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MEDICINE
Basic Sciences

Acupuncture self-administration role in modulating anxiety on mental stress context

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Introduction. The vagus nerve regulates multiple systems, playing an important role in maintaining homeostasis. Literature shows that acupuncture (AC), through anatomical access to the vagus nerve, is a useful method in treating depression and anxiety.

Methods. In this clinical study were included subjects of both genders, aged 19-49 years, who complained of anxiety related to exposure to mental stress. Two groups were created, control (C), which did not receive AC and group that received AC (A). AC was self-administered for one week before mental stress, following instruction on its use. Mental stress consisted of solving difficult mental tasks. Assessment consisted of applying the Anxiety and Depression Scale, the Beck Anxiety Inventory (BAI), determining the total number of hours of sleep and the quality of sleep overnight. Evaluations were made before starting AC administration (T1), before the stressful event (T2), 24 hours after the stressful event (T3).

Results. AC significantly reduce anxiety in group A compared to group C, at T2 and T3. This was proved by both scales and the quality of sleep. There were no significant differences between genders.

Conclusion. AC self-administration may represent a promising therapeutic option in the management of emotional stress, by modulating anxiety in mental stress situations.

Polyphenolic quinazolin-4(3H)-one and catechol hidrazinyl-thiazole derivatives as potent antioxidant agents in a blue light-induced toxicity cellular model of age-related macular degeneration

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Introduction. As human life expectancy increases, there has also been a rise in retinal degenerative diseases, which 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 limited therapeutic options, primarily consisting of antioxidant supplements. Aging is the main risk factor, but genetic and environmental factors, such as excessive exposure to short-wavelength light (blue light), also contribute to the onset and progression of the disease.

Aim. To evaluate the antioxidant capacity of four compounds, two based on thiazole and catechol structures, and the other two based on quinazolinon-aceto-hydrazides and phenolic aldehydes. Individually, these components exhibit significant antioxidant activity, and by effectively targeting oxidative stress, an important contributor to retinal diseases, they may offer therapeutic potential for retinal degeneration.

Methods. The compounds were either synthesized through phenolic aromatic aldehyde condensation or produced via the Hantzsch heterocyclization of thiosemicarbazones. Their antioxidant activity was tested *in vitro* with various abiotic assays, such as total antioxidant capacity and reducing power assays, and in biotic assays using ARPE-19 cells, a human retinal pigment epithelial cell line, also employed for cytotoxicity testing. The *in vitro* antioxidant effects were assessed by quantifying reactive oxygen species activity using an H2O2-induced oxidative stress model, followed by a retinal toxicity model induced by blue light in combination with A2E, a component of retinal lipofuscin and a photosensitizer, using a 450 nm blue light lamp.

Results. The abiotic *in vitro* assays demonstrated high antioxidant activity for all the hybrid compounds compared to ascorbic acid and Trolox. In the blue light cellular model, results varied among representatives of each class, with the most potent antioxidant hybrid belonging to the quinazolinone group.

Conclusion. The hybrid compounds showed strong antioxidant properties in both abiotic and cellular models, while maintaining a good biocompatible profile, making them promising candidates for future *in vitro* and *in vivo* AMD studies.

Understanding reproductive health perspectives: a study of abortion and contraceptive knowledge among future healthcare providers in Romania

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Introduction. Despite increasing global attention to reproductive health, significant knowledge gaps and misconceptions about abortion and contraception exists. Understanding medical students knowledge and their attitudes is crucial for developing effective educational strategies.

Methods. This cross-sectional study, conducted between April and December 2024 at the Iuliu Haţieganu University of Medicine and Pharmacy in Cluj-Napoca, assessed the knowledge and attitudes regarding abortion and contraceptive methods

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among 510 medical students. A validated, self-administered online questionnaire was used, and data were analyzed using descriptive statistics and chi-square tests ($p<0.05$).

Results. 95.88% of participants were aware of abortion, but significant gaps persisted, particularly regarding the legal gestational limit for medical abortion. 65.88% associated abortion with infertility. Support for abortion was high in cases involving maternal health risks (74.12%) or rape (79.22%). Knowledge of contraceptive methods was high for condoms (96.32%) and oral contraceptives (93.37%). Among male students, 64.35% believed condoms reduce sexual pleasure, while 87.85% of female students expressed concern about oral contraceptive side effects. 60.59% considered access to abortion services in Romania insufficient, and nearly 80% supported legal measures to improve accessibility.

Conclusion. Significant knowledge and misconceptions about abortion and contraception exists among future healthcare providers. Gender differences were evident, particularly regarding abortion in non-medical contexts and perceptions of contraceptive methods. Targeted educational interventions are essential to correct misinformation, promote reproductive autonomy, and train medical students to provide comprehensive, unbiased reproductive healthcare.

Biocompatible iron oxide doped materials for magnetic resonance imaging

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Introduction. The present study is focused on the preclinical research of new materials, paramagnetic, biocompatible with the body, non-toxic, resorbable or easily metabolized by the body, contrast agents, for their use in the diagnosis and treatment of tumors, one of the most devastating diseases of the moment.

Methods. A system with a silicon matrix and different concentrations of iron oxide in powder form was synthesized by the sol gel and freeze dry method. Following structural analyses on these materials through DTA, RX, FTIR, EPR, XPS, SEM investigations, the samples were heat treated, washed and immersed in simulated SBF fluid, classifying them based on the information obtained in the parameters indicating the possibility of using them as contrast agents.

Results. The MTT results, showed that a concentration higher than 5% iron oxide, either SG or FD affects cell viability and proliferation, moreover, these substance concentrations lead to cell destruction. The analysis of images and biocompatibility was done at different time intervals. Thus, a first batch was scanned as a control batch. The following batches were scanned in this way, at the time immediately after injection, called time zero, at 2, 24 hours and at 7 days. It is observed according to the images obtained in Figure 2, that at time 0, 2 hours the delimitations of the different living tissues are highlighted much more clearly, so we can say that the contrast increases. At 24 hours the contrast and delimitations of the organs and living tissues are closer to time zero, and at 7 days no differences are observed between the two acquisitions. These images suggest that with the passage of time the iron-based substance injected into the animal model is absorbed or eliminated from the body.

Conclusion. The MRI evaluations confirms that paramagnetic iron oxide ions enhance contrast for T2 relaxation time acquisition protocol. All tissues examined show no changes No signs of inflammation, necrosis or cell damage were observed on examined sections. The use of high-performance MRI with contrast agents doped with paramagnetic iron oxide ions can be an alternative investigation or a complement to MRI diagnosis.

The value of tumor infiltrating lymphocytes in colon cancer patients

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Introduction. TILs represent a key component of the immune microenvironment in cancer. Studies have demonstrated that a high density of TILs is associated with reduced tumor progression, lower rates of lymph node metastasis, and improved overall survival (OS). The aim of this study was to evaluate the density of CD73+ subset of TILs and the Immunoscore in relation to lymph node involvement and lymphovascular invasion in colon cancer patients.

Methods. CD73+ cells were assessed on IHC slides which were digitized using a 3D HISTECH Pannoramic scanner at 40x magnification. Quantitative analysis of the IHC slides was conducted using QuPath software to calculate the percentage of immunopositive cells relative to all nucleated cells in the tumor microenvironment regions. Immunoscore was also calculated. Correlation analysis was performed using Pearson's Coefficient.

Results. 100 patients with colon cancer treated between 2022–2024 were analyzed.We calculated the density of CD73+ intratumoral, tumoral-adjacent and within the distant stroma and total CD73+ density. We calculated the global Immunoscore for CD73+ cells and corelated it with lymph node involvment and lymphovascular invasion. The average number of intratumoral CD73+ cells was 6,55 (0-39,5).The average number of tumoral-adjacent CD73+ cells was 11,54 (0-40,8). The average number of within the distant stroma CD73+ cells was 5,56 (0-30,2). The average total number of CD73+ cells was 11,34 (0-38,1). Correlation between Immunoscore and lymph node involvement was not statistically significant (R=0,0112, p=0,9119). Correlation analysis with lymphovascular invasion demonstrated a weak, but not statistically significant association. (R=-0,0977, p=0,3370, R=-0,1208, p=0,2343).

Conclusion. Assessment of TILs in histopathological evaluation could enhance prognostic accuracy and guide therapeutic strategies for CRC patients, but larger studies need to be done in order to validate its value.

Evaluation of heart failure induction by abdominal aortic ligation and the potential therapeutic effect of Tocilizumab in rats

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Introduction. Heart failure remains a major clinical challenge, with inflammation playing a central role in its progression. This study aimed to evaluate whether abdominal aortic ligation induces heart failure in rats and to investigate whether interleukin-6 receptor blockade with Tocilizumab confers any protective benefit.

Methods. 34 male Wistar rats (G=250±25g) were randomly divided into four groups: group I was sham operated (n =7), group II underwent abdominal aortic ligation (n=13) and groups III and IV received saline solution (n=6) or Tocilizumab – 30mg/kg (n=8) 21 weeks after abdominal aortic ligation. Cardiac function was assessed by echocardiography and electrocardiography after 21 weeks. NT proBNP was measured in blood in parallel with evaluation of myocardial necrosis markers (troponin, CKMB) and oxidative stress parameters (malondialdehyde, superoxide dismutase, catalase) in the cardiac tissue. Statistical analyses were performed using a one-way ANOVA test, with Fischer's test for post-hoc analysis (GraphPad Prism software version 10.6.1).

Results. The results revealed a statistically significant difference in ejection fraction distribution between sham and abdominal aortic ligation groups ($p < 0.05$) without electrocardiographic changes. Cardiac tissue malondialdehyde levels were significantly higher in rats subjected to abdominal aortic ligation compared to sham-operated controls ($p < 0.01$) while Tocilizumab administration resulted in lower MDA levels but statistically insignificant ($p = 0.24$). Additionally, NTproBNP, troponin levels and activity of superoxide dismutase increased in group II.

Conclusions. Abdominal aortic ligation is a reliable model for inducing heart failure in rats. Tocilizumab administration following ligation attenuated cardiac dysfunction and inflammatory response, supporting the hypothesis that IL 6 receptor blockade may offer therapeutic benefit.

Importance of the auriculopuncture on the stress induced by dental treatments

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Introduction. Dental practice is frequently associated with stress and anxiety present in patients who benefit from these medical services. The objectives was the evaluation of auriculopuncture (AP) effectiveness on stress, in patients during a dental check-up (DC).

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Methods. Participants (no=30, age 24-49years) were randomized into 3 groups: control (C no=10); with AP before DC (APB no=17); with AP before until after DC (APBA no=17). AP was applied one session keeping the needels on place, without any anxiolytic medication. Evaluations: heart rate (HR), salivary cortisol (SC), anxiety (A). Evaluations were carried out pre and post DC.

Results. HR, CS and A values were: significantly increased in C, compared to APB and APBA, moderately before DC and significantly after DC; moderately increased post DC, at APB compared to APBA. Under AP, HR and A values were more reduced, both at APB and APBA, compared to SC, especially post DC.

Conclusion. AP applied to patients undergoing DC reduces HR, SC and A, especially if the maintenance of the needles is longer, respectively before and after DC. The impact of AP is more important on HR and A, but it is also present on SC. AP can be a non-traumatic, economical and useful method in modulating the stress associated with dental procedure, DC.

Magnetic resonance spectroscopy for retinal metabolites detection after blue light exposure

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Introduction. The eye is a complex structure, with multiple systems involved in focusing and detecting the light. The retina interacts with light, and excessive exposure, especially to blue light is prone to produce degeneration, mainly through oxidative reactions. This mechanism is involved in Age-Related Macular Degeneration or Diabetic Retinopathy. Acute exposure of the eye to blue light in adult rats induces metabolic changes, which have so far been investigated using invasive methods that require animal sacrifice.

Methods. Our objective was to apply an animal model of oxidative stress and monitor the metabolic changes using 11.7 Tesla 1H-Magnetic Resonance Spectroscopy. We exposed adult rats to high intensity blue light, at 440nm (6000lux) and investigated retinal metabolic changes up to 48 hours post exposure. All experimental procedures were conducted in accordance with the laws regarding the protection of animals used for scientific purposes and the applicable national legislation (ANSVSA Project Authorization No. 414/20.08.2024).

Results. 1H-Magnetic Resonance Spectroscopy enabled the *in vivo* identification of retinal metabolites, demonstrating relatively low inter-individual variability. The

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retinal environment seemed stable, with only slight variations in Lactate and, to lesser extent, Glutamate metabolism. The acquired spectrum highlighted the presence of several essential retinal metabolites, including lipids, Lactate, N-acetylaspartate, Glutamate, Choline, Taurine, Creatine, and Glucose. Blue light induced specific changes, relatable to oxidative stress, and 1H-Magnetic Resonance Spectroscopy allowed to follow the dynamic metabolic changes, post exposure. Apoptosis damage is linked to blue light and could be estimated by the observed reduction in NAA. Glutamate decreased immediately after blue-light exposure. From 20 minutes after exposure, there was a constant increase in Glutamate levels, up to 48 hours. Glucose had a reduction immediately post exposure and stabilization afterwards. At 80 minutes there was still a slight reduction, no change in the next 24 hours, and a rehabilitation at 48 hours. Lactate peak was markedly increased postexposure, at 10 minutes, and continued to increase for the rest of the examinations. In the interval between 80 minutes scan and 24 hours scan there was a small reduction, then Lactate increased again at 48 hours. These changes were related to blue light exposure, inflicting increased damage to retinal pigment epithelium and, to a lesser extent, to photoreceptors.

Conclusion. This was the first *in vivo* spectroscopic study of the retinal tissue, and no animals were sacrificed during the research. MRI spectroscopy could become an early non-invasive marker of retinal damage. In this preliminary study, metabolic retinal changes were observed after acute exposure to blue light. Translation of the technology into humans would allow us to better understand mechanisms of some common eye diseases: Age-related Macular Degeneration, Diabetic Retinopathy, or Glaucoma.

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High-density-lipoprotein cholesterol structure and function under inflammatory conditions

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High-density lipoprotein cholesterol (HDLc) functions at the intersection of cholesterol metabolism and innate immunity, exerting anti-inflammatory effects under normal conditions. However, inflammation can alter HDLc's structure, impairing its function. We aimed to identify literature on HDLc-mediated anti-inflammatory effects *in vivo* and *in vitro* studies and its structural remodeling under the influence of inflammatory and non-inflammatory factors.

Studies on animal models and *in vitro* cell cultures (e.g., macrophages/monocytes, smooth muscle and endothelial cells) show that reconstituted HDLc and its main component, ApoA-I, reduce chemokine and chemokine receptor expression in endothelial cells and smooth muscle cells, inhibit LDL oxidation, and decrease MCP-1 production.

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Under inflammatory conditions, altered HDLc composition contributed to a pro-inflammatory state. In patients with acute phase response following cardiac surgery, a reduction of HDLc levels, accompanied by structural remodeling characterized by increased inflammatory proteins (serum amyloid A, group IIA secretory phospholipase), and decreased ApoA-I, leads to diminished protection against LDL oxidation while preserving cholesterol reverse transport capacity. In patients with active rheumatoid arthritis, elevated HDLc plasma level correlated with an altered phosphosphingolipidome of the HDLc, resulting in pro-inflammatory effects.

Although HDLc is considered a cardioprotective factor due to its anti-inflammatory role, its structure may undergo alterations under the influence of inflammatory factors, leading to dysfunctions in reverse cholesterol transport and inflammation modulation.

Dissection in the 21st century: virtual tables versus traditional methods and their influence on medical students' perception – a systematic review

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Background. Virtual dissection tables (VDTs) have emerged as innovative tools in anatomy education, offering interactive, three-dimensional visualization of anatomical structures. However, their performance in conjunction with traditional teaching methods needs to be further analyzed and synthetized. This systematic review aimed to evaluate the effectiveness, student satisfaction and perceived utility of VDTs compared to cadaveric dissection, lectures, and textbook-based learning.
Methods. A systematic search of literature identified 22 eligible studies involving students of medicine and related healthcare professions. Studies were analyzed in terms of design, cohort characteristics, educational outcomes, and anatomical content coverage. VDTs evaluated included commercial platforms such as Anatomage, Spectra, VH Dissector, and institutional in-house systems.

Results. VDT use was associated with improved academic performance in 86% of studies, with score increases ranging from 8% to 31% over traditional teaching methods. The greatest improvements were observed in musculoskeletal and neuroanatomy modules. Student satisfaction ranged from 64% to 95%, with the majority citing improved spatial understanding, engagement, and repeatability. However, preference for VDT-exclusive learning remained low, reported by only 2.4% to 30.2% of students. Most participants favored a hybrid approach combining VDTs with cadaver-based instruction. Despite these benefits, limitations included high implementation costs (up to $200,000 USD), limited access due to device scarcity, lack of tactile feedback, and significant variation in assessment methods and anatomical content. Additionally, no study conducted a direct comparison between various VDT platforms, nor between commercial and in-house systems.

Conclusion. VDTs represent a valuable complement to traditional anatomy education, enhancing learning outcomes and student engagement across a range of healthcare disciplines. However, their full potential is best realized when used as part of a multimodal curriculum that retains cadaveric dissection. Further research is needed to assess long-term outcomes, clinical outcomes and cost-effectiveness, and to compare different VDT systems.

MEDICINE
Medical Specialties

A rare case of intraprocedural right atrial thrombosis during MitraClip: when vigilance prevents disaster

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Introduction. Transcatheter edge-to-edge mitral valve repair (TEER) represents a major therapeutic breakthrough for severe mitral regurgitation (MR), providing a valuable minimally invasive option for patients with prohibitive surgical risk. Despite its favorable safety profile, intraprocedural thrombotic complications may still occur, and the optimal management of acute thrombus during TEER remains uncertain.

Case presentation. An 87-year-old male with persistent atrial fibrillation and a normally functioning mechanical aortic valve prosthesis (Sorin Carbomedics, size 21) implanted for infective endocarditis, on long-term vitamin K antagonist therapy, was admitted for progressive dyspnea (NYHA class III/IV).Transesophageal echocardiography (TEE) revealed severe mixed-etiology (degenerative and functional) MR, predominantly atrial, with preserved left ventricular function and a small patent foramen ovale. Given the prohibitive surgical risk (EuroSCORE II 7.34%, STS-PROM 15%), the Heart Team referred the patient for a MitraClip procedure. During advancement of the SWARTZ transseptal sheath toward the superior pulmonary vein, TEE revealed a large, mobile, echogenic, snake-like thrombus (>10 cm) in the right atrium, molding along the sheath and extending toward the interatrial septum. In the presence of a hypermobile thrombus and a pre-existing PFO, there was serious concern for imminent embolization. Intracatheter heparin was administered, and after achieving adequate anticoagulation (ACT >350 s), the thrombus completely resolved within ten minutes. The patient remained hemodynamically stable, without signs of embolization. Following confirmation of procedural safety, a MitraClip XTW was successfully implanted at the medial A2–P2 scallops, reducing MR to mild–moderate (mean gradient 3 mmHg). The patient recovered uneventfully, and postprocedural CT excluded pulmonary embolism.

Conclusion. Although a rare complication, acute thrombus formation during TEER carries the potential for devastating embolic consequences. This case highlights the critical need for constant vigilance, rapid intervention, and cohesive multidisciplinary action to prevent fatal outcomes.

A day in the life of young adults: insights from Holter-EEG monitoring

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Introduction. 24-hour continuous EEG recording (Holter-EEG) is an essential method for evaluation the electric brain activity during the sleep-wake cycle, thus aid in diagnosing paroxysmal events. We discuss the indications for Holter-EEG, the

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requirements, the results observed in two patients, as well as limitations and potential technical advancements.

