment and was later referred to gastroenterology due to upper

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tract hemorrhage with melena. Her medical history included arterial hypertension and a heart attack with otherwise unremarkable health records.

She had a sudden onset of decline in her general condition, stayed hemodynamically stable, but had severe anemia. An emergency upper gastrointestinal endoscopy showed grade II esophageal varices with active bleeding, gastric varices and moderate hypertensive gastropathy. Variceal band ligation was performed.

Ultrasonography revealed cirrhosis and a large liver mass involving several segments and the hilar region with portal vein invasion. Further investigations showed an extremely high alpha-fetoprotein level, positive HBs antigen, anti-HCV antibodies and replicating HCV-RNA. Contrast-enhanced CT and MRI with Primovist confirmed HCC.

Cirrhosis management focuses on finding and addressing causative factors to prevent decompensation and complications. This case highlights a cirrhotic patient with active hepatitis C and advanced HCC. Given the relatively young age at diagnosis, the question arises about suitable oncologic treatments and the potential benefit of antiviral therapy.

Conclusion. This case is notable due to the limited treatment options available for a young cirrhotic patient with hepatocellular carcinoma and active hepatitis C infection.

Postnatal management for laparoschisis – a case report

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Introduction. Gastroschisis is an abdominal wall defect with an incidence of 1:3000-4000 live births, usually occurring on the right side of the umbilicus. This defect results in herniation of internal organs without a protective sac.

Intubation is performed under general anaesthesia. Gastric decompression and good muscle relaxation are essential for reducing organs back into the abdomen.

Case report. We present a case of a new-born female weighing 2300 grams, diagnosed with gastroschisis prenatally. At 37 weeks of gestation, she was delivered in a clinic and transported for emergency treatment.

Upon presentation, the bowels were ischemic due to strangulation from crying. The patient was intubated, and a central venous catheter (CVC) was placed. We then decompressed the gastrointestinal system and placed a urinary catheter for diuresis monitoring.

During surgery, the organs were reduced into the abdomen. The post-operative period was uneventful; the patient was extubated on the second day, and enteral nutrition was started on the seventh day with good tolerance. After three weeks, she was discharged with recommendations.

Considerations for patients with gastroschisis include potential respiratory failure after organ reduction due to high intra-abdominal pressure, the risk of associated malformations, temperature and fluid loss while organs are outside the abdominal cavity. Post-operative pain is managed with opiates or caudal anesthesia.

Early complications may include abdominal wall cellulitis, abdominal wall breakdown, gastroesophageal reflux, cholestasis, necrotising enterocolitis, abdominal compartment syndrome, pneumonia, and CVC infections.

Conclusion. Prenatal diagnosis and prompt postnatal intervention with the help of the pediatric anesthesia team increase the chance of survival in gastroschisis patients.

Implications of KDM3A gene variant in a patient with epileptic syndrome: a hidden gem?

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Introduction. Research in genetic epilepsy syndromes offers insight towards a better understanding of the basic mechanisms of epilepsy. Most mutations in epilepsy without structural brain abnormalities lie in ion channels, yet numerous genes involved in functional and developmental processes are recognized using Whole Exome sequencing.

Case report. A thirteen-month-old patient presenting an epileptic syndrome with paroxysmal onset two months after in the context of a gastrointestinal viral infection, with four epileptic crises reported in less than 48 hours was admitted to the neurology section. Seizure, signs of general hypotonia, perioral cyanosis and altered consciousness (2 minutes), followed by postictal sleep were noted. Infectious markers, MRI brain scan and EEG were within the normal range; the patient had normal postnatal evolution. Levetiracetam was prescribed, improving the patient's condition. Using Whole Exome sequencing, the analysis of candidate variants in genes not yet associated with the disease revealed heterozygous status for KDM3A gene c.1940-2A>G.

KDM3A plays a key role in the epigenetic regulation of gene expression, crucial in neurofunctional and neurotransmission processes. Its functions as histone demethylation and neurotransmitter expression regulation contribute to the synaptic plasticity and neuronal response to stimuli. KDM3A mutations result in changes in gene expression, altering histone modification patterns and impacting neurodevelopmental or cognitive functions. This variant is absent in gnomAD, a large reference population database aiming to exclude individuals with severe pediatric disease.

Conclusions. Although an established association between germline variants in the KDM3A gene and human disease is lacking now, the variant's properties imply that a disease association could be linked with further research. Experimental models about demethylation inhibition offer novel perspectives towards personalized therapies in treatment of epilepsy.

The weight of diagnosis: alkaptonuria in a child and ethical challenges in communication

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Introduction. Alkaptonuria (AKU) is an autosomal recessive disorder resulting from a deficiency in homogentisate 1,2-dioxygenase from tyrosine metabolism, leading to the accumulation of homogentisic acid (HGA), which is excreted in urine and subsequently oxidizes, causing a characteristic dark coloration. Long-term complications include: ochronosis (blue-black discoloration of connective tissues) and an increased risk of degenerative arthritis due to HGA accumulation in cartilages. Other affected areas include cardiac valves, the prostate, bones, and kidneys.