Methods. Two patients (F25, known with one episode of lose of consciousness, and F23, presenting with visual hallucinations and suspected sleep paralysis) had their EEG recording for 24 hours (from 12:00 to 12:00 the following day). Twenty-one scalp electrodes were used (in 10-20 system) with simultaneous ECG. The recordings were afterwards interpreted offline by a trained neurologist. The analysis focused on the basal rhythms of wake periods, the sleep stages, as well as identifying epileptiform discharges (EDs).

Results. The first recording revealed a normal, well-organized awake EEG, with a reactive posterior dominant rhythm in alpha frequency band, and no EDs. During the afternoon, a nap was identified as light NREM sleep with few intermittent awakenings. The detection of chewing artifacts for two shorts periods of time in awake state was correlated with two frugal meals. The night recording identified poor deep NREM sleep interleaved with short REM sleep periods. In the second case, the EEG recording showed a beta dominant rhythm in awake state, with frequent movement and environmental artifacts, which partially obscured interpretation. The nocturnal recording was characterized by fragmented, non-restorative sleep, consisting primarily of light NREM sleep and frequent awakenings.

Conclusion. The Holter-EEG recording enables the correlation between specific EEG patterns and daily activities and clinical history. While artifacts remain a limitation, there recordings are invaluable for characterizing paroxysmal events, unexplained loss of consciousness, and chronic sleep disturbances.

The many sides of cannabis consumption

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Introduction. Cannabis consumption is widespread globally, predominantly illicit, but it is legalized in some states.

Case presentation. A 19-year-old female patient, with no prior medical history, a chronic Cannabis user, presents to the Emergency Department (ED) for dizziness following the ingestion of Cannabis edibles (cakes). On the ECG we can find different abnormalities, even some unexpected ones considering the patients age.

Case particularity. This case shows the different actions that Cannabis has on the hearts electrical system depending on the dosage and the way in which it was consumed.

Conclusion. Dangerous habits can lead to perilous pathological conditions and something as simple as removing them from our lifestyle can improve the outcome.

Incidental findings in pneumology evaluation - case presentation

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Lymphangioleiomyomatosis (LAM) is a rare, slowly progressive, low-grade, femalespecific, neoplastic (non-malignant) disease characterized by marked infiltration of the lung parenchyma, including pulmonary lymphatics, pleura, and blood vessels, with atypical smooth muscle cells, which leads to the destruction of normal lung architecture, the deterioration of lung function and the appearance of cystic changes. We present the case of a 41-year-old pacient, active smoker with a 20 pack-year smoking history (1 pack per day), without allergies or any exposure to known respiratory toxins, known with SARS-COV-2 infection (mild form), renal angiomyolipomas, pelvic inflammatory disease and bilateral adnexectomy in her personal pathological history who presented to the Pulmonology Hospital complaining of dry cough for a month. The auscultation of the lungs, highlighted normal vesicular murmur, without detectable rales, SpO2 = 99% without oxigenotherapy. We completed the paraclinical investigations with a computed tomography that concluded to cystical images with thin walls distributed bilaterally in both lung fields, hepatic hypodensities, left tyroid calcification. The pacient required a fibrobronchoscopy that did not highlighted the presence of a pathological processes. A brochioloalveolar lavage was performed. No pathological changes were found in the pulmonary function testing. Blood work: lymphocytosis and incresed d-dimers. Furthermore, we decided to determine the vascular endothelial growth factor D, which was significantly incresed and is specific for the diagnosis of lymphangioleyomiomatosis. At the annual reevaluation, a worsening of renal symptoms and slight worsening of respiratory symptoms is noted, with the initiation of specific therapy. The peculiarity of the case consists in the accidental discovery of a rare pathology during a routine check-up in order to evaluate the post-Covid syndrome and the patients low compliance with the indications.

Diabetes secondary to Alpelisib treatment in advanced breast neoplasm: case report

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Background. Alpelisib is drug used to treat certain types of breast cancer after progression despite hormonal treatment, by inhibiting phosphatidylinositol 3-kinase (PI3K). Hyperglycemia can occur in 60% of treated patients since PI3K is a pathway implicated in both glucose metabolism regulation and cellular proliferation.

Case description. 52 years old women attended our outpatient clinic at Center for Diabetes, Nutrition and Metabolic Diseases, Emergency County Hospital Cluj-Napoca in Apr 2022. The patient was sent by the family physician because of recent high fasting blood glucose levels. The patient had no complains at presentations, no personal nor family history of diabetes mellitus, and was diagnosed with left breast invasive ductal carcinoma in 2008 and treated in Oncology Department ever since. Multiple treatment plans were recommended for the progressive oncological disease; among them, Alpelisib, was newly introduced in Jan 2022. At presentation, the patient had normal body mass index = 23 kg/

m2, blood pressure = 115/62 mmHg, and healthy lifestyle. Diabetes mellitus was diagnosed based on fasting venous blood glucose: 159 mg/dl and 176 mg/dl, both higher than 126 mg/dl. The type of diabetes was questioned and, given the patient's characteristics and previous reports of Alpelisib induced hyperglycemia, the diagnosis was established: secondary diabetes mellitus. Treatment with Metformin 2 g/day and lifestyle optimization were initiated for glycemic control, and Alpelisib was continued. Progressive increase in glycated hemoglobin A1c was noticed in the next 12 months, starting from 6.4% to 7.2% (optimal < 6.5%), lead to addition of the second and third line of antihyperglycemic drugs: Sitagliptin 100 mg/day (inhibitor of dipeptidyl peptidase 4) and Dapagliflozin 10 mg/day (inhibitor of sodium glucose co-transporter 2). The oncologist decided to stop the treatment with Alpelisib in Jan 2024. Further, glycemia levels returned to normal values (90 mg/dl) leading to antihyperglycemic treatment discontinuation.

Conclusion. Our clinical case report describes a patient with hyperglycemia secondary to treatment with Alpelisib for advanced breast cancer. Initiation of antihyperglycemic medication was required for controlling glycemia. The collaboration between oncologist and diabetologist allowed the patient to continue receiving Alpelisib for breast cancer control even in the presence of elevated blood glucose levels that prompted antihyperglycemic medication.

Arrhythmias in children: cardiac and neurological complications

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Introduction. Permanent junctional reciprocating tachycardia (PJRT) is a rare form of atrioventricular reentrant tachycardia, caused by the existence of an accessory pathway.

Case report. A 1 year and 11 month old patient presented to the ER Cluj-Napoca (2018) with severe respiratory distress and cardiogenic shock. Investigations revealed cardiomegaly, NT-ProBNP=26,635pg/mL, troponin=399mg/L, ejection fraction<10% and hemodynamic instability, which is why she was admitted to the ICU. The evolution was complicated by recurrent asystoles and Paroxysmal Supraventricular Tachycardia, requiring cardiopulmonary resuscitation and electrical cardioversion.Echocardiography confirmed severe dilated cardiomyopathy and subtricuspid thrombosis. Etiologically, acute Cytomegalovirus infection was identified. Holter ECG revealed alternation between sinus and junctional rhythm with ventricular extrasystoles; neurological evaluation confirmed severe hypoxic-ischemic encephalopathy. Final diagnoses: cardiogenic shock, dilated cardiomyopathy, orthodromic SVT, right ventricular thrombosis, sepsis, multiple organ dysfunction and severe hypoxic-ischemic encephalopathy.She was referred to a specialized advanced cardiac support service. The patient was diagnosed with bilateral pneumonia and acute respiratory failure (2019), presented with paroxysmal tachycardia, subsequently maintaining sinus rhythm under treatment. Echocardiography (2020) revealed LVEF 60% and normal left ventricle.In 2021, the first transseptal radiofrequency ablation of a right postero-septal accessory pathway was performed at the San Raffaele Institute; due to the persistence of Holter changes, a reintervention with catheter ablation was performed. Antiarrhythmic therapy was discontinued, at the advice of the arrhythmologist. The patient is currently under observation.

Conclusion. Early identification is essential for preventing severe complications, such as cardiomyopathy and cardiorespiratory arrest.

A complex case of Carney Triad complicated by a cerebral aneurysm requiring multidisciplinary management

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Introduction. Carney Triad is a rare, non-hereditary syndrome characterized by the co-occurrence of gastrointestinal stromal tumor (GIST), pulmonary chondroma, and extra-adrenal paraganglioma. Its pathogenesis is epigenetic, primarily involving promoter hypermethylation of the SDHC gene. We present a complex case that underscores the multisystem nature of this condition, highlighting the challenges posed by concurrent, life-threatening vascular anomalies.

Case Presentation. A 32-year-old woman was admitted for evaluation of a 8 cm mediastinal mass and a right paracarotid mass. She presented with hypertensive crises, with systolic blood pressure (SBP) peaking at 200 mmHg. Her medical history included a subtotal gastrectomy for GIST in 2014.

Results. CT confirmed paragangliomas in the mediastinum and neck, alongside pulmonary chondromas and incidental adrenal adenomas. Biochemical testing confirmed a functional, norepinephrine-producing tumor: plasma normetanephrine was significantly elevated at 357.16 ng/L (2.64 times the upper limit of normal), 3-methoxytyramine was mildly elevated at 19.99 ng/L, and Chromogranin A was elevated at 459.3 ng/mL. Cerebral MRI revealed an 8 mm complex cerebral aneurysm at the A2 segment of the right anterior cerebral artery (ACA). No pathogenic mutations were identified (KIT, NF1, PRKAR1A, SDHB, SDHC, SDHD) confirming the sporadic, epigenetic form of Carney Triad. The discovery of the cerebral aneurysm significantly complicated the management plan, necessitating a neurosurgical consultation and a careful risk-benefit analysis regarding surgical intervention versus radiological surveillance.

Conclusion. While a direct pathogenic link to Carney Triad remains speculative, the co-occurrence of a vascular anomaly with functional, catecholamine-secreting paragangliomas and severe hypertension mandates a highly vigilant, multidisciplinary approach. This case warrants proactive cerebrovascular screening and comprehensive management that addresses risks beyond the classic triad.

Recurrent asthma exacerbations in a patient with common variable immunodeficiency

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Introduction. Common variable immunodeficiency (CVID) is a rare immunodeficiency „Iuliu Haţieganu" disorder characterized by impaired B-cell differentiation and defective immunoglobulin production, manifested through recurrent respiratory infections. A large proportion of patients with CVID have a clinical history suggestive of chronic respiratory disease. Although this condition may mimic asthma, a delayed diagnosis of CVID in a patient with known asthma is rarely reported.

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Case report. We present the case of a 51-year-old female patient, non-smoker, with no known allergies and a history of occupational exposure to respiratory irritants (textile factory – for 10 years), presented to the Clinical Hospital of Pulmonology in Cluj-Napoca, complaining of productive cough with mucopurulent sputum, exertional dyspnea of moderate intensity, and fatigue. From a medical history perspective, the patient had been diagnosed with asthma, suspected diffuse interstitial lung disease, chronic allergic rhinitis, and multiple recurrent pneumonias over the past year, despite optimized asthma therapy. On physical examination, decreased breath sounds were noted bilaterally at the bases, with fine crackles at the left basal lung field, and an oxygen saturation of 93% on room air. Laboratory findings revealed leukocytosis with neutrophilia, inflammatory syndrome, mild hypoproteinemia, sputum examination with negative bacteriology and negative for Mycobacterium tuberculosis, negative autoimmune profile, normal thyroid markers, and negative anti-Aspergillus IgG. Pulmonary function tests revealed a mixed ventilatory defect with mild restriction and obstruction, and normal values of diffusing capacity across the alveolar–capillary membrane. On chest CT imaging, there were pulmonary consolidation foci associated with septal thickening, bilateral cylindrical bronchiectasis, and splenomegaly. Bronchoalveolar lavage showed no signs of infection or inflammation. In this context, a primary immunodeficiency was suspected, prompting measurement of immunoglobulin levels, which revealed a severe deficiency of IgG, IgM and IgA. Thus, the patient was referred to the Immunology Department for further evaluation and initiation of immunoglobulin replacement therapy.

Discussion. Although rare, the overlap between asthma and CVID should be suspected in cases of apparently refractory asthma complicated by recurrent infections or bronchiectasis. Measuring serum immunoglobulins can turn a “difficult asthma” into an accurate diagnosis and a targeted therapeutic approach.

Conclusions. Sometimes, the path to asthma control begins by overcoming it—through identifying an underlying cause, such as CVID.

Nosocomial infections caused by *Candidozyma auris*: case study

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Introduction. Nosocomial infections affect the quality of healthcare, patient safety and evolution. *Candidozyma auris*, a newly identified species as an etiological agent in human disease, is an opportunistic germ that easily survives in the environment. The objective of the work was to identify the characteristics of patients who develop infections with *Candidozyma auris*.

Methods. A cross-sectional study was conducted, by including cases of nosocomial infections with *Candidozyma auris* diagnosed during the year 2025, in the Cluj-Napoca Clinical Hospital of Infectious Diseases. The data recorded for each case included personal characteristics, time, episode of nosocomial infection, concomitant diseases and evolution during hospitalization.

Results. In total, 9 cases (4 women and 5 men) were diagnosed, relatively evenly distributed over time, in patients with a mean age of 79.1 years (between 67 and 89 years). The most frequent chronic pathologies were atrial fibrillation, hypertension, dementia and sequelae after stroke. The cases were diagnosed on average after 25.6 days (between 15

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and 36 days) from hospitalization, 4 being blood infections, of which one associated with the central venous catheter and 5 urinary infections, of which 4 cases associated with the bladder catheter. Fluconazole resistance was present in 3 strains of *Candidozyma auris*, 2 identified from urine culture and one strain from blood culture.

The diagnosis upon admission was respiratory infections in 7 patients and urinary tract infections in 2 patients. Portage was present in 6 patients, being with *Klebsiella pneumoniae* (producer of extended-spectrum beta-lactamases and carbapenemases), *Acinetobacter baumannii*, vancomycin-resistant *Enterococcus faecium, Escherichia coli* (producer of extended-spectrum beta-lactamases), *Pseudomonas aeruginosa*. Cutaneous portage of *Candidozyma auris* was identified in 5 patients. The evolution was towards death for 8 patients.

Conclusion. Nosocomial infections with *Candidozyma auris* occurred in patients over 65 years of age, who mainly had chronic cardiovascular or neurological pathology and who presented concomitant portage mainly with *Klebsiella pneumoniae*, *Acinetobacter baumannii* and other antibiotic-resistant strains.

Benefits of core activation exercises for the rehabilitation of low back pain patients

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Introduction. The objective of this study was to demonstrate the benefits and effectiveness of exercises activating the Core area, mainly the abdominal muscles, the lumbar extensor muscles and the glutei muscles in the rehabilitation of patients with low back pain, compared with the Williams method.

Methods. 40 patients with low back pain (age between 22 and 76 years, 24 women and 16 men) participated in this prospective randomized controlled trial. Patients were assigned to Core group (n=20) or to Williams group (n=20). Study participants received 10 sessions of Core or William method rehabilitation, 5 days / week, for 2 weeks. All patients were assessed on the first and on the last day of treatment, by: visual analogue scale (VAS) for pain, Schoeber index for lumbar mobility, Oswestry Disability Index (ODI) for function.

Results. No difference between groups could be identified 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 6.3±1.1 to 2.9±0.8, $p<0.05$ in Core group, and from 6.2±1.7 to 3.9±1.2, $p<0.05$ in Williams group), mobility (Schoeber index increased from 13.5±3.7 cm to 16.6±2.2 cm, $p<0.05$ in Core group, and from 12.9±3.3 cm to 14.5±2.9 cm, $p<0.05$ in Williams group), function (ODI decreased from 30±4.8 to 11.9±2.5, $p<0.05$ in Core group, and from 36.1±6.1 to 28.4±2.6, $p<0.05$ in Williams group). Nevertheless, the improvement was significantly better in Core group than in Williams group: $p=0.01$ for VAS, $p=0.0002$ for Schoeber index and $p=0.02$ for ODI.

Conclusion. Both Core and Williams kinesitherapy methods were effective in the rehabilitation of the patients with low back pain, with supplementary advantantages in favour of Core program, thus representing a promising therapeutic option.

The utility of hematological and inflammatory markers in the evaluation of neonatal sepsis in premature newborns

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Introduction. The newborn has an immature immune system, with reduced antibody production and limited neutrophil and other immune cell function. In premature newborns, this immaturity is even more pronounced, which makes them much more vulnerable to infections, anemia, and other hematological pathologies. The classic markers for infection are C-reactive protein (CRP), which peaks at 24-48 hours, and procalcitonin (PCT), which increases more rapidly and exhibits specific dynamics, making it a valuable marker for early diagnosis. Indices such as the Systemic Immune-Inflammation Index (SII) and the Systemic Inflammatory Response Index (SIRI), which combine values from several types of blood cells (neutrophils, lymphocytes, platelets), can be used in combination.

Methods. The study is a retrospective, analytical, and observational study conducted on a sample of 60 premature newborns hospitalized at the Obstetrics-Gynecology Clinic I in Cluj-Napoca. They were divided into two homogeneous groups: the study group (30 cases with risk factors for early sepsis) and the control group (30 cases without risk factors). Results: ROC analysis revealed modest ability for procalcitonin (AUC = 0.61) and poor ability for PCR (AUC = 0.55), similar to a random prediction. Mean PCR values remain relatively stable in the study group and decrease in the control group. Mean procalcitonin values decrease steadily over time in both groups, but with a higher initial value in the study group. In the study group, there is a statistically significant difference ($p<0.001$) between the means of SII and SIRI of deceased newborns and those who survived. The thrombocytopenia and lactate level at birth are correlated with the cerebral hemorrhage.

Conclusions. Individual inflammatory markers, although used clinically, had a modest predictive capacity for neonatal sepsis. The presence of thrombocytopenia and an elevated lactate level at birth are important risk factors for cerebral hemorrhage.

Effects of prematurity on vitamin D levels in the first month of life-correlations with plasma levels in pregnant women

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Introduction. Vitamin D is an essential nutrient that plays a vital role in bone health and musculoskeletal development. The most important function of vitamin D is the insurance of calcium and phosphate homeostasis, which is essential for bone growth and bone mineral metabolism.

Studies suggest that in both high- and low-income countries, maternal supplementation may be preferred to infant supplementation.

Methods. This is a prospective study that analysed 25OH vitD3 levels in mothers and their newborns in relation to pregnancy-induced pathology, enrolling participants prior to delivery and following them to assess outcomes. The study was conducted during the 5

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months in County Hospital Baia Mare.

The aim is to assess 25OH vitD3 level by age group and its correlation with maternal status.

Results. Data analysis reveals a mean gestational age of 35.76 ± 3.04 weeks. The level of 25OH vit D3 by age group was without statistically significant differences: 0.094 (age group 28-32 was 15.47 ± 7.3 ng/dl, age group 32-36 weeks was 19.73 ± 12.1 ng/dl., age group over 37 weeks was 18.41 ± 7.77ng/dl.). There were statistically significant differences between the 3 VG groups in 25OH vit D3 values at birth compared to 1 month of age, with the lowest values in the group with VG of 28-32 weeks (10.07 ± 4.62ng/dl at birth vs 18.76 ± 4.41ng/dl at 1 month; p = 0.043). There was no statistically significant correlation in the studied sample between maternal vitamin D3 values and vitamin D3 values at birth (Correlation test: p=0.659 >0.05).

Conclusion. At birth At 1 month of age, the serum level of 25 OH vit D3 was significantly lower in all age groups.

Urinary metabolic profile and biomarkers of discrimination between thyroid nodules and thyroid papillary carcinoma

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Introduction. This study aimed to characterize the urinary metabolic profile of patients with papillary thyroid carcinoma (PTC) and benign thyroid disease (BT) compared with healthy controls (C), to identify differentiation biomarkers using multivariate and univariate statistical tools, and to assess the metabolic pathways affected in each pathology. Urine and serum data were further integrated using the Venny algorithm to identify common and specific biomarkers.

Methods. A total of 20 healthy subjects and 60 patients (30 PTC, 30 BT) were included. Urine samples were collected and processed for UHPLC-QTOF-ESI+-MS analysis, which detected 386 molecules, of which 190 were identified across 10 metabolite classes.

Results. PLSDA showed clear separation between C and both pathological groups, and moderate discrimination between PTC and BT. VIP scores and Random Forest analysis highlighted key metabolites differentiating PTC from BT, including guanosine, 6-hydroxymelatonin, homocysteine, taurocholic acid, serotonin, and specific lysophospholipids. Volcano analysis revealed significant fold-change variations, while ROC analysis identified urinary lipid metabolites (LisoPEs, mevalonic acid, glycerophosphocholine, steroid derivatives) with the highest AUC values. In serum, amino acid derivatives and acylcarnitines were more discriminative.

Pathway analysis indicated disturbances in steroid hormone metabolism, sulfur-amino acid metabolism, tryptophan metabolism, and pathways involving alanine, aspartate, and glutamate. Venny integration identified 90 shared metabolites between urine and serum.

In conclusion, non-targeted UHPLC-QTOF metabolomics revealed distinct metabolic signatures in PTC and BT, involving both polar and lipid metabolic pathways. These findings support the identification of potential biomarkers relevant for differentiating malignant from benign thyroid pathology.

Septo-optic dysplasia: a rare cause of short stature in a pediatric patient

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Introduction. Septo-optic dysplasia (SOD), is a congenital disorder that affects early brain development, typically defined as a combination of at least two of the following three features: optic nerve hypoplasia, midline brain abnormalities (absence of the septum pellucidum), and pituitary gland hypoplasia. The incidence of SOD is 1 in 10,000 newborns. In the majority of SOD cases, the underlying cause remains unclear, although both genetic and environmental factors are thought to contribute to its development.

Case report. A 7-year-old boy, born from a pathological pregnancy, known to have hyperopia, amblyopia, exophoria, and convergence insufficiency, requested an endocrine-metabolic evaluation in the context of short stature and weight deficiency. Physical examination revealed short stature (-2.93 SD) and underweight (p 1). Hormonal testing showed markedly low basal GH (0.27 ng/ml) and undetectable IGF-1 (<7 ng/ml); slightly low FT4 (0.94 ng/dl) with normal TSH; ACTH (18.9 pg/ml) and serum basal cortisol (16 µg/dl) with physiological values. The clonidine stimulation test demonstrated no GH response, confirming growth hormone deficiency. X-ray of the nondominant hand revealed a bone age delay of 4 years and 11 months. Pituitary MRI described the pituitary gland as being reduced for age, neurohypophysis ectopia, absence of the septum pellucidum, atrophic optic nerves, suggesting SOD. Treatment with human recombinant GH 0.50 mg/day was initiated.

Conclusions. The case highlights the importance of early diagnosis of SOD and integrated ophthalmological, neurological, and endocrine evaluation, which are essential for the prompt initiation of GH therapy and optimization of the growth and development prognosis.

Diagnostic and therapeutic management of an incidentally discovered adrenocortical carcinoma – a case report

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Introduction. Adrenocortical carcinoma (ACC) is a rare endocrine disorder with a poor prognosis, often associated with hypercortisolism. Therapeutic management includes surgical treatment (en bloc adrenalectomy with locoregional lymphadenectomy) and adjuvant therapy (mitotane, chemotherapy - etoposide, doxorubicin, cisplatin, and various local/anti-hormonal/anti-resorptive therapies).

Case report. We present the case of a 39-year-old female patient in whom a right adrenal adenoma (~10 cm) was incidentally discovered. The clinical features (hirsutism, bufallo hump, facial erythema, obesity, and hypertension - all of recent onset), together with hormonal assays (lack of cortisol suppression after 1 mg dexamethasone, elevated midnight serum cortisol, 24-hour urinary free cortisol, DHEA-S and testosterone, suppressed ACTH;

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plasma metanephrines and normetanephrines, serum aldosterone, plasma renin activity, and aldosterone/renin ratio all within normal limits) and abdominal imaging, established the diagnosis of a right adrenal adenoma with co-secretion of cortisol and androgens, for which a right adrenalectomy was recommended. Histopathological exam confirmed the diagnosis of high-grade right ACC (pT2NxMxL1V1), and treatment with mitotane was initiated, up to 4.5 g/day (a dose poorly tolerated due to gastrointestinal side effects), along with 30 mg/day of hydrocortisone. Postoperative thoracoabdominopelvic imaging showed no signs of tumor recurrence or distant metastases.

Conclusions. Suspicion of ACC should be raised in patients with large adrenal adenomas presenting with clinical signs of rapidly progressing hypercortisolism and hyperandrogenism.

The impact of lifestyle modification on the management and prognosis of obstructive sleep apnea syndrome

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Background. Obstructive Sleep Apnea Syndrome (OSAS) is characterized by partial or complete collapse of the upper airway, leading to sleep fragmentation, intermittent hypoxemia, and sympathetic nervous system activation. The prevalence of OSAS is increasing and closely correlated with the rising incidence of obesity.

Case presentation. A 59-year-old non-smoking female, previously diagnosed with severe OSAS, postponed initiation of CPAP therapy and subsequently used it inconsistently. She presented to our clinic with complaints of excessive daytime sleepiness, fatigue, and morning headaches. Her medical history revealed cardiovascular and metabolic comorbidities and multiple ENT surgical interventions. On physical examination, BMI was 39.7 kg/m², with Mallampati score III. Nocturnal polygraphy during CPAP therapy revealed a persistently elevated Apnea–Hypopnea Index (AHI). Due to ongoing obstructive events, various non-invasive ventilation modes were tested; however, despite increased pressure levels, a high residual AHI persisted. This raised suspicion of an upper airway obstruction contributing to increased resistance. ENT examination revealed no significant obstruction, while sinus CT was normal except for mild nasopharyngeal adenoidal hypertrophy. The patient was switched to auto-CPAP therapy with low-flow supplemental oxygen, achieving partial improvement in residual AHI and nocturnal oxygen saturation. At six-month follow-up, the patient had achieved a voluntary weight loss of 25 kg through nutritional counseling and regular physical exercise. This resulted in marked improvement in daytime symptoms, reduction of antihypertensive therapy, and normalization of spirometric parameters. Given the substantial weight reduction, a new polygraphy confirmed severe OSAS, yet auto-CPAP titration without supplemental oxygen provided effective correction of apneic events and desaturations.

Discussion. Weight loss reduces upper airway collapsibility, improves oxygenation, and positively influences cardiovascular parameters. Lifestyle intervention has clinically meaningful reduction in AHI.

Conclusion. Lifestyle modification represents a major component of therapeutic success in a patient with severe OSAS. Weight loss significantly improved adherence to positive airway pressure therapy, long-term prognosis, and overall quality of life.

Complex management of post-prolonged intubation tracheal stenosis associated with obstructive sleep apnea syndrome – a case report

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Introduction. Post-intubation tracheal stenosis represents a severe complication in patients with acute respiratory failure following COVID-19, requiring prolonged mechanical ventilation. The management of these patients is often difficult, involving repeated interventions and a multidisciplinary approach.

Methods. We present the case of a 55-year-old hypertensive and obese female patient with a history of severe COVID-19 infection (2021), complicated by acute respiratory failure that required prolonged orotracheal intubation, subsequently developing post-intubation tracheal stenosis. The patient experienced recurrent episodes of respiratory failure, treated with successive endoscopic dilatations. Due to the recurrence of the stenosis, placement of a Montgomery T-tube was decided to maintain tracheal patency.

During follow-up, the patient presented to our department for the evaluation of suspected sleep apnea syndrome. A cardiorespiratory polygraphy was performed, revealing severe obstructive sleep apnea syndrome (OSA) (AHI = 30.2/hour of sleep, ODI = 45.5/hour). A titration with autoCPAP 5–15 cmH_2O was performed, resulting in a residual AHI of 7.3/hour of sleep. Fixed-pressure therapy was attempted, but the patient could not tolerate it due to air leaks around the Montgomery tube; therefore, she continued therapy with autoCPAP.

Results. The placement of the Montgomery T-tube allowed stabilization of respiratory function and reduction of acute respiratory failure episodes.

Implementation of CPAP therapy was initially challenging, requiring pressure adjustments to prevent air leakage through the external limb of the Montgomery tube. After careful calibration of parameters, the therapy was well tolerated, with symptomatic improvement.

Conclusion. This case highlights the complexity of treating post-intubation tracheal stenosis, particularly in post-COVID-19 patients, where tracheal inflammation and fibrosis may be exacerbated. Placement of a Montgomery T-tube represents an effective solution for maintaining airway patency, while identifying and managing comorbidities such as OSA are essential for optimizing respiratory prognosis and improving patient quality of life.

Effectiveness of preoperative rehabilitation in the recovery of patients with anterior cruciate ligament reconstruction

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Introduction. The aim of this paper was to assess the potential effects of preoperative rehabilitation programs in the management of patients with anterior cruciate ligament reconstruction.

Methods. 42 patients with low back pain (age between 25 and 40 years, 19 women

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and 23 men) participated in this prospective randomized controlled trial. Patients were assigned to the Study Group (SG, n=22) or to the Control Group (CG, n=20). Patients from both groups received 10 sessions of post-surgical rehabilitation, 3 days / week, but only patients from SG had also 10 sessions of pre-surgical rehabilitation, 3 days / week. All patients were assessed on the first and on the last day of treatment, by: Single-Leg Hop Test and Triple Hop Test for knee muscle strength, stability and proprioception, International Knee Documentation Committee (IKDC) questionnaire for pain and function.

Results. No difference between groups could be identified in any of the parameters at baseline. At the end of treatment patients in both groups obtained significant improvement in all parameters: Single-Leg Hop Test increased from 122±10 m to 164±14 m, $p<0.05$ in SG, and from 119±17 m to 151±12 m, $p<0.05$ in CG, Triple Hop Test increased from 315±21 m to 450±17 m, $p<0.05$ in SG, and from 308±12 m to 392±16 m, $p<0.05$ in CG, IKDC increased from 58±4 to 82±7, $p<0.05$ in SG, and from 54±3 to 71±7, $p<0.05$ in CG. Nevertheless, the improvement was significantly better in SG than in CG: $p=0.04$ for Single-Leg Hop Test, $p=0.04$ for Triple Hop Test and $p=0.02$ for IKDC index.

Conclusion. Preoperative rehabilitation increased the effectiveness of the postoperative kinesitherapy program in recovering muscle strength, stability, proprioception and functionality in patients with anterior cruciate ligament reconstruction.

Congenital ichthyosis with transient neurological symptoms in a CYP4F22-positive neonate: a diagnostic dilemma

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Introduction. Autosomal recessive congenital ichthyosis (ARCI) caused by CYP4F22 mutations typically presents with skin barrier abnormalities and scaling, without associated neurological manifestations. When a neonate with ichthyosis develops acute neurological deterioration, the differential diagnosis is broad and can include neuro-ichthyosis, metabolic disease, epileptic encephalopathy, or infectious encephalitis.

Case presentation. We report a neonate suspected of having ichthyosis due to a collodion membrane, ectropion, and eclabium. Whole exome sequencing was performed, with results pending for six weeks. At three weeks of age, the infant developed fever and acute neurological symptoms, including abnormal posturing, spasticity, and reduced responsiveness. The initial electroencephalogram was interpreted as burst–suppression, suggesting severe encephalopathy, and was first considered in the context of ichthyosis-associated metabolic disease. Antiseizure therapy produced no improvement, and lumbar puncture was deferred. At the insistence of the parents (both physicians), empiric antiviral therapy was administered, after which the infant became responsive. Neuroimaging did not reveal lesions, metabolic investigations were unremarkable, and whole exome sequencing later confirmed a CYP4F22 mutation. Subsequent EEG review at a tertiary center clarified that the initial pattern did not represent true burst–suppression. Although initial suspicion suggested a syndromic metabolic disorder, this diagnosis was inconsistent with the clinical course, as the infant fully recovered, EEG normalized, and antiseizure medications were discontinued.

Conclusion. This case highlights the challenges of interpreting acute neurological events in neonates with rare genetic disorders. Misinterpretation of early

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EEG findings and uncertainty regarding etiology can generate significant and lasting parental anxiety about prognosis, sequelae, and relapse risk. The case underscores the critical importance of diagnostic clarity for guiding management and providing families with reassurance, while emphasizing the need for multidisciplinary evaluation and prompt consideration of treatable emergencies, such as infection, in unexplained neonatal encephalopathy.

Pulmonary aspergilloma: diagnostic and therapeutic approach

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Introduction. Pulmonary aspergilloma represents a localized form of aspergillosis, characterized by the colonization of a pre-existing pulmonary cavity by fungi of the Aspergillus genus. These fungi proliferate within the cavity, forming a compact fungal mass ("fungus ball"). The diagnosis is supported by positive anti-Aspergillus IgG antibodies and confirmed through imaging investigations.

Case presentation. We present the case of a 69-year-old male, former smoker (40 pack-years), abstinent for 4 years, with no occupational exposure to respiratory irritants and no documented allergies. The patient had a history of pulmonary tuberculosis (exact date unknown), COPD stage IV, risk group E, chronic respiratory failure requiring long-term oxygen therapy with non-invasive ventilation at home, extensive bronchiectasis, and diffuse bilateral reticulonodular pulmonary fibrosis.

The patient presented with sudden-onset moderate hemoptysis and productive cough.

Clinical examination revealed bilateral vesicular breath sounds, wheezes in the left upper lobe, and SpO_2 = 96% on 3 L/min oxygen via a 24% Venturi mask. Laboratory findings showed leukocytosis with neutrophilia, marked inflammatory syndrome, mild normochromic macrocytic anemia, and elevated anti-*Aspergillus fumigatus* IgG (184 mg/L). Arterial blood gases were within compensated parameters: pH 7.39, pCO_2 38.5 mmHg, pO_2 92 mmHg, HCO_3 23.27 mmol/L, SaO_2 97%.

Chest CT scan revealed bilateral apical fibrotic sequelae, suggestive of chronic post-tuberculous lesions, and a cavitary lesion measuring 53/38/22 mm with a central hyperdense mass in the left upper lobe, highly suggestive of an aspergilloma. Additional findings included a 35/23 mm parenchymal nodule in the left upper lobe, hilar calcifications, a 22 mm right lower hilar nodule, and scattered micronodules, completing a complex pulmonary imaging pattern.

Treatment was initiated with hemostatic agents, resulting in hemoptysis remission, and systemic antifungal therapy - initially Voriconazole, followed by Itraconazole - alongside prophylactic antibiotics (Amoxiplus) for bacterial infections. The patient showed favorable clinical, biological, and imaging evolution. However, recurrent hemoptysis and progression of respiratory failure remain important long-term concerns requiring close follow-up.

The association of a history of pulmonary tuberculosis, fibrotic sequelae, and a cavitary "fungus ball" on CT, along with elevated anti-*Aspergillus fumigatus* IgG, confirmed the diagnosis of post-tuberculous pulmonary aspergilloma. Hemoptysis remains the predominant and potentially life-threatening manifestation, caused by erosion of vessels

within the cavity wall. Therapeutic management is complex and should be individualized according to symptom severity, pulmonary comorbidities, and overall functional status. In this case, the presence of severe COPD and chronic respiratory failure limited surgical options, leading to a conservative approach with antifungal therapy and supportive care.

Conclusion. Pulmonary aspergilloma occurs as a late complication in patients with pulmonary tuberculosis and residual cavitary lesions. Diagnosis relies on the correlation between thoracic imaging and specific serologic markers. Treatment should be tailored to disease severity and comorbidities, while the prognosis remains guarded in patients with advanced chronic lung disease, requiring close monitoring and multidisciplinary management.

The role of holistic approach in the diagnosis and management of neonatal inherited disorders

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Introduction. Diagnosing inherited disorders is often a challenge for neonatologists. These conditions are often asymptomatic immediately after birth, the newborn presents a normal transition to life outside the womb.The clinical symptoms occur after 1-3 days of life, and the diagnosis involves multidisciplinary collaboration.

We present the case of 2 newborns with inherited diseases whose diagnosis and management involved a holistic approach.

Case report 1. Term newborn, 38 weeks of gestation, 2250g, Apgar score 8, known as kidney malformation, present of 7th day of life hyperglycemia with poor response to insulin treatment in high doses. Diabetology consultation is performed, continuous insulin treatment and glucose level monitoring with Dexcom one + is initiated. The poor evolution of the case raise suspicion on genetic form of diabetes. Genetic testing for monogenic diabetes confirmed the patient heterozygous for KCNJ11 gene that encodes a subunit of the ATP-sensitive K+ channel. Follow up of the child by diabetologist was done. The one year follow up of the children revealed a normal neurological outcome and good control of glucose level.

Case report 2. Term male, newborn, 39 weeks of gestation, 3300g birth weight, Apgar score 8/9, known with antenatal subependymal cysts, good neonatal transition. On second day of life presents signs of respiratory distress, persistent lactic and hyperammonemia. The head ultrasound confirms the multiple cysts. Based on clinical and laboratory findings raise the suspicion of metabolic disorder of urea cycle or energy metabolism disorder. The urine analysis by MRI spectrometry oriented the diagnosis pyruvate carboxylase deficiency which was confirmed by genetic testing. The sequence analysis revealed a PC c.1825+1G>A homozygous form, a variant not reported before. Pyruvate carboxylase deficiency is characterized by the accumulation of lactic acid and other potentially toxic compounds in the blood. The type B of the disease-severe neonatal form associates lactic acidosis, neurological impairment and survival for less than 3 months.

The patient had a pure neurological outcome and died before 1 month of age.

Genetic counseling of parents was applied in both cases.

Conclusion. In both patients the diagnosis and management of rare diseases needed multidisciplinary cooperation. Genetic testing was necessary for the accurate diagnosis and counseling of parents.

Cardiovascular manifestations of tuberous sclerosis complex - from rhabdomyomas to electrocardiographic abnormalities (a case series)

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Introduction. Tuberous sclerosis complex is an autosomal-dominant genetic disorder characterized by benign tumors affecting the brain, heart, lungs, kidneys and eyes. Among the cardiovascular manifestations, cardiac rhabdomyomas are the most common and may represent the first diagnostic sign of the disease. These lesions can be associated with arrhythmias, conduction abnormalities or outflow tract obstruction.

Objective. Presenting the clinical features, with a focus on cardiovascular manifestations in 11 patients diagnosed with tuberous sclerosis, highlighting the importance of cardiologic monitoring during follow-up.

Methods. Eleven patients who underwent cardiologic evaluation: electrocardiography (ECG), echocardiography and ECG Holter monitoring were included. The characteristics of the cardiac rhabdomyomas (number, location, size), the presence of rhythm abnormalities and clinical outcomes were analyzed.

Results. Five patients were diagnosed antenatally with cardiac rhabdomyomas, detected on fetal ultrasound. In the remaining cases (n=6), the mean age at symptom onset was 6 months.