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Case report. The patient is a two-year-old male with no significant medical history until his parents noted a change in the color of his urine-soaked diapers, which darkened after a few hours of light exposure. The urine analysis using nuclear magnetic resonance (NMR) spectroscopy confirmed AKU due to elevated HGA. Following diagnosis, ethical concerns arose regarding communication with the family; the parents expressed frustration towards the physician, feeling that receiving a diagnosis for an untreatable condition was more burdensome than relieving.

This case highlights the utility of NMR spectroscopy in diagnosing metabolic disorders and emphasizes the importance of diagnostic communication for which the treatment is not available yet. Vitamin C has been tested as a potential treatment but studies indicated that it may increase HGA production and urinary excretion, making it unsuitable option. Nitisinone has shown promise in reducing HGA levels in adults AKU patients, with ongoing research evaluating its safety and efficacy in children.

Conclusions. This case underscores the complexities of managing rare disorders, highlighting the need for accurate diagnosis and compassionate communication when addressing chronic conditions with limited treatment options during childhood.

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Epidermolysis bullosa associated with pyloric atresia and aplasia cutis congenita – a case report

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Introduction. Epidermolysis bullosa (EB) is a group of inherited bullous disorders characterized by blister formation in response to mechanical trauma. According to skin morphology, epidermolysis bullosa has been classified into four subtypes.

Case report. We present the case of a male preterm newborn at 32 weeks of gestation by cesarean section subsequent to abnormal findings at fetal ultrasound, such as enlarged stomach, hypertelorism and short limbs.

At birth, the patient's clinical examination presented cutaneous aplasia on the lower limbs and bilaterally under ears, outer ear agenesis, nasal septum hypoplasia, micrognathia, multiple blisters on the face, trunk and limbs, lower limbs deformities and absence of toenails.

Amid the ultrasounds performed in the medical care unit, the head ultrasound showed enlarged interhemispheric and subarachnoid space; the abdominal ultrasound revealed digestive tract anomalies such as the significantly distended stomach occupying the abdominal cavity.

The patient was referred to the pediatric surgery department and died at the age of five days due to severe postoperative complications.

Genetic testing was performed on peripheral blood samples using Next Generation Sequencing (NGS). The interpretation revealed two different homozygous null variants affecting ITGB4 and KRT10 genes. The ITGB4 mutation explains the clinical phenotype: junctional epidermolysis bullosa with pyloric atresia. KRT10 gene mutation is associated with congenital ichthyosiform erythroderma.

Conclusions. The novelty of the ITGB4 and KRT10 gene mutation association is explained by the context of consanguinity, the parents being second-degree cousins. As genetic testing is available, familial planning is recommended, knowing the 25% risk of transmitting the recessive autosomal disease to other descendants.

How right colon cancer hides: silent symptoms for an advanced disease

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Introduction. Most colon neoplasms are adenocarcinomas and glandular malignancies. Although diagnostic tools continue to improve, early discovery is still a challenge. Non-specific symptoms are often the only clue for a progressive disease.

Case report. A 57-year-old woman was admitted for anemia-related symptoms including fatigue, dizziness and 7 kg of weight loss in a year. The patient reported no blood in the stool, the abdomen was normal and a CT done a year prior showed no modifications. Labs confirmed hypochromic microcytic anemia. A fecal occult bleeding test was positive. GI tract endoscopies were performed, revealing an ulcero-infiltrative tumor located in the cecum and ascending colon junction, covering 60% of the circumference. Biopsy confirmed adenocarcinoma (G2). CT showed a cecal wall thickening with an 18 mm mesenteric lymph node. A hemicolectomy was performed, also removing a portion of the ileum and of the ascending colon. Histopathological examination confirmed an adenocarcinoma pT3N0Mx, with no node metastasis. The patient's course was favorable, she was prescribed iron supplements and was discharged.

This case highlights the difficulty of early detection of colon cancer in patients presenting non-specific symptoms (anemia and weight loss, no bleeding, transit issues or pain) and supports current literature on right colon cancer being more silent, showing the importance of GI examination in older patients with anemia. The clean CT a year prior suggests either rapid tumor growth or how small lesions can be missed, with colonoscopy remaining the gold standard in detection. Delayed diagnosis also means postponed treatment, particularly critical in oncologic cases.

Conclusion. Although increasingly common, colon cancer can hide behind ambiguous symptoms and waste time that should be used for treatment. Medical workers must remain vigilant even in the face of common symptoms to ensure the best healthcare for patients.