Cardiac rhabdomyomas were present in all patients, primarily located within the ventricles: left ventricle (LV) (n=1), right ventricle (RV) (n=2), both LV and RV (n=5) and LV, RV and left atrium (LA) (n=3). Multiple cardiac masses were identified in most cases, except for two patients with a solitary lesion. None of the patients showed significant hemodynamic dysfunction.

Electrocardiographic abnormalities (n=3) included pre-excitation, early repolarization and premature ventricular beats; two patients required antiarrhythmic therapy.

All patients also presented extracardiac involvement: cutaneous (n=11), renal (n=6), neurological (n=11), psychiatric (n=4) and ophthalmologic (n=3).

Conclusion. Cardiovascular manifestations are common in tuberous sclerosis. Although cardiac rhabdomyomas typically have a benign course and may regress spontaneously, the associated risk of arrhythmias and hemodynamic complications require ongoing cardiologic follow-up.

Pharmacological treatment options of gambling disorder

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Introduction. Gambling Disorder (GD) involves neurobiological dysregulation in brain circuits governing reward and impulsivity, affecting the dopaminergic, serotonergic, and glutamatergic systems. Although Cognitive-Behavioural Therapy (CBT) is the mainstay, pharmacological options are needed for patients with an insufficient response.

Methods. This review synthesized data from Randomised Controlled Trials (RCTs), meta-analyses, and systematic reviews published in PubMed. Efficacy was assessed using

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validated scales like the YB-BOCS-PG (Yale-Brown Obsessive Compulsive Scale Modified for Pathological Gambling), gambling frequency, and functional improvement.

Results. Opioid Antagonists (Naltrexone, Nalmefene) is the most promising class. Naltrexone reduces craving and pleasure by blocking the reward pathway. RCTs confirm that Naltrexone (especially at 100–150 mg/day) is significantly more effective than placebo in mitigating craving and gambling behaviour. Anticonvulsants (Topiramate, Lamotrigine) modulate glutamatergic and GABAergic systems, significantly reducing impulsivity and excitement. Topiramate is a strong therapeutic option for impulse-driven GD. Antidepressants (Selective Serotonin Reuptake Inhibitors, such as paroxetine, escitalopram, fluvoxamine) correct serotonergic dysregulation, primarily useful for patients with comorbid depression and anxiety. Atypical Antipsychotics should be reserved for patients with comorbid psychotic or severe affective disorders due to limited direct evidence for GD symptom reduction.

Conclusion. Naltrexone and Topiramate emerge as the most robust pharmacological options, supported by evidence for reducing craving, impulsivity, and gambling engagement. Treatment selection requires personalization, considering the patient's symptom profile, presence of comorbid psychiatric disorders, and tolerability of adverse effects.

The role of predictive and prognostic markers in the personalized approach to patients with obstructive sleep apnea syndrome

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Introduction. Obstructive sleep apnea syndrome (OSA) is a common but often underdiagnosed sleep disorder characterized by repeated interruptions in breathing during sleep, followed by intermittent decreases in oxygen saturation. People with OSA experience fragmented sleep and multiple nocturnal and diurnal symptoms, with a significant negative impact on their overall health and quality of life. Given the significant complications of this pathology, its increasing prevalence in the general population, the methods developed for diagnosis, and the difficult access to them, it is necessary to create preventive models by identifying the predictive factors of this pathology, with the aim of increasing awareness and expanding the possibilities for investigating this pathology.

The main objective of the study is to analyze the correlations between the presence of certain predictive and prognostic factors and the severity of obstructive sleep apnea syndrome.

Methods. The study group included 30 consecutively selected patients with an increased risk of sleep apnea, quantified using the STOP-BANG questionnaire and the Epworth Sleepiness Scale (ESS). The data studied included: anthropometric indices, presence of comorbidities, nocturnal cardiorespiratory polygraphy parameters, fractional nitric oxide level in exhaled air (FeNO), and average and maximum End Tidal CO2 (EtCO2) levels assessed by continuous nocturnal capnography.

Results. In the analyzed group, the mean age at diagnosis was 55.60±10.55 years, with a predominance of males (80%). 90% of subjects had varying degrees of obesity, 33.3% had excessive daytime sleepiness (EDS> 10 points), and 63.3% had at least one associated cardiovascular pathology. 53.65% of subjects had severe OSA. The mean FeNO level in the study group was 26.03±17.387 ppb, without being influenced

by the presence of comorbidities, OSA severity, or body mass index (BMI). The mean EtCO2 level was 44.70 ±3.879 mmHg, with 43% of subjects having values above the physiological limit. There was a statistically significant correlation between BMI and ESS (r=0.562, p=0.001), apnea-hypopnea index (AHI) (r=0.578; p=0.001), and the presence of cardiovascular comorbidities (p=0.004). In addition, patients with severe OSA were found to have higher EtCO2 levels compared to those with moderate OSA (p=0.001), with a statistically significant correlation between the desaturation index (ODI), time spent at oxygen saturation ≤90% (T90%), and EtCO2 level (r=0.584, p=0.001, and r=0.584, p=0.001, respectively). Following the study, statistically significant correlations were reported in the group of patients diagnosed with OSA between anthropometric indices and OSA severity, and as a predictive and severity marker, EtCO2 plays a central role, having significant relationships with the parameters identified by nocturnal cardiorespiratory polygraphy and with anthropometric indices.

Conclusion. Nocturnal CO2 level monitoring can play a crucial role in the complex assessment of patients with obstructive sleep apnea syndrome, especially in those with identified risk factors (obesity, associated cardiovascular pathology). The use of this parameter in current clinical practice can facilitate the adjustment of appropriate, individualized treatment and reduce the risk of worsening the pathology and the occurrence of other associated complications. Future studies on large groups of patients are needed to investigate the complex relationships between these identified markers (FeNO, EtCO2) and the severity of obstructive sleep apnea syndrome and associated comorbidities in order to develop effective screening and diagnostic models.

Glioblastoma - a relentless challenge in neuro-oncology

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Introduction. Glioblastoma is the most aggressive primary brain tumor in adults (WHO grade IV), marked by rapid progression and poor prognosis, with a median survival of about one year despite multimodal treatment. This case highlights the diagnostic and therapeutic challenges in managing glioblastoma in the context of pulmonary lesions.

Case Report. We report the case of a 75-year-old male, active smoker, with controlled hypertension and COPD, who presented with progressive left occipital headache, right-sided paresthesia and weakness, and visual disturbance on the left side. Neurological exam revealed right hemiparesis (4/5) and left hemineglect. Two months later, symptoms progressed to gait instability, asthenia, and weight loss. Neurological reevaluation identified right central facial palsy, bilateral Babinski sign, and right hemifacial myoclonus, indicating rapid neurological decline. Cranial CT/MRI demonstrated multifocal lesions, including a large left fronto-parietal mass with necrosis, irregular margins, and extensive vasogenic edema, suggesting multifocal glioblastoma or metastasies. Thoraco-abdominal CT identified a spiculated right lower-lobe pulmonary mass and multiple micronodules, raising suspicion of pulmonary metastases. He received dexamethasone, levetiracetam, and supportive care. Oncological team advised biopsy, but CT-guided biopsy was not feasible due to anatomical limitations.

Conclusion. This case illustrates the complex interplay between glioblastoma and a suspected pulmonary metastasis, highlighting the challenges in therapeutic decision-making. Despite aggressive supportive care, the patient experienced a rapid

clinical decline- underscoring the poor and the challenge of therapeutic triage in the presence of competing pathology. Early involvement of neurology, neurosurgery, oncology, and palliative services is essential to optimize symptom control and quality of life.

From genes and modifiers to therapy

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Introduction. Understanding how genetic mutations and modifier genes influence disease expression is central to translational medicine. Advances in molecular genetics have redefined monogenic disorders, showing that phenotype and therapeutic response depend on complex gene–environment and modifier interactions.

Methods. Data were obtained through a PubMed literature search (last five years), selecting the most representative studies addressing gene–modifier interactions and therapeutic strategies in monogenic diseases were analyzed to highlight key translational links between genotype, modifier effects, and therapeutic strategies.

Results. IEMs illustrate the metabolic variability modulated by secondary pathways, while SMA models integrate genetic, biochemical, and therapeutic insights. Loss of SMN1 function is partially compensated by SMN2 and other modifiers, shaping disease severity and treatment outcome. This knowledge led to the development of gene replacement and splicing-modifying therapies. In IEMs such as phenylketonuria, Pompe, Fabry, mitochondrial disorders etc, genotype–phenotype correlations and modifier effects guide enzyme replacement, substrate reduction, and emerging mRNA or gene-editing therapies. Telomere biology also modulates tissue resilience; mutations in TERT, TERC, or DKC1 link defective maintenance to premature aging and organ failure.

Conclusions. Integrating gene defects, modifier pathways, and molecular therapies defines a translational continuum from mechanistic discovery to individualized treatment. This framework transforms rare genetic diseases into models for precision medicine, promoting early diagnosis, tailored interventions, and improved clinical outcomes. Population-specific mutation patterns in Romania may guide research on rare disorders and contribute to reference genome initiatives such as ROGEN.

Relationship between core rebalancing and shoulder functional improvement in patients with shoulder pain

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Introduction. The objectives of the study were to evaluate the benefits of introducing core strengthening exercises into a shoulder rehabilitation program in patients with painful shoulder, in order to increase mobility, relieve pain, and reduce disability.

Methods. 45 patients with shoulder pain (age between 40 and 70 years, 31 women and 14 men) took part in this prospective randomized controlled trial. Patients were assigned to Core group (n=25) or to Control group (n=20). All patients received 10 sessions of kinesitherapy, 5 days / week, for 2 weeks. Shoulder exercises and core strengthening exercises were prescribed for patients of the Core group, meanwhile patients of the Control group only performed shoulder exercises. All patients were assessed on the first and on the last day of treatment, by: visual analogue scale (VAS) for pain, Disabilities of the Arm, Shoulder and Hand (DASH) index for function, Shoulder Pain And Disability Index (SPADI) for pain and function.

Results. No difference between groups could be identified 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 6.9±1.3 to 4.5±1.1, $p<0.05$ in Core group, and from 6.5±1.2 to 4.8±1.6, $p<0.05$ in Control group), function (DASH index decreased from 58±5.9 to 43.1±4.2, $p<0.05$ in Core group, and from 54.1±4.9 to 42.6±6.9, $p<0.05$ in Control group), pain and function (SPADI decreased from 68.4±5.7 to 46.2±6.1, $p<0.05$ in Core group, and from 64.9±6.3 to 44.1±3.2, $p<0.05$ in Control group). At the same time, the improvement was significantly better in Core group than in Control group: $p=0.05$ for VAS, $p=0.02$ for DASH index and $p=0.01$ for SPADI index.

Conclusion. Shoulder exercises were effective in patients with painful shoulder for reducing pain and increasing function, but including additional Core strengthening exercises in the rehabilitation program led to supplementary benefits.

Monitoring of tick-bitten patients for development of *Borrelia burgdorferi sensu lato* infection – an observational study

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Introduction. Lyme borreliosis is the most common tick-borne zoonosis in Europe and North America, caused by *Borrelia burgdorferi sensu lato*. In Romania, epidemiological data regarding the actual seroconversion rate of the infection are limited. The objective of this study is to assess the risk of *Borrelia burgdorferi* infection development in patients exposed to tick bites.

Materials and methods. A total of 86 patients with recent tick bites from the Transylvania region were enrolled after providing informed consent. Standardized questionnaires were administered to assess living environment, diet, occupational and

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recreational exposures. Biological samples were collected within the first 1–3 days post-bite and again at 4–6 weeks follow-up. Serological testing included detection of *Borrelia burgdorferi*-specific IgM and IgG antibodies using ELISA and Western Blot techniques. Additional laboratory investigations were performed to rule out potential cross-reactive or interfering pathogens: Mycoplasma IgM, rheumatoid factor (RF), rapid plasma reagin (RPR), anti-TPO antibodies, HBs antigen, and HCV antibodies.

Results. Preliminary clinical and serological data have been processed. Variations were observed between baseline and follow-up serological testing, as well as interindividual differences in immune reactivity. Complete interpretation of results depends on the final analysis of all included markers.

Conclusions. The findings to date highlight the need for sustained serological monitoring in patients exposed to tick bites.

MEDICINE
Surgical Specialties

Deep neck space infections: a multidisciplinary approach in the management of a major emergency

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Introduction. Deep neck space infections represent a severe and potentially fatal pathology requiring rapid recognition and coordinated management. These infections, which often arise from dental or upper respiratory sources, can spread quickly through the fascial planes of the neck and lead to life-threatening complications such as mediastinitis, sepsis, or internal jugular vein thrombosis. Because of their anatomical complexity and proximity to major vascular and neural structures, early diagnosis and timely intervention are essential.

This study summarizes the experience of the ENT Department of the Cluj-Napoca County Emergency Clinical Hospital in diagnosing and managing deep neck infections, with emphasis on the diagnostic role of contrast-enhanced CT, the therapeutic approach, and clinical outcomes over a five-year period.

Methods. A retrospective analysis was conducted on patients diagnosed with deep neck infections between 2020 and 2024. Data included demographic characteristics, predisposing factors, presenting symptoms, imaging findings, type of treatment, and outcomes.

Diagnosis was established through clinical examination and contrast-enhanced cervical CT, which defined the extent of infection and guided the surgical plan.

All patients received broad-spectrum intravenous antibiotics, typically beta-lactams combined with metronidazole or clindamycin. Surgical drainage was indicated in cases of abscess formation, airway compromise, or poor response to conservative therapy.

Two surgical approaches were used depending on abscess location and extent: the transoral route for medial or localized collections and the cervical route for extensive or lateral involvement.

Results. Fifty-five patients were included in the study: 32 men and 23 women, aged 19 to 85 years (mean age 46.6). The most frequent predisposing factors were recent upper respiratory tract infection (40%), dental infection (33%), and diabetes mellitus (17%).

The dominant symptoms at presentation were high fever (90%), cervical swelling and pain (86%), odynophagia (82%), and trismus (72%).

Contrast-enhanced CT was decisive for diagnosis and treatment planning, accurately identifying the location and spread of infection.

Forty-three patients (78%) required surgical drainage, while 12 (22%) were treated successfully with antibiotics alone. Among those operated, 60% underwent a transoral approach and 40% a cervical approach. The average length of hospital stay was 8.1 days, ranging from 3 to 30.

Most patients recovered completely under combined medical and surgical treatment. Complications, such as septicemia or airway obstruction, occurred mainly in patients with delayed presentation. No deaths were recorded.

Conclusion. Deep neck infections remain a serious otolaryngologic emergency that demands early recognition and coordinated multidisciplinary management. Prompt initiation of empirical antibiotic therapy and accurate imaging assessment are key to preventing complications. Surgical drainage remains the mainstay of therapy when abscess formation or airway compromise occurs.

The five-year experience at the Cluj-Napoca County Emergency Clinical Hospital highlights the value of a standardized, multidisciplinary approach integrating clinical assessment, radiologic guidance, and surgical expertise to reduce morbidity and improve patient outcomes.

Case report: to be or not to be a Warthin's tumor?

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Introduction. Primary squamous cell carcinoma (PSCC) of the parotid gland represents less than 1% of all salivary gland neoplasms. This case report aims to raise awareness about this topic and the differential diagnoses that should be considered in cases of masses involving the parotid region.

Methods. A 65-year-old caucasian, non-smoking woman was hospitalized for a painless, right parotid mass that progressively increased over the last six months and that measured 10x6 cm, with areas of different consistency, mobile with respect to the overlying erythematous skin, but fixed with respect to the deep tissues. Previously, the patient had already undergone two neurosurgical interventions for a right orbital sebaceous carcinoma. Features of facial nerve palsy were absent, and cervical lymph nodes were not palpable. A provisional clinical diagnosis of Warthin's parotid tumor was made. The contrast-enhanced head and neck computed tomography revealed a pseudo-encapsulated, oval, and inhomogeneous mass, with a central area of cystic appearance, starting from the lower region of the superficial lobe of the right parotid gland. Our team performed a partial superficial right parotidectomy and a modified right radical neck dissection with preservation of the spinal accessory nerve and sternocleidomastoid muscle, with no complications during postoperative recovery. The histopathological report revealed the diagnosis of primary squamous cell carcinoma of the superficial lobe of the parotid gland, pT4aN2bL1V0R0. Two months after the surgery, the patient was referred to a radiotherapy clinic for adjuvant treatment.

Results. PSCC of the parotid gland is an aggressive malignancy that affects males twice as often as women and has a mean age of presentation around 60 years. Other salivary gland lesions that can be confused with PSCC include Warthin's tumor, high-grade mucoepidermoid carcinoma, and metastatic squamous cell carcinoma from a primary skin carcinoma. The particularities of our case are the female gender, the patient's history of orbital sebaceous carcinoma, the lack of facial nerve involvement at presentation, and the cystic component of the tumor.

Conclusion. An extended clinical and histological examination is mandatory to differentiate a PSCC tumour from other similar conditions. Future prospective studies should assess new early diagnostic techniques and identify effective curative treatments for each stage of the disease.

When rare pathology meets new technology: PTeye™ autofluorescence for parathyroid mapping in total thyroidectomy indicated after thyroglossal duct carcinoma

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Introduction. Thyroglossal duct cysts (TGDC) occur in up to 7% of the population, with carcinoma developing in only 1–2% of cases, typically arising from

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ectopic thyroid tissue along the embryologic descent of the gland. In certain cases, total thyroidectomy is warranted due to the presence of papillary thyroid carcinoma in the orthotopic thyroid. This procedure carries a specific risk of parathyroid injury, and to enhance surgical safety, intraoperative near-infrared autofluorescence has emerged as a valuable tool for real-time identification and preservation of the parathyroid glands.

Case report. A 41-year-old male patient, with a prior history of a Sistrunk procedure in 2016 and subsequent surgery for an anterior cervical tumour (histology: Papillary thyroid carcinoma arising in a thyroglossal duct remnant; BRAF V600E positive), presented electively for a completion total thyroidectomy. There was no significant family history of thyroid or endocrine disease. The surgical approach employed an anterior cervical incision. Given the critical risk of parathyroid gland injury in total thyroidectomy, intraoperative surveillance was enhanced with the PTeye™ system, a fibre-optic near-infrared autofluorescence device for real-time identification and monitoring of the parathyroid glands. In support of this approach, a recent multicenter randomized trial demonstrated that fibre-based near-infrared autofluorescence increased the mean number of parathyroid glands identified during thyroidectomy (3.3 glands vs 2.8 in control; $P < .001$) without increasing operative time.

Conclusions. To sum up, both the rarity of the disease (TGD carcinoma) and the innovative method for improving surgical management of complications make this case unique and emphasise the importance of constantly improving the medical devices for a better outcome for the patient as well as training as many physicians in order to be used at a larger scale, PTeye being used only in Cluj-Napoca, Romania.

Imaging challenges in the case of a gastric gastro-stromal tumor with a particular location and development

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Gastrointestinal Stromal Tumors benefit from standardized criteria for diagnosis and treatment. However, given their particular location and histological profile, they represent real challenges. We present the case of a patient with a Subcardiac Gastric Gastro-intestinal Stromal Tumor, developed abdomino-mediastinally, for whom an Upper Polar Gastrectomy was performed through thoraco-phreno-laparotomy, which imposed multiple pre- and post-therapeutic imaging difficulties.