Dealing with infective endocarditis

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Introduction. Infective endocarditis represents the inflammation of the endocardium, frequently affecting elderly patients. The development is associated with several predisposing factors, including valvular disease, prosthetic valves, dental procedures and non-sterile venous injections.

Case report. A 16 year old female presented to the emergency room with left hypochondriac pain unrelived by analgesics, fever, chills and weight loss. She reported recently being tattooed and pierced. On examination, a IV-V grade systolic murmur, with axillary and posterior thoracic irradiation, was audible, while on palpation, she felt pain in the right iliac region. The transthoracic echocardiogram revealed a vegetation of 15/14 mm on the anterior mitral valve, with severe mitral regurgitation, suggestive of infective endocarditis according to Duke criteria, leading to antibiotherapy. The CT-angiography showed a mycotic aneurysm with intimal dissection in the right common iliac and proximal external iliac arteries, right external iliac artery occlusion due to thrombosis, multiple splenic infarcts, along with mycotic aneurysm in the medial cerebral artery. Therefore, the patient underwent endovascular stent grafting for the aneurysm, followed by mechanical mitral valve replacement, via median sternotomy.

Regarding this case, the development of mycotic aneurysms is indeed a clinical challenge. The vegetation of the mitral valve can release septic emboli through the vasa vasorum, causing infection, arterial wall weakening and dilatation, thereby increasing the risk of rupture. Her intracranial aneurysm can cause bleeding and neurological deficits.

Conclusion. Despite the patient's age and lack of any cardiac conditions, it is important to consider tattooing and piercing as potential causes of infective endocarditis, leading to severe complications that are difficult to treat.

Case study: managing Zenker's diverticulum in the elderly

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Introduction. With a reported prevalence of 0.01 to 0.11%, Zenker's diverticulum is the most frequent kind of esophagal diverticulum and usually occurs in older patients. Regurgitation and dysphagia are the most common symptoms.

Case-report. We present the case of an 82-year-old woman with Parkinson's disease who was admitted for a fall without loss of consciousness. The physical exam revealed facial traumatic marks, but the pulmonary exam was normal. Inflammation markers were increased and a computerized tomography (CT) scan of the thorax displayed two consolidation foci in the left lung. Sputum microbiology discovered Klebsiella species.

The patient also reported dysphagia, already present for several months, that aggravated until complete aphagia.

Upper GI endoscopy, attempted without sedation, could not pass the upper oesophagal sphincter and found saliva stagnating in the hypopharynx. Stenosis of the pharyngo-esophageal junction was suspected, but the neck CT scan displayed a

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pharyngo-esophageal diverticulum on the left side. Upper GI endoscopy confirmed the presence of Zenker's diverticulum.

Antibiotic treatment, temporary oxygen supplementation and parenteral feeding were necessary.

Peroral endoscopic myotomy for Zenker's (Z-POEM) was performed in a tertiary-level endoscopy unit with technical and clinical success.

A tissue eventration through the Killian triangle known as Zenker's diverticulum (ZD) is thought to be brought on by cricopharyngeal muscle dysfunction. One of the primary complications of the illness is aspiration pneumonia.

Z-POEM has shown encouraging outcomes and might be superior to other endoscopic procedures in several ways, such as having a lower chance of recurrence.

Conclusion. This case underscores the importance of recognizing Zenker's diverticulum in elderly patients and the efficacy of its endoscopic interventional treatment.

Breast surgery meeting artificial intelligence. A new perspective for the future

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Introduction. Nowadays, multidisciplinarity is a keyword in Breast Cancer management, due to the heterogeneity in terms of histology, molecular subtypes and response to treatment. The increased rate of false-negative results in imaging techniques remains problematic, combined with the risk of underestimating the aggressiveness of the tumor after tissue sampling. Artificial Intelligence (AI) might be a solution to all these problems. The aim of this review is to analyze the suitability of AI in breast management strategies.

Material and methods. Articles between 2020 and 2024 from the PubMed database were selected based on their title and content, using the keywords "ARTIFICIAL INTELLIGENCE" AND "BREAST SURGERY". To be included, articles had to be available in English. Articles were divided into groups depending on the contribution of AI.

Results. Out of the total number of 161 results, only 25 respected the predefined conditions and were included in the analysis process. Concludingly: AI supports breast imaging by simplifying the workflow; AI algorithms can detect occult lesions and decrease the rate of false-negative results; it can process histopathological results and guide therapy. One meta-analysis stated that the concordance rate between the analysis of clinical decision support systems (CDSS) and multidisciplinary team meetings (MDMS) was 72.8% for stage I-II, respectively 84.1% for stages III-IV, $P \leq 0.00001$.

Conclusion. Despite the advantages brought by AI in breast surgery, every decision should be validated by specialists, due to ethical and legal implications. The significant workflow of clinicians makes AI to be suitable for use in CDSS. AI models can radically transform breast cancer management, improving the detection of lesions and treatment. AI-assisted decision-making for breast cancer will probably be implemented in the future, but the "main character" is, undoubtedly, the physician.

Artery-only fingertip replantations - insights from a three-case series

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Introduction. In traumatic upper-extremity amputations, the decision for microsurgical replantation is influenced by factors like stump condition, amputation level, and the patient's health. Advances in microsurgery now enable very distal replantations, including those beyond the distal interphalangeal joint (DIP). According to Tamai's classification, distal amputations are categorized as zone I, distal to the lunula, and zone II, between the lunula and DIP. In some cases, venous repair is unachievable due to vessel size or damage, making artery-only replantations susceptible to venous congestion.

Case report. This series includes three patients who presented to the Emergency Department with guillotine-type distal finger amputations. A 42-year-old male presents with a Tamai I amputation of the fifth finger, a 57-year-old male with a Tamai II amputation of the thumb, and a 56-year-old male with a Tamai I amputation of the third finger. Each fingertip is reattached via artery-only microsurgical anastomosis, with immediate patency confirmed by milking test and by puncturing the fingertip to verify capillary bleeding. Before vessel declamping, an intravenous heparin bolus is administered, followed by antispastics, anticoagulants, and antiplatelet therapy. Venous drainage is maintained by regularly incising and dressing the fingertip in heparinized gauze to promote continuous bleeding for the initial 5 days.

Postoperative management for artery-only replantation is challenging due to venous congestion, which can be managed through fingertip incisions or leech therapy to establish venous outflow.

Conclusion. Artery-only fingertip replantations are feasible despite venous congestion challenges. Precise microsurgical anastomosis is critical for success, while strategies like external bleeding or leech therapy support positive outcomes in traumatic amputations.

Acute descending necrotizing mediastinitis of oropharyngeal origin – case presentation

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Introduction. Acute descending necrotizing mediastinitis (ADNM) is a severe condition that can arise as a complication of infections in the oro-pharyngeal regions, spreading to the mediastinum. Despite advancements like CT imaging, modern antibiotics and aggressive drainage, ADNM has a high mortality rate due to rapid infection spread.

Case report. A 55-year-old man presented with a diffuse floor of the mouth infection originating from tooth 4.8 causing bilateral cervical swelling. Broad-spectrum antibiotics were initiated. Persistent purulent discharge and gas bubbles in the upper mediastinum led to his transfer to Thoracic Surgery. Clinical examination and imaging confirmed the infection, complicated by acute descending necrotizing mediastinitis, congestive pericarditis, liver microabscesses, pleuro-pulmonary inflammatory syndrome, multi-

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organ failure and sepsis. A right thoracotomy with mediastinal drainage, pericardotomy and left pleurotomy was performed. Samples collected during the intervention confirmed Enterococcus, S. epidermidis and Acinetobacter, guiding antibiotic adjustments. Supportive measures included thrombosis prophylaxis, gastric acid suppression, liver support, electrolyte management and hypercaloric nutrition. Oral and maxillofacial treatment involved antiseptic lavage, excision of necrotic tissue and tooth extraction. After 19 days, wounds showed signs of healing, though organ insufficiency remained.

ADNM is a life-threatening complication of diffuse odontogenic infections. Early antibiotics, microbiological testing and urgent surgical intervention—including aerobiotic conditions and oxygen-releasing lavages—are critical for improving outcomes.

Conclusions. A thorough understanding of the potential complications of diffuse and spreading infections of odontogenic origin is essential. Early diagnosis and aggressive treatment can improve survival rates.

A rare glimpse into hereditary nephritis: the diagnostic journey of a young male with Alport syndrome

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Introduction. Alport syndrome is a genetic disorder caused by mutations in COL4A3, COL4A4 and COL4A5 genes, affecting type IV collagen. It is characterized by progressive kidney disease, hearing loss and ocular abnormalities, primarily impacting the glomerular basement membrane.

Case report. We present the case of a 35-year-old male diagnosed with chronic kidney disease (stage G3bA3) in 2022, renovascular hypertension, mixed dyslipidemia and under investigation for nephritic syndrome. His family history reveals renal anomalies – his grandfather had a single functional kidney due to congenital hypoplasia. His medication includes Furosemide, Perindopril and Atorvastatin. Laboratory tests indicated impaired renal function, while urinalysis revealed proteinuria and hematuria. As IgA Nephropathy was initially suspected, immunological tests were conducted with a final negative result. Considering the clinical findings, a genetic etiology was suspected, Alport Syndrome emerging as a likely cause. Ophthamologic and otolaryngologic evaluations showed no abnormalities, but a renal biopsy indicated irregularities consistent with Alport Syndrome. The treatment plan was adjusted to include a combination of both ACEi and ARB, along with Dapagliflozin to support renal function and optimize blood pressure control.