Particular postoperative course after multimodal treatment of metachronous rectal peritoneal carcinomatosis

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Metachronous peritoneal carcinomatosis benefits from standardized therapeutic criteria. The need for aggressive surgery and the intraperitoneal dissemination modality influence the postoperative evolution. We present the clinical evolution of a patient with Metachronous Rectal Peritoneal Carcinomatosis, for whom Total Ileo-colectomy and Intraperitoneal Intraoperative Chemotherapy were performed, who, under conditions of Short Bowel Syndrome, developed Paralytic Ileus.

Aggressive presentation of a rare pancreatic neoplasm: a case report of emergency surgical management

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Introduction. Pancreatic neuroendocrine tumors (PNETs) are rare neoplasms originating from the hormone-producing cells of the pancreas. Often, asymptomatic neoplasms can occasionally present with severe, acute complications. This case report highlights the importance of timely diagnosis and surgical intervention in preventing life-threatening outcomes.

Methods. A 58-year-old female was transferred to our emergency room in shock with diffuse peritoneal irritation and positive FAST-US. Computer tomography revealed a pseudopapillary tumor in the pancreatic tail with active bleeding and massive hemoperitoneum. During exploratory laparotomy, a massive hemoperitoneum and a cystic tumor with active bleeding from a breach in the anterior tumor wall were found. The tumor was compressing the inferior splenic pole, causing splenic ischemia. The

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surgical approach involved rapid packing for tamponade, splenic mobilization and entry into the omental bursa. A retropancreatic tunnel was created behind the pancreatic body, followed by en bloc corporeocaudal splenopancreatectomy using a linear stapler. Hemostasis was achieved, two drains were placed intraperitoneally, and the abdomen was closed in a standard manner.

Results. Postoperatively, the patient was monitored in the ICU, where she remained hemodynamically stable and recovered well. On postoperative day 3, she was transferred to the surgical ward and discharged in good condition by day 7. Histopathology confirmed a grade 2 pancreatic neuroendocrine tumor (pT3 pN1 L1 V0 PN1 R0).

Conclusions. Hemorrhagic complications of pancreatic neuroendocrine tumors are rare, but prompt surgical intervention significantly improves patient outcomes and reduces mortality.

Beyond high-risk groups: evaluating the role of NIPT in routine surveillance of low-risk pregnancies

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Introduction. Non-invasive prenatal testing (NIPT) is a screening test that analyzes fetal DNA fragments (cfDNA) circulating in the maternal blood to estimate the risk of chromosomal abnormalities in the fetus. Even if it is highly accurate, it is not a diagnostic test. NIPT does not actually test whole fetal cells, but the fetal DNA fragments that come mainly from the placenta, from the apoptotic syncytiotrophoblast cells. The mixed cfDNA is sequenced and is used to detect over or under-representation of chromosomes. Because of the origin of the DNA, NIPT reflects the placental genome, which usually matches the fetus, but it might be different in cases like confined placental mosaicism, maternal chromosomal abnormalities or vanishing twins. Standard panels test trisomy 21, 18, 13 and sex chromosomes aneuploidies. Some panels add microdeletions/wide-genome testing, but performance is weaker and more controversial. Confirmation of diagnosis is recommended to be made through invasive testing (chorionic villus sampling (CVS) or amniocentesis) followed by DNA testing techniques.

Methods. We made a retrospective study from our database, including 1073 NIPT tests conducted between April 2014 and August 2025. We included low-risk pregnancies, and the testing being performed between 10 and 22 weeks of gestation. NIPT was used for counseling together sonographic appearance.

Results. From the 1073 NIPT tests performed, we had 25 positive results, 11 for trisomy 21, 2 for trisomy 13, 1 for trisomy 15, 1 for trisomy 18, 2 for XXX syndrome, 1 for Klinefelter syndrome, 3 for Monosomy X and 4 for chromosomal deletions. Invasive testing through amniocentesis was proposed to all NIPT abnormal results, but was performed in only 13 patients, 4 patients had a normal result following invasive diagnosis, 8 had a conformation of the diagnosis, 1 patient had a different triploidy. From the NIPT positive cohort, 5 patients were assisted at birth in our facility, 3 underwent a medical termination of pregnancy and 4 patients had a miscarriage between 14 and 19 weeks of gestation. From the live-births, 1 baby had a genetic testing after birth that confirmed the diagnosis, and one baby had Down syndrome features. From the fetuses resulted after miscarriage or pregnancy termination, 6 had specific characteristics for the

suspected syndrome.

Conclusions. Our series has the merit to analyze a decent number of patients from low-risk pregnancy. The availability of NIPT test with extremely good sensitivity for Down syndrome is important for the management of low-risk pregnancy and has the advantage of being non-invasive. NIPT is not a diagnostic test therefore amniocentesis or cordocentesis is needed for follow-up.

Uterine arteriovenous malformations – a rare pathology with an integrative approach

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Introduction. Uterine arteriovenous malformations (AVMs) are a rare but potentially life-threatening cause of abnormal uterine bleeding (≈2%), characterized by direct communications between uterine arteries and veins without an intervening capillary network. Most cases are acquired, occurring in young women following intrauterine procedures, pregnancy, or obstetrical interventions. Early diagnosis is essential, as curettage performed in an undiagnosed AVM may lead to massive hemorrhage and emergency hysterectomy.

Methods. Two young patients presenting with episodes of menorrhagia and metrorrhagia, both with a history of previous deliveries and uterine curettage, were evaluated. Transvaginal Doppler ultrasound, contrast-enhanced MRI and CT revealed tortuous vascular structures within the myometrium, highly suggestive of uterine arteriovenous malformations. The diagnosis was confirmed by angiography, which demonstrated abnormal arteriovenous communications with high-flow shunts. Bilateral selective uterine artery embolization was subsequently performed via femoral access, using microparticles under fluoroscopic guidance.

Results. In both cases, cessation of bleeding was achieved, with rapid hemodynamic stabilization and preservation of uterine integrity. Post-procedure and two-month follow-up angio-CT confirmed a marked reduction in pathological vascular flow, without complications. Further embolization sessions were proposed to optimize the therapeutic outcome; however, the patients declined, given the significant improvement and reduction of metrorrhagias.

Conclusion. Selective uterine artery embolization is a safe and effective therapeutic option for uterine AVMs, allowing hemorrhage control and preservation of reproductive potential. A significant postprocedural reduction in vascular flow is typically observed, and in persistent cases, up to five re-embolization procedures may be performed with favorable outcomes. This minimally invasive approach enabled successful conservative management of uterine arteriovenous malformations.

Intestinal obstruction as the initial manifestation of primary intestinal malignant melanoma. Diagnostic challenges and multidisciplinary management

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Introduction. Intestinal malignant melanoma is an exceptionally rare neoplasm, with differentiation between primary and metastatic forms often being difficult. Presentation as intestinal obstruction is uncommon and poses significant diagnostic and therapeutic challenges.

Methods. We report the case of a 35-year-old male admitted with intestinal obstruction initially suspected to be caused by a jejunal lymphoma. Abdominal CT revealed a large jejunal mass with locoregional lymphadenopathy and distant metastases.

Results. Emergency surgery was performed to relieve the obstruction, identifying a jejunal tumor with transmural invasion, perforation, and generalized peritonitis. Segmental resection and peritoneal lavage were carried out. Histopathology confirmed malignant melanoma (S100, SOX10, HMB-45 positive). Dermatologic and PET-CT evaluations revealed no cutaneous or mucosal primary lesion. The case was staged as IV, and combined immunotherapy (Nivolumab + Ipilimumab) was initiated with favorable early outcome.

Conclusion. This case underlines the rarity of intestinal melanoma presenting with bowel obstruction, the difficulty in distinguishing primary from metastatic disease, and the importance of multidisciplinary collaboration between surgery and oncology in managing such complex cases.

Functional reconstruction after oral cancer surgery: a case of tongue reconstruction using a buccinator-based myomucosal flap

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Introduction. Oral oncologic surgery aims not only for complete tumor excision but also for optimal functional rehabilitation. Local flaps play a crucial role in preserving tongue mobility, sensitivity, and speech outcomes.

Methods. We present the case of a 61-year-old patient with a history of oropharyngeal squamous cell carcinoma (cT2N2bM0) treated by radiochemotherapy in 2024, with good loco-regional control. At one-year follow-up, the patient developed a right level III lymph node enlargement. Clinical and imaging evaluation revealed a second primary tumor on the right lateral tongue. Surgical management included wide excision of the lingual lesion, bilateral selective neck dissection (levels I–III), and reconstruction of the tongue defect using an anterior buccinator-based myomucosal flap.

Results. The procedure was well tolerated, with favorable postoperative evolution. The flap ensured good coverage, preserved lingual sensitivity, and allowed satisfactory mobility, facilitating speech and swallowing recovery.

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Conclusion. Local myomucosal flaps represent a reliable reconstructive option in oral oncologic surgery, allowing functional restoration while maintaining oncologic safety. The buccinator-based flap offers excellent results for medium-sized tongue defects, balancing form and function.

Entangled beginnings: prenatal ultrasound diagnosis of amniotic band syndrome with anencephaly

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Introduction. Amniotic band syndrome (ABS) represents a rare, sporadic congenital disorder resulting from early rupture of the amniotic sac, leading to fibrous bands that can entangle fetal structures and cause a wide spectrum of deformities. Central nervous system anomalies, though uncommon in ABS, carry severe prognostic implications. Early prenatal detection through ultrasound is essential for accurate diagnosis, parental counseling, and pregnancy management.

Methods. We report a case of ABS diagnosed prenatally at 20 weeks of gestation. A detailed fetal anomaly scan using two-dimensional and three-dimensional ultrasonography revealed severe cranial vault defect consistent with anencephaly and multiple amniotic strands attached to the cephalic pole. No other major visceral anomalies were identified. Serial follow-up ultrasounds were performed to monitor fetal growth and viability.

Results. The pregnancy was complicated by intrauterine fetal demise at 34 weeks of gestation. Cesarean section was performed due to prior uterine surgery. The delivered stillborn fetus exhibited severe cephalic extremity malformations and evidence of fibrous amniotic adhesions involving the head, confirming the prenatal findings.

Conclusion. This case highlights the critical role of detailed prenatal ultrasonography in identifying atypical presentations of ABS and neural tube defects. Early and accurate diagnosis facilitates appropriate counseling regarding the poor prognosis and guides obstetric management. Recognition of ABS as an etiologic factor in anencephaly is essential to differentiate it from primary neural tube closure defects and to prevent unnecessary genetic concern in future pregnancies.

Recurrent loss of consciousness in the aftermath of a suicide attempt: a functional etiology hidden in plain sight

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Background. Intentional drug overdose remains a critical presentation in emergency medicine, often reflecting impulsivity, emotional dysregulation, and comorbid

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substance misuse. When recurrent loss of consciousness follows such an event, the diagnostic pathway typically prioritizes cardiogenic and neurogenic causes. Yet, when every test returns normal, the clinician faces a diagnostic paradox.

Methods. A 43-year-old woman was admitted following the voluntary ingestion of ten moxonidine (Physiotens) tablets combined with alcohol in a suicidal attempt. During prehospital management, she experienced recurrent syncopal episodes approximately every five minutes, each followed by transient confusion, temporospatial disorientation, perseverative speech, retrosternal pain radiating to the neck and left shoulder. Upon arrival, she was hemodynamically and respiratory stable.

Comprehensive investigations—ECG, cardiac biomarkers, echocardiography, cranial CT, chest radiography, and full laboratory and toxicology panels—revealed no abnormalities. Neurological examination showed no focal deficits, preserved cranial nerve function, and normal coordination. Despite exhaustive evaluation, no organic cause for the recurrent syncopal events could be identified. A complete somatic and psychiatric assessment was performed that revealed emotional lability, impulsivity, low frustration tolerance, and poor insight, consistent with an emotionally unstable (impulsive type) personality disorder and harmful alcohol use.

The episodes were therefore interpreted as psychogenic pseudosyncope, a functional condition that clinically mimics true syncope but occurs in the absence of hemodynamic or neurological changes. Such presentations challenge both diagnostic reasoning and interdisciplinary collaboration, as the clinical appearance of "collapse" masks an underlying psychological mechanism.

Conclusion. This case illustrates the complexity of recurrent transient loss of consciousness when cardiologic and neurologic findings are normal. According to ESC guidelines, psychogenic pseudosyncope should be considered in patients with normal diagnostic results but high psychosocial stress or personality pathology. The recognition of this functional etiology is essential—not only to prevent unnecessary investigations but also to redirect attention toward psychiatric care and suicide prevention, where the true urgency lies.

Comparative evaluation of back-wall and side-wall errors in non-living and live microsurgical training models during the EANS - Iuliu Hatieganu UMPh course

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Introduction. Technical errors such as back-wall and side-wall stitches are leading causes of anastomotic failure in microsurgery. The European Association of Neurosurgical Societies (EANS) microsurgical training course, organized at "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, provides a progressive curriculum starting with non-living chicken models followed by live rat vessels. This study aimed to compare performance on both models and evaluate whether non-living training offers comparable skill transfer to the live setting.

Methods. Residents and medical students performed end-to-end microvascular anastomoses during two sequential training sessions: one on chicken thigh arteries (non-living) and one on live rat femoral vessels. The presence of back-wall and side-

wall stitches was recorded for each attempt. Results were analyzed separately for each model and comparatively for participants (identified by unique alphanumeric codes) who completed both stages. All anastomoses were documented through high-resolution photographs and video recordings for post-course review and error verification.

Results. A total of 64 chicken and 29 rat anastomoses were evaluated. On chicken models, back-wall errors occurred in 25% and side-wall errors in 26.6% of cases. On rat vessels, back-wall errors increased to 41.4%, while side-wall errors decreased to 3.4%. Among 27 participants who completed both sessions, total error counts improved in 15%, remained stable in 55%, and worsened in 30%. The higher rate of back-wall stitches on live models likely reflects the additional technical challenge posed by pulsatile, fragile vessels under physiological conditions.

Conclusions. Training on non-living chicken models is highly effective for acquiring basic microvascular skills and identifying common side-wall errors. However, the transition to live rat models remains crucial for mastering vessel handling, flow control, and back-wall prevention under realistic tissue dynamics. The EANS–UMF Cluj-Napoca course, integrating both models with systematic photo-video documentation, offers a comprehensive, ethically balanced approach to developing microsurgical proficiency.

A single-institutional analysis of laparoscopic 3D radical cystectomy with intracorporeal urinary diversion

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Introduction. Robotic radical cystectomy has become the standard treatment for localized muscle-invasive bladder cancer, demonstrating clear benefits over the open approach through reduced intraoperative blood loss, lower morbidity and shorter hospitalization. However, in centers with limited access to robotic surgery, the laparoscopic approach remains a viable alternative, offering comparable results to robotic surgery. This study aims to evaluate the perioperative and postoperative outcomes of laparoscopic radical cystectomy (LRC) performed at our institution.

Methods. We prospectively identified 124 patients who underwent LRC between 2017 and 2025 at our institution. The choice of urinary diversion was individualized based on patient age, comorbidities, and clinical tumor stage. Perioperative parameters included operative time, estimated blood loss (EBL), and intraoperative complications, while postoperative outcomes included transfusion rate, length of hospital stay (LOS), and early and late complications. Median follow-up was 12 months.

Results. The median operative time was 210 minutes in the cutaneous ureterostomy (CU) group, 360 minutes in the ileal conduit (IC) group, and 450 minutes in the neobladder (NB) group. Median EBL was 300 mL (IQR 200–450 mL), and 26 patients required perioperative transfusions. Two intraoperative complications occurred: one uretero-ileal anastomotic twist requiring reanastomosis and one accidental bilateral mono-J stent removal during stoma creation. Major complications occurred in 18.6% of CU patients, 12.9% of IC patients, and 9% of NB patients. The median LOS was 8 days (IQR 7–12). At 12 months, uretero-ileal strictures were observed in seven IC and one NB patient.

Conclusion. Laparoscopic radical cystectomy respects the principles of minimally invasive surgery and provides outcomes comparable to those achieved with the robotic approach. It represents a safe and effective alternative in centers where access to robotic surgery is limited.

Perioperative outcomes of 3D laparoscopic radical cystectomy with intracorporeal ileal conduit: a single-center experience

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Introduction. The ileal conduit remains the most commonly performed urinary diversion following radical cystectomy, offering lower rates of long-term complications and an overall better quality of life for patients. When performed through a fully intracorporeal minimally invasive approach, this technique can further enhance postoperative outcomes, particularly in patients with significant comorbidities. The aim of this study was to evaluate the outcomes of laparoscopic intracorporeal urinary diversion following radical cystectomy.

Methods. A total of 64 patients who underwent 3D laparoscopic radical cystectomy with intracorporeal ileal conduit reconstruction between January 2017 and February 2025 were included. For the ileal conduit, a 15-cm segment of ileum was isolated approximately 20 cm proximal to the ileocecal valve. Bowel isolation and anastomosis were performed using laparoscopic staplers in all cases. The left ureter was transposed to the right side, and ureteroileal anastomoses were constructed using the Bricker technique with 3-0 Vicryl sutures. Both ureters were catheterized with 7 Ch Mono-J stents.

Results. The median duration for intracorporeal urinary diversion was 180 minutes (IQR 90–210). Most postoperative complications were minor; however, major complications occurred in 7 patients (12.9%), with two requiring surgical reintervention—one for urinary fistula and one for postoperative bleeding. Ureteral stents were typically removed 4 weeks after surgery. At a median follow-up of 12 months, uretero-ileal stenosis was identified in 13.7% of patients (unilateral in 5 cases and bilateral in 2 cases).

Conclusion. The 3D laparoscopic approach is feasible for intracorporeal urinary diversions, ensuring complete minimally invasive approach in radical cystectomies, in centers access to Da Vinci system is limited. Once the learning curve is overcome, performing a laparoscopic intracorporeal urinary diversion offers significant advantages to the patient with a less economic burden.

Laparoscopic 3D radical cystoprostatectomy with ileal conduit diversion for muscle-invasive bladder cancer: a case report

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Introduction. Radical cystectomy with urinary diversion remains the standard curative approach for muscle-invasive bladder cancer (MIBC) following neoadjuvant chemotherapy. The advent of three-dimensional (3D) laparoscopy has enhanced spatial perception and precision in complex pelvic procedures, reducing surgical trauma and improving recovery. We present the case of a 56-year-old male with muscle-invasive urothelial carcinoma showing squamous and sarcomatoid differentiation, treated by 3D laparoscopic radical cystoprostatectomy with bilateral pelvic lymphadenectomy and

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ileal conduit urinary diversion after systemic therapy.

Methods. The 56-year-old patient had a pT2G3 urothelial carcinoma with squamous and sarcomatoid features, diagnosed after transurethral resection of the bladder tumor. Staging revealed no distant metastases on FDG PET-CT. The multidisciplinary team recommended radical cystoprostatectomy. Surgery was performed laparoscopically in 3D mode (non–nerve-sparing) with extended bilateral lymphadenectomy and ileal conduit diversion under general anesthesia.

Results. A transperitoneal five-port approach was used. Both ureters were dissected and sectioned near the bladder. The posterior plane was developed via the Douglas pouch with identification of seminal vesicles and preservation of Denonvilliers' fascia. Lateral and anterior dissections were completed with clipping of vesical and prostatic pedicles, division of the dorsal venous complex, and urethral sectioning. The specimen, including bladder, prostate, and lymph nodes, was extracted through a left iliac incision. A 15 cm ileal segment, isolated 20 cm from the ileocecal valve, served as the conduit. Intestinal continuity was restored by mechanical ileoileal anastomosis; ureteroileal anastomoses were performed with 4-0 Vicryl over mono-J stents. Operative time was 360 minutes with minimal blood loss; one unit of packed red cells was transfused on postoperative day 1. Recovery was uneventful, with early bowel function and clear urine output. Final pathology: invasive urothelial carcinoma G3 with squamous and sarcomatoid differentiation, pT3aN1MxL1V1PN1R0.