Typically diagnosed in childhood, this disorder can present subtly, delaying recognition. Although there is no confirmed family history of Alport Syndrome, a potential genetic link exists because of the patient's grandfather's condition.

Conclusions. This case illustrates the complexity of Alport Syndrome in atypical presentations without classic symptoms. The delayed diagnosis emphasizes the necessity for thorough evaluations and increased suspicion in patients with renal impairment and family history of renal anomalies.

A rare complication with an uncommon etiology: venous hypertension caused by venous retrograde outflow in the arteriovenous fistula

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Introduction. Venous hypertension is a rare complication of an arteriovenous (AV) fistula that usually appears in the context of high flow. It is caused, in the majority of cases, by central venous stenosis. Rarely, it can appear secondary to retrograde outflow from the fistula into a collateral vein.

Case report. A 56-year-old woman with chronic kidney disease (CKD) that undergoes hemodialysis is referred to the clinic for a left-hand ulceration. Past medical history includes left nephrectomy for pyonephrosis. The patient has a functional left brachiobasilic fistula. On clinical examination, in the left limb, edema, venous collateral circulation and a dorsal hand ulceration with erythema and necrosis zones were noted. Laboratory examinations and bacterial cultures showed no signs of infection. Ultrasound revealed an elevated brachial artery flow, with a low resistivity index. Angiography ruled out central venous stenosis, but revealed a big collateral vein near the fistula, with a retrograde flow that led to inefficient venous drainage and thus venous hypertension. The treatment was surgical, and it consisted of the ligation of the venous collateral. This resulted in the resolution of the venous hypertension, with rapid improvement of the condition and a full recovery.

Venous hypertension is often diagnosed late since it is a rare complication of a fistula. Uncommon causes of hypertension, such as retrograde outflow into a collateral vein, can also delay the diagnosis. The differential diagnosis is made with central venous stenosis, arterial steal syndrome, and ischemic neuropathy.

Conclusions. Venous hypertension represents a rare complication of an AV fistula. High flow through the fistula is an important risk factor. While the most common etiology is central venous stenosis, other conditions, such as retrograde outflow through a venous collateral may be taken into account.

From eczema to diagnosis: a clinical journey in breast oncology

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Introduction. Paget's disease of the breast is a rare type of cancer that develops in the nipple, and sometimes in the areola. It may be isolated to the nipple (ductal carcinoma in situ), or it may be accompanied by invasive breast cancer in the lactiferous ducts of the same breast.

Case report. A 70-year-old woman presents to the oncology department with erythema of the left nipple, having previously undergone a three-month course of treatment for eczema prescribed by her dermatologist with no improvement. The only symptom reported was the erythema with no associated pain, swelling or discharge. Mammography revealed multiple calcifications in the nipple and a round opacity within the mammary gland. An ultrasound confirmed the presence of the nodule measuring 2.1 cm, and elastography indicated a hard consistency of the nodule, characteristic of a

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malignant lesion. MRI findings showed contrast uptake in the lesion. A needle biopsy of the nodule confirmed the presence of invasive ductal carcinoma, while a punch biopsy of the nipple revealed Paget cells, indicative of Paget's disease of the breast. The patient will be treated with chemotherapy followed by a mastectomy.

Paget's disease of the breast, while rare, can easily be mistaken for more common skin conditions, such as wounds, breastfeeding-related injuries, or eczema, leading to delays in diagnosis. In this case, the patient's initial treatment for eczema highlights the importance of maintaining a high suspicion of malignancy in atypical skin presentations, particularly when standard treatments fail.

Conclusions. This case underscores the importance of recognizing Paget's disease of the breast as a potential indicator of malignancy, particularly in patients presenting with atypical nipple changes as well as the need for a multidisciplinary approach in managing breast cancer including oncologists, surgeons, and pathologists, to ensure comprehensive care.

Alternative approach to MRSA treatment: are antibiotics a relic of the past or an undisputed necessity?

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Introduction. Methicillin resistant Staphylococcus aureus (MRSA) is a Gram-positive bacterium that is notorious for its antibiotic resistance. Its ability to develop more effective ways of evading antibiotics and its vast presence makes it a treat to public health. A relatively new treatment option is bacteriophage (phage) therapy. Recent studies show that phage therapy is an effective therapy with few side effects and high specificity. Besides being efficient at targeting MRSA, it also has astonishing results in biofilm formation, which further contributes to their usage.

Material and methods. Out of a total of 311 articles on both Embase and PubMed using the keywords "MRSA" and "phage therapy", 84 have been excluded due to our selected time frame. 42 have been excluded for lack of coherence, 104 for lack of relevance to the subject and 36 for incomplete or unreliable data, leaving us with 45 articles.