Conclusion. Laparoscopic 3D radical cystectomy with ileal conduit diversion is a safe, effective, and oncologically sound technique for MIBC, providing precise dissection and favorable postoperative recovery even in complex cases.

Biliary drainage for the preoperative management of periampullary neoplasms: a retrospective cohort study

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Introduction. Preoperative biliary drainage (PBD) in patients with periampullaryneoplasms remains a debated topic, with various techniques available andconflicting evidence regarding their impact on postoperative outcomes. This study aimedto assess, in a high-volume pancreatic surgery center, whether the choice among endoscopic,surgical, or no preoperative biliary drainage influences postprocedural and postoperativecomplication rates.

Methods. A retrospective cohort study was conducted at the Surgical Department of the "Octavian Fodor" Regional Institute of Gastroenterologyand Hepatology in Cluj-Napoca, Romania, between January 2017 and May 2023. Atotal of 655 patients undergoing pancreaticoduodenectomy or total pancreatectomy forresectable periampullary tumors were divided into three groups: no PBD, endoscopic PBD,and surgical PBD. Clinical, procedural, and postoperative variables were collected andstatistically analyzed.

Results. Endoscopic drainage was associated with a significantlyhigher rate of postoperative intra-abdominal abscesses, postoperative pancreatic fistula(POPF), and pancreaticojejunostomy fistula compared to surgical drainage and no PBD.Patients in the endoscopic group also exhibited significantly higher rates of positive bilecultures, particularly with pluribacterial populations. Procedure-related complications,such as

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pancreatitis and cholangitis, were significantly lower in the surgical drainage group.No significant differences were found among groups regarding postoperative hospitalstay, relaparotomy rates, or 90-day mortality.

Conclusion. Surgical biliary drainage was associated with lower perioperative morbidity compared to endoscopic drainage. While endoscopic drainage remains the most commonly used approach, surgical drainage may offer a safer alternative in selected patients. Prospective randomized controlled trials arewarranted to validate these findings.

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Melanoma of the hard palate – a small tumor with extensive lymphatic spread - case report

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Introduction. Mucosal melanomas of the head and neck are rare, most originating from the sinonasal area (70%) followed by the oral cavity (20%). Melanoma originating from the hard palate mucosa is exceptionally rare, accounting for approximately 0.2% to 8.0% of all melanoma cases and 0.5% of all oral cancers. Early symptoms are often subtle or go unnoticed, leading to delayed diagnosis and a worsening prognosis.

Imaging Findings and Procedure Details. We present the case of a 62-year-old male who developed progressive cervical swelling without additional symptoms, including weight loss, night sweats, dysphonia, dysphagia, or dyspnea.

Initial MRI revealed multiple right cervical nodal conglomerates extending to the supraclavicular region, characterized by marked heterogeneity with areas of necrosis and contrast enhancement and noticeable for the presence of spontaneously hyperintense signal on T1-weighted images. Signs of extracapsular extension were also noted.

The patient underwent three core biopsies of these nodal conglomerates, all of which were inconclusive, identifing only necrotic tissue. A follow-up MRI detected a 15 mm spontaneously T1 hyperintense mucosal lesion in the right hard palate without bone invasion or evidence of perineural spread along the palatine nerves. Clinical examination revealed subtle dark pigmentation at the corresponding mucosal site. A biopsy of the

lesion confirmed the diagnosis of malignant melanoma (BRAF negative) and a US-guided fine-needle aspiration cytology (FNAC), confirmed metastatic melanoma.

Spontaneously hyperintense lymph node metastases are rare and suggest the presence of fat, high protein content, or paramagnetic components. In the head and neck, its presence suggests nodal metastases from papillary thyroid cancer, mucinous adenocarcinoma, or melanoma (melanotic). It may also result from hemorrhage secondary to prior interventions (FNAC or biopsy).

Unfortunately, after surgical resection and radiation therapy, the patient experienced rapid disease progression, developing lung metastases and local progression with involvement of the nasopharyngeal mucosa.

Recognizing the imaging hallmarks of metastatic melanoma in the head and neck region is essential for timely intervention and improved patient outcomes.

Conclusion. Primary oral mucosal melanoma remains a significant diagnostic challenge. The presence of spontaneous hyperintense components both on lymph node metastasis and primary lesion on MR imaging may suggest this diagnosis.

Radiotherapy - surgery time interval influence immediate postoperative outcome in rectal cancer patients

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Introduction. Preoperative radiotherapy has been long time accepted as a preoperative standard of care in patients with rectal cancer. However there is still a debate related to the optimal time interval between radiotherapy and surgery with more recent arguments for a longer period of time, namely 10 to 12 weeks. The aim of this study was to evaluate in a prospective manner the immediate postoperative outcome in patients operated at least 10 weeks after radiotherapy.

Methods. Twenty five patients have been included, 15 male and 10 female with a mean age of 68 years (48-78), The mean BMI was 27 (24-34). Postradiotherapy the mean tumor stage was yT2 N1 (T1-T3, N0-N2) All patients underwent a complete biologic and MRI preoperative evaluation. Fiftheen patients underwent laparoscopic rectal resection while 10 were resected through a laparotomy. In all patients there was a similar standrdized procedure. We evaluate the length of postoperative hospital stay, the ICU stay and postoperative complications according to Clavien Dindo classification.

Results. Intraoperative local inflammation and adhesions were evaluated by the surgeons with a score from 1 (no morphological changes) to 4 (severe adhesions, intens einflammatory tisues). The mean score was 2 (1-3). Postoperative therapy and evaluation was similar to all patients There were no postoperative deaths. Thea mean length of hospital stay was 12 days (6-24) with a significant longer period for patients with laparotomy 16 (9-24). There were 2 postoperative type I leakages, managed conservatively, and 12 other complications classified as Clavien-Dindo 1 and 2. All patients were discharged at home , with a good physical performance score.

Conclusion. A period of at least 10 weeks between radiotherapy and surgery in patients with rectal cancer insures a favourable outcome of these patients independently of their age, BMI or preoperative tumor stage.

New techniques in macular hole surgery - vitrectomy and inverted flap

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Introduction. Macular hole is an important cause for vision loss in elderly. Conventional treatment involves posterior vitrectomy with complete peeling of the internal limiting membrane from the retinal surface. This may result in incomplete or low surgical success, either anatomically, or functionally. The purpose of the study is the evaluation of a new surgical technique for macular hole closure.

Methods. This is a retrospective observational study approved by the Ethics committee of UMF Cluj. 32 eyes were operated in 2024-2025 for full thickness macular hole, with 23G posterior vitrectomy and inverted flap (internal limiting membrane), followed by expandable gas injection (C2F6). Minimum follow-up was 6 months. Anatomical success was assessed with retinal examination (including ocular coherence tomography - OCT) and functional success was assessed with visual acuity measurements and microperimetry (for macular sensitivity at 8 and 20 degrees).

Results. The patients were mostly females (59%), with mean age 69 years. Interventions were performed on macular holes, stages 2 (41%), 3 (50%), and 4 (9%). Most were holes with large diameter, on average the basal diameter BD was 834 ± 356 µm.

Most of the macular holes were successfully closed (>90%). Our personal data (unpublished) suggested a closure rate of less than 50% with the conventional surgery. This would mark a dramatically increase in anatomical closure rate. Visual acuity was better in most patients (best corrected visual acuity increased from 0.9LogMar to 0.68LogMar ($p<0.001$)). At the end of the follow-up, most of the patients had the external limiting membrane (measured on OCT) healed (1/3 totally restored, and another 1/3 partially restored) and almost 50% had the retinal ellipsoid zone restored, at least in part. Preoperative OCT biomarkers for postoperative visual improvement were detected: basal diameter, minimum linear diameter, and traction hole index. Postoperative OCT biomarkers for visual improvement (both visual acuity and microperimetry, in the central 8 degrees) were the status of the ellipsoid zone and the external limiting membrane.

Conclusion. Macular hole surgery with posterior vitrectomy and inverted flap had a high rate of success, both anatomically (closure rate more than 90%) and functionally (improved visual acuity and macular sensitivity). OCT biomarkers were identified for the prediction of functional outcome.

Extent of resection and recurrence in craniopharyngiomas: a meta-analysis of the literature and retrospective review of a single-center experience

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Introduction. Craniopharyngiomas are benign epithelial tumors of the sellar region, presenting a bimodal age distribution and arising from Rathke's pouch remnants. Their management remains controversial: while gross total resection (GTR) offers

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curative potential, it carries a higher risk of hypothalamic and endocrine morbidity. Conversely, subtotal resection (STR) minimizes surgical morbidity but is associated with a higher recurrence rate, which can be mitigated by postoperative radiotherapy (RT). The present meta-analysis and single-center retrospective review aim to evaluate how the extent of resection influences recurrence rates and long-term outcomes in patients with craniopharyngioma.

Methods. A systematic literature search (2000–2025) identified 35 retrospective studies meeting inclusion criteria: ≥20 patients, defined extent of resection, and ≥24 months of follow-up. Data on recurrence, follow-up, and adjuvant RT were extracted. Heterogeneity was assessed using I^2 statistics, and relative risk (RR) of recurrence was calculated for GTR versus STR. Additionally, a retrospective review of 97 cases treated at our neurosurgical center between 2000–2025 was performed, analyzing surgical approach, resection rate, and recurrence patterns.

Results. The meta-analysis included 3,392 patients (62% GTR, 38% STR). Recurrence rates were 17% for GTR, 67% for STR, and 24% for STR + RT. Heterogeneity was low for GTR (I^2 = 24%) and substantial for STR (I^2 = 53%). The pooled risk ratio favored GTR (RR ≈ 0.22, I^2 = 0%). Our institutional data mirrored these findings, with 15% recurrence after GTR and 72% after STR at a median follow-up of 6.5 years.

Conclusion. Gross total resection remains the most effective strategy for minimizing recurrence in craniopharyngiomas. When total removal is not feasible due to hypothalamic, visual loss or other deficits regarding the area of resection, subtotal resection followed by radiotherapy offers comparable tumor control with reduced morbidity. Long-term outcomes depend on careful surgical planning and multidisciplinary management.

Extramedullary plasmacytoma of the nasal cavity – a case report

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Introduction. Extramedullary plasmacytoma (EMP) of the nasal cavity is a rare plasma cell neoplasm characterised by monoclonal proliferation of plasma cells in soft tissue areas outside the bone marrow, with no evidence of systemic multiple myeloma. This malignancy primarily affects the head and neck region, especially the sinonasal tract.

Methods. A 67-year-old male patient presented with unilateral nasal obstruction, mucopurulent rhinorrhea, and proptosis. Nasal endoscopy revealed a mass filling the left nasal cavity, extending into the nasopharynx. The patient was scheduled for surgery, but returned to our department one week later with an acute dacryocystitis. CT and MRI showed tumour extension into the left orbit and indicated an extremely well-vascularised tumour. Twenty-four hours before surgery, a selective embolisation was performed to decrease intraoperative bleeding.

Results. A successful endoscopic resection of the tumour was performed with minimal bleeding. Destruction of the lamina papyracea was noticed during surgery.

The histopathology report revealed an extra-medullary plasmacytoma. Multiple myeloma was ruled out. The patient was referred to the Haematology Department for adjuvant treatment.

Conclusions. EMP should be considered in the differential diagnosis of nasal cavity tumours. A definitive diagnosis involves detailed evaluation, including histopathological confirmation by immunohistochemistry, as well as systematic exclusion of multiple myeloma.

Medial congruent vs. medial pivot: comparing robotic and conventional functional alignment in TKA

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Introduction. Total knee arthroplasty (TKA) remains the gold standard for advanced osteoarthritis. Robotic-assisted TKA (rTKA) systems like ROSA aim to enhance precision, optimize implant placement, and improve outcomes. This study compares functionally aligned rTKA using the ROSA system with conventional kinematically aligned medial pivot TKA regarding implant positioning, function, and satisfaction.

Methods. We conducted a prospective multicenter trial of patients with advanced osteoarthritis undergoing TKA, treated with either ROSA Zimmer Persona MC (robotic, functional alignment) or MicroPort Evolution Medial Pivot (conventional, kinematic alignment). All procedures were performed by a single high-volume knee surgeon. Independent observers evaluated radiographic, clinical, and satisfaction outcomes. Primary endpoints included polyethylene insert thickness, alignment outliers (>2° from the mechanical axis), and patient-reported scores (KSS, FJS-12) preoperatively and at 6 months, under full ethical and GDPR compliance.

Results. Polyethylene thickness did not differ significantly between groups. The robotic system achieved greater precision and fewer alignment outliers, though experienced manual alignment also maintained low deviation. Both groups showed comparable improvements in function and satisfaction. Medial pivot implants yielded slightly higher FJS-12 scores, suggesting better joint awareness, while robotic cases achieved marginally greater range of motion. No significant differences were observed in radiographic findings or early complications at 6 months.

Conclusions. Both functionally aligned robotic and conventional kinematic TKA achieved excellent short-term outcomes. Robotic assistance improved surgical precision and range of motion, whereas conventional medial pivot TKA offered slightly higher patient-reported satisfaction and joint awareness.

PHARMACY

Tracking inflammation in long-COVID: a non-invasive device for cytokine detection versus ELISA

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Introduction. Long COVID is a multisystem condition that persists after SARS-CoV-2 infection and is difficult to diagnose due to its non-specific symptoms. Elevated levels of IL-6 and TNF-α reflect ongoing inflammation, making them useful biomarkers for its detection. The aim of this work was to develop a novel method for the simultaneous detection of IL-6 and TNF-α and to apply it to the analysis of real saliva and sweat samples.

Methods. The platform consisted in a screen-printed working electrode, functionalized with gold and platinum nanostructures and with two distinct aptamers, labelled with different redox probes: ferrocene and methylene blue. Saliva and sweat samples were collected from long COVID patients (n=10) and healthy controls (n=5) and were tested using the developed aptasensor and ELISA, the gold standard method.

Results. The optimized platform was able to detect the two cytokines in a range from 5–5000 pg/mL, with a limit of detection of 1.6 pg/mL. Saliva and sweat samples were analyzed with no pretreatment using the aptasensor. The results were compared to those obtained using the standard ELISA method. ANOVA regression showed strong significance with consistent parallelism and linearity (TNF-α: $p = 0.965$; IL-6: $p = 0.999$). All results were within confidence intervals, confirming accurate system performance. Bland–Altman plots demonstrated a strong agreement between the aptasensor and the ELISA control.

Conclusion. An electrochemical aptasensor for the dual detection of IL-6 and TNF-α was successfully developed and applied to the analysis of raw saliva and sweat samples, demonstrating good agreement with the standard ELISA control method.

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Thermoreducible shape memory polymer decorated with gold nanoparticles as SERS substrate for glucose detection

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Introduction. Our study presents a simple and rapid fabrication method of a surface-enhanced Raman spectroscopy (SERS) substrate for glucose detection, using thermoreducible shape memory polymer disks decorated with gold nanostars (AuNSs) for Raman signal enhancement. AuNSs were functionalized with 4-mercaptophenylboronic acid (4-MPBA) used as Raman probe molecule and selective glucose receptor.

Methods. AuNSs were obtained through a wet chemical synthesis method using tetrachloroauric acid, silver nitrate and ascorbic acid as reducing agent. A certain

volume of concentrated AuNSs was drop-casted on shape memory polymer disks and heat treated on a hot plate until full contraction, to generate a compact and solid AuNSs layer. The SERS substrate was functionalized with 4-MPBA and exposed to glucose at different physiologically relevant concentrations. The effect of various interferences on the SERS signal was tested, as well as the reproducibility and stability of the SERS signal over time. SERS data was collected using a Raman spectrometer.

Results. Thermal reduction of the shape memory polymer reduced the distance between AuNSs, creating numerous new hot spots, resulting in an enhanced Raman signal of the probe molecule. SERS substrate demonstrated quantification capabilities in glucose detection, revealing a linear relationship between clinically relevant glucose concentrations and monitored analytical signal. The substrate depicted high signal reproducibility and selectivity for the analyte of interest and quantification performance up to five days after fabrication.

Conclusions. The study demonstrated the potential use of modified shape memory polymers as SERS substrates for selective glucose detection at clinically relevant concentrations. The rapid obtained, cost-effective and reproducible SERS substrates, prone to mass production, promise integration into a novel SERS based sensor for blood sugar levels monitoring.

Prehistoric plants - geological past and biological present

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Over hundreds of millions of years, certain plant species have managed to survive major extinctions and climatic changes, retaining traits similar to their prehistoric ancestors. The identification of ancient plants involves paleoethnobotanical, isotopic, genetic, and taxonomic investigations, among others. The oldest living plants in the world, which existed millions of years ago, include: ferns (Pteridophyta, 360 million years), lycopsids (Lycopodiophyta, 410 million years), cycads (300 million years), Magnolia species (95–130 million years), Equisetum spp., Ephedra spp., Piper nigrum, Wollemia nobilis, Welwitschia mirabilis, Ginkgo biloba, Andryala laevitomentosa, and others. Some of these plants are used in medicine, nutrition, and industry, representing a living bridge between the planet's biological past and the human present. Thus, Ginkgo biloba is one of the oldest medicinal plants in the world, a key species in traditional Chinese medicine, with its extracts being primary ingredients in numerous pharmaceutical preparations. Ephedra, another ancient genus, documented from the Early Cretaceous period, offers historical insights into the evolution, taxonomy, and biogeography of the genus, its age estimated at 120–125 million years. In conclusion, ancient plants form a living connection between the distant past and the present, representing valuable current resources not only from a scientific standpoint but also from ecological, medical, cosmetic, nutritional, and cultural perspectives.

Solid phase synthesis of linear and cyclic peptides

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Introduction. Peptide synthesis has gained significant development in the pharmaceutical field and represents an important tool in the creation of new peptide drug candidates with improved functions. Short peptides are most commonly obtained by solid phase peptide synthesis (SPPS) which has numerous advantages compared to solution-phase procedures in terms of efficiency and yield. SPPS is based on repetitive processes requiring covalent attachment of a protected amino acid to solid support, deprotecting the functional group involved in forming the peptide bond, followed by coupling the next amino acid that has been previously activated.

Peptide structures can be modified to increase their metabolic stability, binding affinity and selectivity in interaction with pharmacological targets. Cyclic peptides represent promising candidates for therapeutic and diagnostic applications due to their exceptional stability, bioavailability and binding specificity.

The aim of this study was to develop both a linear and a cyclic peptide with potential applications in cancer diagnosis and therapy.

Methods. SPPS was applied by Fmoc/t-Bu strategy, using 2-chlorotrityl chloride resin. The peptide cyclisation was investigated on solid support and in solution, exploring the oxidative cyclisation through disulfide bridges between terminal cysteine units. The obtained peptides were analyzed by HPLC-MS.

Results. The optimal reaction conditions were established for both the solid-phase coupling and the oxidative cyclisation in solution. Positive electrospray ionization mass spectrometry (ESI-MS) analysis detected the peptides in their protonated form, as single charged ion [M+H]+ and doubly charged ion [M+2H]2+.

Conclusion. Both linear and cyclic peptides with potential applications in cancer diagnosis and therapy were obtained by SPPS followed by cyclisation in solution. ESI-MS analysis confirmed the structures of the synthesised peptides.

Biomimetic electrochemical sensor for antibiotic detection

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Introduction. Antibiotics represent a very important pharmaceutical class, being widely used for the prevention and the treatment of bacterial infections in humans and veterinary medicine. Unfortunately, their misuse and overuse can lead to side effects, allergies, the spread of the antimicrobial resistance and contamination of the environment. This highlights the importance of antibiotics detection in pharmaceutical formulations, in biological samples (to ensure the proper treatment) and in environmental samples. Cefuroxime is a second-generation cephalosporin, with a broad-spectrum antimicrobial activity indicated in the therapy of a wide range of severe infections. The purpose of this study was to develop a novel electrochemical sensor based on molecularly imprinted polymer (MIP) for the selective and sensitive detection of cefuroxime.

Methods. The MIP film was prepared by electro-polymerization of 3,4-etylenedioxytiophene (EDOT), as a functional monomer, and cefuroxime, as the

template, in the presence of gold nanoparticles (AuNPs) and titanium carbide MXene on a screen-printed carbon electrode modified with multiwalled carbon nanotubes (MWCNT-SPE). The developed MIP was characterized by scanning electron microscopy (SEM) and by electrochemical techniques.

Results. Factors influencing the sensor response, such as the concentration of monomer and template, the number of polymerization cycles, the template removal and the incubation, were optimized. The developed sensor presents a low detection limit of 10-9 mol L-1 and could achieve linearity against logarithm of concentration over a wide range of concentration (10-9 mol L-1 to 10-4 mol L-1). Furthermore, the sensor proved to be selective, and it was successfully applied to detection of cefuroxime from human serum and sea water, with good recoveries.

Conclusion. A sensitive and selective MIP-based sensor was developed for the detection of cefuroxime, using EDOT as monomer, in the presence of AuNPs and titanium carbide MXene on MWCNT-SPE. The sensor was optimized and fully characterized. The MIP-based electrochemical sensor was successfully applied to real samples analysis.

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Evaluation of the phytochemical profile and biological potential of extracts obtained from *Aronia melanocarpa* using various mixtures of natural deep eutectic solvents

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Introduction. Aronia melanocarpa fruits (black chokeberry, Rosaceae family) are renowned for their nutritional value, possessing a rich profile of bioactive compounds with antioxidant, anti-inflammatory, cardioprotective, and antidiabetic properties. The aim of this study was to optimize the extraction of these compounds using „green" solvents and to evaluate the resulting phytochemical composition using HPLC-MS/MS.

Methods. For the extraction, Natural Deep Eutectic Solvents (NaDES) were utilized, formulated with choline chloride as the hydrogen bond acceptor (HBA) and lactic acid, glycerol, or D-fructose as hydrogen bond donors (HBDs). A D-optimal experimental design (5 factors, 3 levels) was applied, resulting in 31 experiments to determine the most effective solvent mixture.

Results. HPLC-MS/MS analysis of the extracts confirmed the presence of 19 distinct bioactive compounds. The D-optimal design identified the NaDES mixture composed of choline chloride and lactic acid as the most effective extraction solvent. This specific solvent yielded the highest concentrations of several bioactive compounds, including hyperoside, isoquercitrin, and various cyanidins. Significant concentrations of major phytochemicals were quantified, including cyanidin-3-O-

galactoside (199.221 µg/mL), chlorogenic acid (175.984 µg/mL), protocatechuic acid (45.598 µg/mL), isoquercitrin (22.892 µg/mL), and procyanidin C1 (6.759 µg/mL).

Conclusion. These findings validate the use of NaDES as a „green," sustainable, and highly effective alternative to conventional solvents for the recovery of bioactive compounds from Aronia melanocarpa fruits.

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Aptamer selection using real-time quantitative PCR assisted SELEX technology for targeted therapy of hepatocellular carcinoma

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Introduction. Despite advances in screening and therapeutic strategies, hepatocellular carcinoma (HCC) is predominantly diagnosed at advanced stages and relies mainly on systemic therapy. Developing effective therapies for HCC remains challenging due to limited drug penetration, chemoresistance and toxicity to healthy cells. Aptamer-based nanotechnology represents a promising strategy for targeted drug delivery, combining the pharmacokinetic advantages of nanotherapeutics with the high specificity of aptamers [1]. This study presents the selection and characterization of novel DNA aptamers targeting glypican-3 (GPC3), a tumor surface biomarker of HCC, using magnetic beads (MBs)-based SELEX.

Methods. Recombinant GPC3 was immobilized onto MBs via various conjugation chemistries and SELEX parameters were optimized to mimic physiological conditions. Selection progress was monitored by real-time quantitative PCR (qPCR), melting curve analysis and enrichment assay. The enriched DNA pool was sequenced for primary structure determination and aptamer affinities were assessed by isothermal titration calorimetry.

Results. Distinct aptamer sequences with high affinity for GPC3 were successfully isolated. Integration of qPCR in the SELEX workflow enabled real-time monitoring of enrichment and minimized primer-dimer formation. Among the identified sequences, AP1F and AP4G exhibited nanomolar affinities, showing improved performance compared with with the only previously reported GPC3-binding aptamer.

Conclusions. The obtained aptamers will be further investigated for the development of MBs-based targeted delivery systems incorporating tyrosine kinase inhibitors.

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Electrochemical aptasensor for detecting Lipocalin-2 in liquid biopsy samples – an innovative approach for monitoring breast cancer patients

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Introduction. Breast cancer (BC) is the most diagnosed cancer and a leading cause of cancer-related death in women, with 2.3 million new cases in 2022. Early detection and monitoring are essential for better outcomes. Electrochemical biosensors provide high sensitivity, portability, and low costs, making them ideal for liquid biopsy applications. Lipocalin-2 (LCN2), a glycoprotein regulating iron metabolism, is overexpressed in BC and stimulates proliferation, metastasis, and ferroptosis resistance. This study presents a novel electrochemical aptasensor for LCN2 detection to support early BC diagnosis.

Methods. The sensor employs two DNA aptamers, capture and reporter - specific to LCN2. Gold electrodes were nanostructured through electrochemical oxidation and reduction to increase surface area and aptamer loading. Sensor fabrication and operation were analyzed using cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS), confirming each modification step and target binding.

Results. Nanostructuring enhanced electroactive surface area and charge transfer. CV and EIS confirmed aptamer immobilization and functionalization efficiency. Upon LCN2 binding, notable impedance increases indicated specific aptamer - protein interaction. The biosensor exhibited high sensitivity, wide dynamic range, and reproducibility, detecting LCN2 at clinically relevant levels with minimal nonspecific adsorption. The dual-aptamer design and nanoporous interface improved recognition and electron transfer efficiency.

Conclusion. The developed aptasensor allows rapid, sensitive, and specific detection of LCN2, showing strong potential for liquid biopsy and early BC diagnostics. Its simplicity, scalability, and analytical reliability make it a promising tool for point-of-care and clinical applications.

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Novel antimicrobial Thiazolyl-Methylthio-1,3,4-Thiadiazole hybrid compounds: synthesis, computational prediction, biological assessment, and 2D-QSAR study

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Introduction. The antimicrobial resistance represents an emerging threat against the global public health and is regarded as a silent pandemic. Contributing to the increasing demand for novel antimicrobial compounds, herein we presented the synthesis, *in silico* and *in vitro* antimicrobial evaluation, and the 2D-QSAR study of two series of twenty thiazolyl-methylthio-1,3,4-thiadiazole hybrid compounds (6a-j and 8a-j).

Methods. The compounds were obtained through a multi-step reaction process. The structures were confirmed through I R, M S, 1 H N MR a nd, 1 3C N MR spectral analysis. Computational studies consisted of molecular docking, molecular dynamics simulations, and druggability prediction. The compounds were evaluated *in vitro* through minimal inhibitory concentration (MIC) determinations. The 2D-QSAR study was conducted using the Free-Wilson model.

Results. All compounds showed antibacterial and antifungal activities. Compounds 8a-j showed similar or superior activity to ciprofloxacin (MICs = 15.62-125 µg/mL) against *Escherichia coli* ATCC 25922 (MIC = 15.62 µg/mL) and *Enterococcus faecalis* ATCC 29212 (MICs = 31.25-62.5 µg/mL). Compounds 6d-h showed superior activity to ciprofloxacin against Salmonella derby (MIC = 31.25 µg/mL) and *E. faecalis* (MIC = 62.5 µg/mL). The antifungal activity against Candida albicans ATCC 10231 was similar to fluconazole (MIC = 15.62 µg/mL) in most cases. The antifungal activity was less potent against Aspergillus brasiliensis ATCC 16404 (MICs = 31.25-62.5 µg/mL) compared to C. albicans. All compounds had good druggability properties. The scaffold had a significant contribution to the antimicrobial activity of these compounds.

Conclusion. Based on the results, twenty novel compounds with antimicrobial activity were developed. Overall, series 8a-j had better antibacterial activity, while series 6a-j had better antifungal activity.

Optimization of nanostructured lipid carriers loaded with herbal extracts for wound care - a Quality by Design approach

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Introduction. The aim of this study was to optimize the formulation of nanostructured lipid carriers (NLCs) loaded with a complex herbal extract (CHE) using the Quality by Design approach and Design of Experiments methodology.

Methods. A Fractional Factorial Design Resolution III (N = 11 experiments)

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was used for optimization. Formulation factors included: type of solid lipids (palmitic acid, cetearyl alcohol) and liquid lipids (caprylic/capric triglycerides, isopropyl myristate), solid lipid concentration (5–15%), Tween® 80 concentration (2–5%), and the effect of addition of Span® 85 (1%). The solid:liquid lipid ratio was 50:50, and CHE concentration was 20%. For characterization of NLCs were studied: particle size (PS), polydispersity index (PDI), zeta potential (ZP), encapsulation efficiency (EE), and occlusion factor (OF). The optimized formulation was further analyzed for pH, viscosity, texture, and results were compared with those of blank NLCs (without CHE) and a commercially available wound care product. The morphology of the optimized formulation was evaluated by electron microscopy. The *in vitro* release profile of CHE from the optimized NLCs was also evaluated.

Results. Cetearyl alcohol decreased PS and PDI while increasing OF; palmitic acid increased EE and reduced ZP. Caprylic/capric triglycerides decreased PS and increased EE. The optimized formulation contained 5% cetearyl alcohol, 5% caprylic/capric triglycerides, 5% Tween® 80, 1% Span® 85, 20% CHE, and water. The optimized formulation exhibited PS suitable for dermal penetration, low PDI, negative ZP, and high EE and OF. The pH, viscosity, and texture parameters of the optimized formulation, commercially available wound care product and blank formulation were comparable. Electron microscopy confirmed spherical and uniform NLCs. The optimized formulation showed a sustained release of CHE up to 72 h.

Conclusion. The optimized CHE-loaded NLCs showed adequate properties for wound care.

DENTAL MEDICINE

Screening of daytime and nocturnal bruxism based on self-assessment questionnaires in patients wearing aligners

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Introduction. Bruxism is a parafunctional activity involving teeth grinding or clenching during sleep or wakefulness, with multifactorial etiology. Early identification is essential to prevent damage to the stomatognathic system. This study aimed to assess the prevalence and self-reported symptoms of daytime and nocturnal bruxism in aligner-wearing patients compared to non-wearers using a standardized self-assessment questionnaire.

Methods. This observational, cross-sectional study collected data through an anonymous online questionnaire covering: (1) demographics, (2) bruxism history, (3) recent symptoms, and (4) related manifestations (TMJ pain, muscle tension, morning discomfort, joint sounds). Additional items addressed aligner use, treatment duration, and daily wear time. Statistical analysis included Chi-square and t-tests (significance set at $p < 0.05$).

Results. Out of 184 responses, 120 valid questionnaires were analyzed (60 aligner users, 60 controls), mostly females aged 21–30, and 43% reported a history of bruxism, and around half reported recent nocturnal symptoms. Aligner wearers were less likely to report a history of bruxism ($p = 0.0427$), but there was no significant association with recent nocturnal symptoms ($p = 0.9296$). A small subset (25%) of aligner wearers without prior bruxism reported new nocturnal symptoms after starting treatment. Significant associations were found between bruxism and TMJ pain ($p < 0.001$), morning clenching/discomfort ($p = 0.0015$), and temple pain ($p < 0.05$).

Conclusion. Aligner therapy was not associated with an increased prevalence of bruxism; however, a small proportion developed new nocturnal bruxism symptoms during treatment, suggesting a potential trigger effect in susceptible individuals.

Self-reported bruxism, whether previous or recent, was significantly associated with muscular and temporomandibular symptoms, underscoring the importance of early recognition of these manifestations in clinical evaluation.

Self-assessment questionnaires provide relevant information about patients' perception of their symptoms; however, they are not sufficient for a definitive diagnosis and should be correlated with clinical examinations and objective methods such as electromyography (EMG) or Polysomnography (PSG).

Metabolomics applications for diagnosing peri-implantitis

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Introduction. Peri-implantitis (PI) is a prevalent inflammatory condition affecting dental implants, leading to increased treatment costs, patient dissatisfaction, and potential implant failure. Novel biomarker-based approaches may contribute to early detection, thereby decreasing the burden of the disease. The aim of this review was to assess *in vivo* studies using metabolomics to identify the metabolic profiles and potential biomarkers of peri-implantitis.

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Methods. The protocol for this study was registered with PROSPERO (CRD42025634865). Five databases and grey literature sources (PubMed, Scopus, Web of Science, ProQuest, and Google Scholar) were searched using keywords related to metabolomics and peri-implantitis. Studies were selected by independent, inter-calibrated researchers. Data were extracted using predefined, custom forms. The risk of bias was assessed using the ROBINS-I tool.

Results. An electronic literature search retrieved 543 articles, of which five were selected. All studies were published within the last five years of the search. All but one study used untargeted metabolomics, and all studies identified metabolites associated with peri-implantitis or distinct metabolomic profiles of peri-implantitis. SCFAs and lysine metabolites were recurring in the results, confirming the findings of previous metabolomic studies on periodontal disease.

Conclusion. Metabolomics has not been widely used to study peri-implantitis. Evidence from existing studies confirms the findings of metabolomics studies on periodontitis. Several metabolites related to PI are associated with immune response, tissue degradation, and cellular energy pathways. Integrating -omics technologies into peri-implantitis diagnosis may facilitate biomarker discovery and improve early detection strategies.

New diagnostic tool for early tooth decay detection using Raman/ SERS spectroscopy. A preliminary study

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Introduction. Dental carriers represent the most widespread chronic infectious disease worldwide. Considering the major influence of oral cavity's condition on systemic homeostasis, the development of low-cost, non-invasive, painless, and highly specific diagnostic platforms becomes imperative to compensate for the numerous shortcomings of currently used diagnostic methods (X-ray imaging, DIAGNOdent, intraoral camera etc.). Thus, ultrasensitive spectroscopic techniques for the analysis of (bio)liquids may represent a promising solution for meeting the aforementioned criteria. In this study we have employed Surface-Enhanced Raman Spectroscopy (SERS) analysis of the salivary samples in order to investigate their molecular fingerprint pattern in tooth decay conditions with the aim of developing a rapid diagnosis method.

Methods. A total of 20 subjects aged between 18 and 25 years were included in the study. They were divided into four equal groups, as follows: the control group (composed of patients who, at the time of examination, showed no signs of odontoparodontal health impairment, i.e., with clinically healthy oral cavities); Group I (comprising patients with 1–5 tooth decays); Group II (comprising patients with 6–10 tooth decays); and Group III (comprising patients with more than 10 tooth decays). Saliva samples were collected under fasting conditions. For SERS analysis, 1 μL of saliva was deposited onto the solid plasmonic substrate. The analyte was allowed to dry at room temperature before spectra acquisition. SERS spectra were recorded using a Renishaw inVia Reflex confocal multi-laser Raman spectrometer (Renishaw™, Wotton-under-Edge, UK).

Results. The acquired SERS spectra revealed distinct tropism in the variations of the concentrations of certain molecules of interest, depending on the cariogenic

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context of the subjects' oral cavities. In the absence of carious processes, a molecular fingerprint characteristic of the homeostatic state of the oral cavity was observed. Under pathophysiological conditions, the morphology of the acquired SERS spectra differs substantially from the previous mentioned situation. Thiocyanate emerges as a relevant biomarker with retrospective and diagnostic value, reflecting past behaviors associated with current oral health status. Patients with poor dental health, characterized by a high number of carious lesions, show increased salivary thiocyanate activity compared to healthy individuals. Elevated thiocyanate levels in patients with apparently good oral health may indicate undetected pathology or an increased risk.

Conclusion. These findings support the integration of SERS salivary analysis as a complementary diagnostic and monitoring tool in dentistry. Further studies on larger cohorts are required to validate and refine the method.

Design and implementation of a digital dental imaging database – Dentihub

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This is an innovative proof of concept platform incorporating an imaging database used to store and integrate all types of digital dental images produced by various medical hardware in different formats (dicom, stl, bmp, jpeg). The aim was twofold: develop a secure-cloud imaging repository that integrates, stores, shares and processes medical imaging data and establish an inventory of image files acquired from CBCT devices, intraoral scanners and facial scanners in different formats (dicom, stl, bmp, jpeg) specific to digital dentistry. All images will be hosted on the platform, with the analysis of their characteristics: type, format, size and compatibility. The technical capacities of this infrastructure will also allow processes like merging, superimposition and advanced virtual planning using these different file types. Electronic archives of multiple imaging file types will be made compatible with the necessities of big-data management and cloud computing in order to cope with the calculations involved in 3D planning and AI data management. Image anonymization for a secure interface of the Digital Hub. The platform will ensure the compliance with ethical principles by using the Basic Application Level Confidentiality Profile, a conservative approach that hides all confidential data related to the following attributes: identity and demographics of the patient, identity of responsible parties or family members, identity of the staff and the organizations involved in the application or execution of the procedure, as well as dates and time of the procedure.

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Development of artificial intelligence tools for dental and maxillofacial imaging

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A large dataset of anonymized panoramic radiographs was manually annotated by multiple calibrated researchers to develop a deep learning algorithm for comprehensive dental condition identification. The annotated images included various dental situations such as dental treatments, carious lesions, apical periodontitis, root fragments, bone resorption, intra-bony lesions, and tooth impactions. Model development was performed using the TensorFlow library, employing deep neural network architectures. The workflow began with automated segmentation using U-Net, followed by the training of a deep learning classifier for diagnostic categorization (Yolo). Model performance was evaluated using both internal (leave-one-out cross-validation) and external validation datasets. Evaluation metrics included the DICE coefficient, sensitivity, precision, and F1-score.

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Validation of dental morphology analysis methods: from analog to digital algorithms

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Introduction. Determining dental morphology precisely is essential in the planning of prosthetic and orthodontic treatments. Comparing analog and digital measurement methods represents an important step toward standardizing morphometric evaluation.

Objective. This study aims to characterize the morphology of permanent human

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teeth by integrating and comparing three measurement methods: analog (electronic caliper), 3D digital (ExoCAD), and GIS-based geometric analysis (Geographic Information System) adapted for dental morphology, complemented by AI-assisted interpretation.