Results. While most bacteria possess a complex clustered regularly interspaced short palindromic repeats (CRISPR) sequences, in order for MRSA to acquire new antibiotic resistant genes, it needed to get rid of the CRISPR system. By doing so, its susceptibility to lytic phages increased. Besides the phages lytic proprieties, they also have an important role in biofilm degradation. Endolysins are proteins synthesized in the later stages of phage replication that inhibit cell wall synthesis and biofilm production. The most notable of these lysins are LysK, CHAP_K, LysRODI, SAL200, LysP108, MR-10, produced by different phages that can be used in phage cocktails as potential treatments.

Conclusions. Phage therapy is a promising and highly effective new treatment option which yields good results with few adverse effects. While the phage resistance has been observed, it comes at the cost of antibiotic susceptibility. This way both therapies can be used simultaneously to treat MRSA infections. Although the research is showing auspicious results, more time is needed for phage therapy to prove its effectiveness.

Homocysteine, methylation, and MTHFR: understanding their interplay and health implication

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Introduction. Methylation is a critical biochemical process influencing gene expression and regulation, including histone modifications and non-coding RNA interactions. Homocysteine, an amino acid linked to methionine metabolism, serves as a key indicator of methylation status and is closely associated with the activity of the methylenetetrahydrofolate reductase (MTHFR) enzyme. The 677C>T polymorphism leading to reduced enzyme activity can lead to elevated homocysteine levels, impacting methylation processes. The MTHFR enzyme is important for maintaining cellular homeostasis, because of its essential roles in the one-carbon cycle which include methionine and folate metabolism and protein, DNA, and RNA synthesis.

Methods. A review of recent literature (last five years) was conducted to analyze the role of homocysteine in methylation and its epigenetic consequences, selecting ten representative publications.

Results. High homocysteine (Hcy) levels are linked to various health issues, including cardiovascular diseases (CVD), neurodegenerative disorders (e.g., Alzheimer's disease), autoimmune conditions, osteoporosis, and certain cancers (e.g., breast and colorectal cancer). Key genes affected by abnormal methylation due to the MTHFR 677TT genotype include SLC6A4 or TP53 (a tumor suppressor gene whose silencing can contribute to tumorigenesis).

Conclusion. Understanding the interplay between homocysteine levels, methylation processes, and genetic factors like MTHFR variants is essential for developing targeted preventive healthcare strategies. This review highlights the increased risk of cardiovascular diseases and cancers associated with impaired methylation due to elevated homocysteine levels. Further therapeutic approaches that would optimize methylation pathways could mitigate health risks related to hyperhomocysteinemia.

Oncolytic viruses as novel therapeutic agents in pancreatic cancer – a literature review

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Introduction. Pancreatic Cancer (PC) is one of the deadliest types of cancer, with a 5-year survival rate of 8-10%, underlining the dire need for novel therapies. Oncolytic viruses infect and lyse cancer cells specifically and are promising agents in the treatment of cancer.

Material and methods. We conducted a search for articles published on PubMed using the terms "oncolytic viruses" and "pancreatic cancer", along with corresponding MeSH terms, and by reviewing their reference list.

Results. The review included 264 articles, focusing on 24 preclinical studies and 9 clinical trials on oncolytic virotherapy for pancreatic cancer (PC). Eight promising virus families were identified. Newcastle disease viruses (e.g., NDV-LaSota, Hitchner-B1, and

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Ulster NDV) showed strong specificity and oncolytic potential, with strains like NDV R75/98 arresting tumor growth and preventing recurrence for three months. Reovirus effectively lysed PC cells, sparing healthy cells and reducing liver metastases (2/6 vs. 6/6 in the controls). Pelareorep improved overall survival (OS) in trials when combined with gemcitabine, surpassing FOLFIRINOX. Measles virus enhanced the tumor reduction capacity of Resminostat, gemcitabine, and Olaparib. Herpes simplex virus boosted ganciclovir's anticancer effect, increasing mice survival by 30% and showing promise as monotherapy in trials. Influenza viruses (H7N3, H5N1, H1N1) induced higher apoptosis than gemcitabine. A modified vaccinia virus inhibited angiogenesis by induced endostatin-angiostatin synthesis and targeted survivin, enhancing OS. Parvovirus H-1PV improved gemcitabine's cytotoxicity in trials. While ONYX-015 (adenovirus) was ineffective in two trials, mutants LOAd703 and VCN-01 are under investigation.

Conclusion. Oncolytic viruses are novel agents that could be used to increase survivability in PC, but further studies are required due to the scarcity of clinical trials.

A familial case of MEN2A: everything started from hypertensive episodes

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Introduction. Multiple endocrine neoplasia (MEN2) is a rare autosomal-dominant hereditary cancer syndrome. It is clinically characterized by the presence of medullary thyroid carcinoma (MTC), pheochromocytoma and primary hyperparathyroidism and at least two of the classical clinical features are required for the diagnosis of MEN 2A.

Case report. A 34-year-old female patient presented at the cardiologist accusing hypertensive episodes associated with flush, headache, palpitations. Lab Results showed an increased level of calcitonin and a high level of metanephrines. Also, at an adrenal ultrasonography were found some masses so a CT was performed. At a thyroid ultrasonography, calcified nodules were found. With these Results, the diagnosis of MEN2 syndrome was suspected.

Genetic testing for mutations for RET gene was performed on patient and all first-degree relatives. Genetic testing identified the presence of the pathogenic heterozygous mutation of codon 634 at the level of exon 11. The patient s children were also tested and are negative for the mutation, instead the patient s mother has the RET mutation.

After diagnosis, the patient underwent total thyroidectomy with right lateral-cervical lymphadenectomy for medullary thyroid carcinoma, partial parathyroidectomy and bilateral adrenalectomy. The histopathological examination of the operative parts revealed the presence of a pheochromocytoma on the right adrenal gland (PASS score = 3) and three pheochromocytomas on the left adrenal gland (PASS score = 0). Following the surgical intervention, the patient received substitutive treatment with levothyroxine 100 micrograms, hydrocortisone 25 mg and fludrocortisonum 0.1 mg.

The patient's mother was diagnosed with medullary thyroid carcinoma and primary hyperparathyroidism. For these conditions, the patient underwent total thyroidectomy with lymphadenectomy and subtotal parathyroidectomy. After the intervention, patient received substitution with levothyroxine.

Multiple endocrine neoplasia type 2A (MEN2A) is a rare syndrome that presents as medullary thyroid carcinoma, pheochromocytoma, and hyperparathyroidism. Different mutations lead to different levels of activation and MEN2 is therefore characterized by a

strong genotype-phenotype correlation.

Conclusions. The particularity of this case stays in the way it was diagnosed, beginning from hypertensive episodes and ending with a dignosis of MEN2A at a mother and daughter. It is well known that rarely pheochromocytoma may be the first manifestation of MEN2.

Phenotypic diversity in hypertrophic cardiomyopathy – a family story

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Introduction. Hypertrophic cardiomyopathy (HCM) is the most frequent heritable cardiovascular disease characterized by substantial heterogeneity in clinical manifestation, genetic aetiology, and outcome, even among family members.

Material and methods. We report the case of a family, a mother (34) and two children (13 and 15) diagnosed with HCM, with genetic analysis indicating the presence of a variant of uncertain significance (VUS) in the MYBPC3 gene. The index case is the mother, diagnosed with HCM after cardiac investigations to determine the underlying cause of a syncopal episode. The echocardiographic examination revealed LV hypertrophy and LVOT obstruction. The genetic testing identified a VUS, c.3413G>C (p.Arg1138Pro) in MYBPC3. Cardiac screening was requested for the children. The first child, asymptomatic at the time of the examination, had an echocardiographic appearance suggestive of nonobstructive HCM. The targeted genetic testing revealed the same variant identified in their mother. In addition, the patient presents lower limb hypotrophy. The neurological examinations showed no abnormalities. The second child was also initially asymptomatic. Echocardiography showed significant LV hypertrophy. Genetic testing confirmed the variant found in their mother. In association, the patient presents short stature, for which the endocrinologist recommended treatment with growth hormone.

Results. Clinical and genetic screening enabled the diagnosis of two asymptomatic children and their inclusion in a follow-up program. The various phenotypes of HCM observed in the two children and the association with other manifestations (short stature or lower limb hypotrophy) are due to causal mutations, modifier genes and environmental factors.

Conclusion. Current management focuses on the early identification of patients at risk through clinical and genetic screening of family members and the timely initiation of treatments to avoid disease progression and complications.

Co-occurrence of breast and ovarian cancer in patients with gBRCA1 mutation: a case report

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Introduction. BRCA1 is a critical gene involved in the maintenance of genomic stability, particularly in the repair of double-strand DNA breaks. Mutations in the BRCA1 gene are strongly associated with an increased risk of breast and ovarian cancers, as well as pancreatic and prostate cancer. This case report presents an instance of a patient with a gBRCA1 mutation, highlighting the clinical evolution and personalized management strategies.

Case report. The presented case is that of a 57-year-old woman diagnosed in 2014 with right breast carcinoma (cT3N0M0, stage IIB). She underwent neoadjuvant chemotherapy, was subjected to radical surgery, and subsequently received adjuvant radiotherapy. In 2020, the disease recurred in the left breast (cT4bN1M0, stage IIIB), at which point she was again treated with neoadjuvant chemotherapy, underwent radical mastectomy, and received adjuvant radiotherapy. In 2021, she was diagnosed with low-grade serous ovarian carcinoma (cT3N0M0, stage IIIB). The patient was treated with 6 cycles of Paclitaxel and Carboplatin, followed by total hysterectomy with bilateral salpingo-oophorectomy, classified as Figo stage IIIB, and received adjuvant treatment with Bevacizumab. In June 2023, the patient presented with mediastinal lymph node recurrence, and histopathological examination revealed metastases of triple-negative breast carcinoma positive for PDL-1. First-line (L1) treatment was initiated with Paclitaxel and Pembrolizumab. In February 2024, a brain MRI showed 6 cerebral lesions consistent with infracentimetric metastases, prompting the initiation of stereotactic radiotherapy (SAbR) for the brain, followed by targeted therapy with Olaparib. The disease progressed in the brain, necessitating repeated SAbR and a cycle of Sacituzumab Govitecan. At the last specialty consultation, a significant improvement in general condition was noted, with a performance status index of ½, and it was decided to continue the current treatment.

The case underscores the increased risk of breast and ovarian cancers in patients with gBRCA1 mutations and highlights the importance of genetic screening and proactive management strategies. The resilience of BRCA1-mutated tumors presents significant treatment challenges. While therapies such as Olaparib can be effective, tumors may develop resistance over time, as demonstrated in this patient's recurrent disease despite multiple treatment regimens.

Conclusion. This case emphasizes the need for personalized treatment approaches and ongoing research into the mechanisms of resistance to improve outcomes for patients with hereditary breast and ovarian cancer syndromes.

Neuroendocrine gastric tumor with rare metastasis to the liver and ovaries: a case study and diagnostic approach

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Introduction. Gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs) are a rare and heterogeneous group of tumors originating from the diffuse neuroendocrine system, with an increasing incidence in recent years. They account for over 55% of neuroendocrine neoplasms and tend to develop rapidly, with more than 50% of patients presenting with lymph node metastases at diagnosis.

Material and methods. This case study reports on a 72-year-old female patient who presented to the medical clinic for diffuse abdominal pain and rectoragy. A comprehensive diagnostic workup was conducted, including a contrast-enhanced computed tomography (CT) scan, laboratory tests, endoscopy, abdominal ultrasound, and biopsy.

Results. Endoscopic examination revealed a 3 cm polypoid lesion. Biopsy and ultrasound findings indicated hepatomegaly with multiple heterogeneous formations in both liver lobes and bilaterally enlarged ovaries. These findings suggested a presumptive diagnosis of GEP-NEN with hepatic and ovarian metastases. The diagnosis was further supported by CT imaging and elevated CA-125 levels in laboratory tests.

Conclusion. GEP-NENs are aggressive tumors that can lead to multiple complications in a short period, resulting in increased morbidity and mortality. Further studies and the development of new screening and diagnostic methods are necessary to better understand and manage this pathology.

Telomerase polymorphisms in cancer: recent findings

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Introduction. Telomerase, which is essential for maintaining telomere length and promoting cellular immortality, is often dysregulated in tumors. Recent studies identified significant associations between polymorphisms in the telomerase reverse transcriptase (TERT) gene and various cancers, highlighting their potential as biomarkers and therapeutic-targets in oncology.

Material and methods. We performed a literature review of 7 representative articles (published during the last 5 years on human subjects) retrieved from the PubMed database, using keywords (”Telomerase”[Mesh]) AND ”Polymorphism, Genetic”[Mesh]) AND ”Neoplasms”[Mesh].

Results. This review includes studies on telomerase polymorphisms across several cancer types: (a) Glial cancer: TERT-promoter-mutations are more prevalent in glioblastomas than in lower-grade gliomas in Chinese population; (b) Lung cancer: three articles reported a higher risk of lung cancer, particularly non-small-cell-lung-cancer associated with the rs4975616 variant in Caucasians compared to Asians. TERT amplification was also observed in lung tumors. Additionally, a meta-analysis linked the rs2736100 (A > C) allele to increased lung-cancer-risk; (c) Breast cancer: three studies

found a focal-amplification of TERT as a prognostic factor in ER+/HER2 metastatic-breast-cancer. A rare breast-cancer-type, low-grade fibromatosis-like-metaplastic-carcinoma, was associated with TERT overexpression and the c.-124C>T mutation. In triple-negative-breast-cancer, the rs10069690 CC genotype correlated with high TERT-expression and poor-prognosis; (d) Colorectal cancer: one article associated hTERT polymorphisms rs2853669 and rs2736098 with colorectal cancer risk in Chinese Han population; (e) Liver cancer: another study with rs2736098 and rs2739100 polymorphisms linked hepatocellular carcinoma with proliferation and telomere shortening.

Conclusion. These findings highlight the significant role of telomerase polymorphisms in various cancers and their potential as biomarkers for risk assessment and prognosis.