Methods. The study was conducted on dental models obtained from 10 patients included in the research, representing complete maxillary and mandibular arches. Each analyzed tooth underwent morphometric evaluation through a complex methodology. All measurements were performed under controlled conditions to minimize operator variability. (1) Analog measurements: the coronal dimensions were recorded directly on the models using a digital electronic caliper (precision 0.01 mm). The following parameters were measured: mesiodistal diameter (MD), buccolingual diameter (VO), clinical crown height, cusp slope length, sagittal occlusal ridge length. (2) Intraoral scanning: the dental arches of the patients included in the study were scanned using the Medit i700 intraoral scanner, and the 3D data were exported to ExoCAD software. The same dimensions were measured, the intercuspal angles were evaluated, and a three-dimensional assessment of crown morphology was performed. (3) GIS geometric analysis: the digital models were imported into AutoCAD. Using a GIS module, the cusp tips and the bases of dental fossae were identified. In addition, slopes were calculated using spatial geometric analysis methods.

Results. The results showed a consistent tendency for overestimation in the analog method compared to ExoCAD. For canines, the mean analog–digital differences were: mesiodistal diameter (MD) +0.57 mm, buccolingual (VO) −0.02 mm, crown height +0.39 mm. For incisors, the differences were: MD +0.10 mm, VO +0.52 mm, crown height +0.19 mm. For molars, MD showed +0.67 mm, and VO +0.04 mm.

The GIS software yielded dimensional values close to those of ExoCAD, within clinically realistic variation ranges (±0.2–0.3 mm), supporting the accuracy and repeatability of digital measurements. The analysis of cusp slopes in GIS showed stable functional values, with the canine cusp angle around 85° ±4°, the mesial slope inclination approximately 42° ±3°, and for molars, the cusp slope angle around 45° ±4°, with mesial and distal slopes between 37° and 40°.

Analog measurements were relevant for linear diameters; however, ExoCAD and GIS software revealed subtle differences in the three-dimensional geometry of dental crowns and allowed calculation of occlusal slopes, which are technically inaccessible through manual measurement.

Conclusion. ExoCAD and GIS software provide convergent and reproducible results, while analog measurement tends to slightly overestimate values. The integration of 3D modeling and GIS analysis enables a more accurate characterization of functional morphology, representing a clinically relevant approach for the design of prosthetic and aesthetic restorations and the establishment of occlusal guidance.

Modern orthodontic technologies: deep bite treatment with aligners

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Aligners represent a new, modern alternative for orthodontic treatment. Recent advancements in the field of biomaterials, along with innovations in aligner planning and manufacturing technology, digitalization, and artificial intelligence, have significantly contributed to the evolution and refinement of this therapeutic method.

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From the patient's perspective, the main advantages are comfort, superior esthetics, the ability to maintain good oral hygiene, and the absence of dietary restrictions. However, effective treatment requires a deep understanding of biomechanics, which is different from classical biomechanics (aligners only work on the „pull" principle), as complex tooth movements can be difficult to control and less predictable compared to those achieved with fixed appliances.

In cases of deep bite, correction is achieved thru posterior tooth extrusion, incisor intrusion, or a combination of these, but studies show limited accuracy of intrusion, approximately 40%. Although the use of new materials like SmartTrack and bite ramps has improved outcomes, the actual reduction in overcorrection often remains lower than digitally planned. For the treatment of these malocclusions, aligners do not work on their own, solely based on the elasticity of the material they are made from. Attachments and auxiliary elements are necessary to increase the treatment's effectiveness, as illustrated by the presented cases.

The integration of digital workflow and artificial intelligence in clinical planning (e.g., ClinCheck, 3Shape, Dexis) represents an important step toward treatment individualization, but software plans should be interpreted with caution. Clear aligners are an esthetic and comfortable solution, with increasingly promising clinical results, but success depends essentially on case selection, the clinician's experience, and a rigorous understanding of the system's biomechanical limitations.

The relevance of dental age in estimating skeletal maturity in patients with Class II malocclusion, in the context of orthodontic treatment

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Introduction. The aim of the study was to determine a correlation between skeletal age and dental age in patients with Class II malocclusion undergoing orthodontic treatment. Skeletal age assessment is usually performed by analyzing the degree of maturation of the cervical vertebrae on lateral cephalometric radiographs or by wrist radiography. The possibility of estimating skeletal age based on dental age, thus avoiding additional radiation exposure, could be a valuable diagnostic tool in orthodontic practice – especially for patients with Class II malocclusion, where the timing of orthodontic treatment plays a crucial role in achieving optimal therapeutic outcomes.

Methods. The study included 73 patients (31 boys, 42 girls, aged 6 to 15) with Class II malocclusion. Dental age was determined using the Demirjian method and the method of dental eruption chronology, based on panoramic radiographs. Skeletal age was estimated from lateral radiographs by evaluating the degree of maturation of the cervical vertebrae (CVM). Statistical analysis was performed using SPSS version 29 software, and statistical significance was set at $p < 0.05$.

Results. The mean chronological age was 12.03 ± 2.2 years, while the mean dental age was 13.28 ± 2.36 years using the Demirjian method, and 12.07 ± 2.48 years using the eruption chronology method. CVM stages 3 and 4 were the most frequently encountered. No significant differences were identified between sexes for chronological, dental, or skeletal age. Dental age was generally higher than chronological age, with the largest differences observed in CVM stages 3 and 4. Strong positive correlations were observed

between CVM and chronological age (r = 0.81), and between CVM and dental age (r = 0.72–0.78, p < 0.001), respectively.

These results confirm the existence of a correlation between dental, chronological, and skeletal age in patients with Class II malocclusion. Although limited by a small sample size, the study confirms that dental and skeletal parameters can effectively reflect a patient's biological development.

Conclusion. The study demonstrated a significant correlation between dental age, chronological age, and cervical vertebral maturation stages in patients with Class II malocclusion. Dental age has proven to be a valid indicator for estimating skeletal maturity, suggesting its potential as a complementary diagnostic tool in orthodontic evaluation – particularly valuable when aiming to optimize treatment timing without exposing patients to additional radiation.

Patient perspective on orthodontic treatment need

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Introduction. The concept of oral health-related quality of life (OHRQoL) captures the everyday impact of oral diseases across various dimensions, including functional limitations and emotional and social well-being. Malocclusion is a public health concern with a high prevalence across various populations, leading to physical and psychological implications that affect oral health-related quality of life. Social interactions are also influenced by malocclusion, affecting both how individuals are perceived by others and how they perceive themselves. Therefore, individuals' self-perception of their oral health plays an important role in understanding the impact of malocclusion on quality of life.

Methods. Data were collected using a questionnaire of 30 items, organized into four distinct sections: patient information, questions on self-perception, questions on functional limitations, questions on knowledge and awareness of the need for orthodontic treatment.

Results. The current study highlights the impact of gender and age on individuals' self-perception of malocclusion, while also examining the influence of urban versus rural residence on the acceptance of orthodontic treatment. Female participants and older individuals tended to perceive their dentition as more attractive. No significant differences were observed between urban and rural students in terms of their self-assessment of dental appearance.

Conclusion. There is an increasing trend of adult patients seeking orthodontic treatment, particularly those requiring oral rehabilitation. Facial aesthetics play a crucial role in personal attractiveness and self-esteem, profoundly influencing health, social interactions, emotional well-being, and professional relationships.

Condylar and mandibular kinematics in bruxism: insights from optical jaw tracking systems

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Introduction. Eccentric bruxism is a parafunctional activity involving tooth grinding, mainly during sleep. This study compared condylar parameters, sagittal condylar inclination (SCI) and Bennett angle (BA), respectively mandibular and condylar kinematics during functional and parafunctional movements in bruxers and non-bruxers. A secondary aim was to validate a digital method for quantifying eccentric bruxism using an optical jaw tracking system (Modjaw®).

Methods. Subjects diagnosed with eccentric bruxism according to validated clinical criteria formed the study group, while demographically matched non-bruxers served as controls. Each participant underwent two Modjaw® recordings to verify repeatability. Functional movements (anterior guidance, mastication) and simulated eccentric bruxism were recorded. SCI, BA, and the trajectories of the inferior interincisal point (IIP), left condyle (LC), and right condyle (RC) were analysed in frontal, sagittal, and horizontal planes to determine mastication and bruxism areas. Statistical tests evaluated repeatability, intergroup differences, and diagnostic accuracy.

Results. Forty participants (20 bruxers, 20 non-bruxers, 10F/10M) were included. The recordings showed high repeatability and reliability. No significant differences were found between groups for functional mandibular movements or condylar parameters. However, parafunctional movements in bruxers exhibited wider and more irregular trajectories than in controls. ROC analysis confirmed high diagnostic accuracy in differentiating bruxers from non-bruxers.

Conclusion. Mandibular and condylar kinematics during functional movements were similar between groups. The Modjaw® system proved to be a reliable digital tool for quantifying eccentric bruxism, supporting early detection before clinical signs occur.

Effects of occlusal splints on mandibular and condylar kinematics in patients diagnosed with temporomandibular disorders

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Introduction. Temporomandibular disorders (TMD) represent complex musculoskeletal conditions involving the temporomandibular joint (TMJ) and associated structures. Occlusal splints are widely used in TMD therapy, yet their effects on mandibular kinematics remain under discussion. This study aimed to evaluate the therapeutic effects of occlusal splint therapy on mandibular and condylar movements in patients with TMD, using an optical jaw tracking system (Modjaw®).

Methods. Patients diagnosed with TMD according to RDC/TMD criteria underwent occlusal splint therapy. A control group was included. Digital splints were fabricated using a full digital approach. Mandibular kinematics was recorded before (T0) and after therapy

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(T1) using the Modjaw® system. Displacements of the interincisal point and both condyles were recorded during mastication and maximal functional movements. Statistical analysis compared intra-group and inter-group differences.

Results. After occlusal splint therapy, patients with TMD showed significant improvements in mandibular function. The range of mandibular motion and masticatory areas increased, while movement patterns became more symmetrical. No significant changes were observed in the control group.

Conclusion. Occlusal splint therapy produced improvements in TMJ and mandibular kinematics during mastication and maximal movements, as observed with the Modjaw® system. A holistic approach to TMD management should address both pain relief and functional improvement of the TMJ kinematics.

An observational study on pain occurrence after root canal treatment: role of operator experience when using a bioceramic sealer

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Introduction. Post-operative pain (POP) is a frequent outcome following root canal treatment, influenced by both clinical and patient-related variables. This study aimed to assess the occurrence and severity of POP after root canal treatment with a bioceramic sealer, performed by operators with varying experience levels.

Methods. A total of 115 patients participated in this prospective observational study. Treatments were conducted by operators of two experience levels: postgraduate students (PGSs) and endodontic specialists (ESs). Procedures followed standardized protocols across two visits— one for instrumentation and one for obturation. The obturation was carried out using the continuous wave condensation technique and Total Fill Hi-Flow BC Sealer (TFHF). POP, chewing discomfort, and sleep disturbance were recorded at 24, 48, and 72 hours after both the instrumentation and obturation sessions using a numeric rating scale (NRS).

Results. POP was significantly higher after the instrumentation phase than after obturation ($p < 0.001$), with pain intensity decreasing progressively over time in both phases. No significant differences were found between PGS and ES groups in terms of POP, chewing discomfort, or sleep disturbance at any time point. Sealer extrusion had no significant effect on POP ($p > 0.05$).

Conclusion. Operator experience did not significantly affect POP when standardized clinical procedures were followed. The use of TFHF with the continuous wave condensation technique resulted in low levels of post-operative pain.

The impact of non-steroidal anti-inflammatory drugs on tooth movement during orthodontic treatment

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Introduction. Orthodontic pain represents one of the most prevalent adverse effects associated with orthodontic therapy. Analgesic agents commonly employed for its management include acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs exert their analgesic effect primarily through the inhibition of prostaglandin synthesis. However, this pharmacological action may concurrently impede orthodontic tooth movement (OTM) by altering the normal process of bone remodeling.

Methods. This review included experimental and clinical studies published between 2004 and 2024 that investigated the effects of either local or systemic administration of NSAIDs on OTM. An initial database search identified 152 articles. Following the rigorous application of predefined inclusion and exclusion criteria, a total of 22 studies met the eligibility requirements and were included in the final analysis.

Results. Clinical research indicates that aspirin and ketorolac can slow OTM, while ibuprofen's impact varies among studies. In contrast, tenoxicam, nabumetone, etoricoxib, and rofecoxib generally show no significant effect on OTM. Both clinical and experimental findings suggest that etoricoxib may be a particularly suitable option for managing orthodontic pain. It could serve as an alternative to acetaminophen, which does not interfere with OTM.

Conclusion. Effective pain control is crucial for ensuring patient comfort and adherence throughout orthodontic treatment. Nonetheless, the use of NSAIDs should be approached cautiously, as they may affect OTM by modifying bone remodeling mechanisms. Among the selective COX-2 inhibitors, etoricoxib stands out as a promising analgesic option with minimal impact on OTM when administered at clinically appropriate doses. Given the scarcity of high-quality human studies, additional research is needed to develop evidence-based recommendations for NSAID use in orthodontics.

NURSING AND HEALTH SCIENCES

Social determinants of overweight and unhealthy eating: results of a cross-sectional survey

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Introduction. Social determinants of health (SDOH) are economic and social conditions which shape the health inequities in a population and have been associated with health status. This cross-sectional survey investigated the SDOH in relation to overweight and obesity in a sample from Romanian population.

Methods. Individuals ≥18 years old completed an online questionnaire between March 2021 and February 2022. Self-declared data on age, weight, height, SDOH (gender, place of residence, employment status, and education), and eating behavior were collected. Food and beverage intake over the past 12 months was evaluated by a food frequency questionnaire. Based on these items and using the principal component analysis with orthogonal varimax rotation, 3 dietary patterns were identified (Prudent, Western, and Risky). SDOH predictors of overweight and unhealthy eating were identified by logistic and linear regression.

Results. Data of 432 adults aged 36.8±11.6 years were analyzed. Most of them were women, living in an urban area, having a university degree and employed. Mean BMI was 25.0±5.0 kg/m2 and the prevalence of overweight and obesity was 25.7% and 16.4%, respectively. Among the SDOH analyzed, male gender (OR=3.789, %CI:2.424-5.922, p<0.001) and employment status (OR=0.815, 95%CI:0.668-0.994, p=0.043) were predictors for overweight and obesity. Among dietary patterns, the Risky one, characterized by a high intake of processed meat, high fat food, and alcoholic beverages was associated with overweight and obesity (OR=1.594, 95%CI:1.214-2.094, p<0.001). SDOH predictor of this dietary pattern was male gender (regression coefficient β=0.382, p<0.001).

Conclusion. This survey identified among SDOHs the male gender and unemployment or retirement as risk factors for overweight and obesity. A risky behavior characterized by a high alcohol intake and unhealthy diet was identified among those with overweight and obesity also associated with male gender.

Adams-Oliver syndrome caused by DOCK6 mutations: a case report and multidisciplinary management considerations

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Introduction. Adams–Oliver syndrome is a rare genetic disorder characterized by aplasia cutis and transverse limb defects. DOCK6 mutations are associated with autosomal recessive forms of the disease. We report a Romanian pediatric case with a moderate phenotype.

Methods. Clinical, imaging, nutritional, and genetic data were evaluated. Sanger sequencing was used for the analysis of the DOCK6 gene. Paraclinical tests, cranial ultrasonography, echocardiography, nutritional assessments, and nursing care evaluations were performed according to standard clinical protocols.

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Results. The two-year-old patient presented with vertex aplasia cutis, alopecia, cutis marmorata, and a terminal defect of the right hand. Investigations revealed a patent foramen ovale and mild pulmonary stenosis. A slight delay in neurological development was also noted, with psychomotor abilities corresponding to those of an 18-month-old child. Genetic testing identified two heterozygous DOCK6 mutations (c.4106+2T>C and c.3063C>G). The patient consistently tracked at the 3rd percentile for weight, which raised concerns about nutritional adequacy and growth potential. Clinical evolution was favorable, with no major short-term complications. The maternal history of hereditary thrombophilia represents a distinctive feature of this case.

Conclusion. This case confirms the phenotypic heterogeneity of Adams–Oliver syndrome and the relevance of DOCK6 mutations. Growth status supports the need for early nutritional screening and personalized interventions. Multidisciplinary management, including the essential role of nursing in skin-lesion care and family education, is critical. Genetic counseling is required to assess the recurrence risk of Adams–Oliver syndrome in other family members. The findings highlight the need for further investigation into the potential connection between DOCK6 mutations and hereditary thrombophilia.

The impact of nutritional strategies on hormonal imbalances in polycystic ovary syndrome

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Introduction. Polycystic ovary syndrome (PCOS) is an endocrine-metabolic condition, of multifactorial etiology, characterized by hyperandrogenism, chronic anovulation, infertility, obesity, insulin resistance and polycystic ovaries .This heterogenous group of disorders represents the most frequent cause of infertility in female aged between 14 and 40 years. There are multiple causes including genetic predisposition, unbalanced diet, sedentary lifestyle, stress.

Treatment options vary depending on age, associated pathologies and the desire to conceive in the near future. These include a healthy lifestyle, medication, and possibly surgery (if the first two options are not successful).

Methods. Our study included 80 patients, aged between 14 and 40 years, diagnosed with polycystic ovary syndrome according to the Rotterdam criteria.

Of these, 30 patients were treated with birth control pills, 20 patients with metformin,15 patients with birth control pills and metformin, 10 patients were only recommended a balanced diet and healthy lifestyle, and 5 patients required surgery. Of the total number of patients, 55 followed strict nutritional recommendations, wich included a low glycemic index diet rich in vegetables, fruits, whole grains, high quality proteins, healthy fats, while avoiding sugary products and processed foods. In addition, supplements such as inositol, omega 3, and vitamin D were recommended.

Results. Patients who underwent drug treatment combined with nutritional recommendations showed improvement in symptoms, hormonal profile, and quality of life.

Conclusion. A balanced diet combined with regular exercise, stress management, and maintaining optimal body weight is the natural and effective solution for alleviating symptoms and improving the quality of life for women with polycystic ovary syndrome.

Feasibility of major interventions in emergency abdominal surgery

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Aim. It is known that emergency surgical procedures, in much weaker or not at all preoperatively prepared patients, present a higher rate of morbidity and mortality. For this reason, it is attempted not to carry out major interventions without prior preparation of the patient, even more so for oncological interventions or those in major hepato-bilio-pancreatic sphere that require multi-organ resections or vascular resections.

This paper aims to present several cases from both the oncological and benign pathologies that, due to the presentation in the surgery unit with complications of the underlying disease: hemorrhages or peritonitis, required emergency surgical intervention.

All these cases were solved surgically and followed up postoperatively for at least 1 year, depending on the pathology for which they presented themselves in the emergency unit.

Methods. 5 cases were analyzed; 2 cephalic duodenopancreatectomies performed for: D3 duodenal neoplasm invading the uncinate process and the transverse colon with vascular effraction at the level of the inferior pancreatico-duodenal trunk and a second case of a giant duodenal gyst with vascular effraction at the level of the middle colic artery; an aorto-duodenal fistula; a perforated superior rectal neoplasm with left ureteral invasion and generalized peritonitis; an acute gangrenous cholecystitis with cholecysto-choledoco-duodenal fistula, vascular effraction at the level of the right hepatic artery and abscess at the level of the hepatic hilum.

The patients were hospitalized through the emergency unit of the Clinic of Surgery III Cluj-Napoca and in all surgeries the main surgeon was the same, only the rest of the team was different.

Results. From the point of view of the rate of occurrence of postoperative morbidities and their complexity, they did not go beyond the limits cited by the literature in the case of scheduled interventions.

The only constant that changed was the length of hospitalization, which increased by approximately 3 days compared to that in the conditions of a scheduled intervention.

We note that the patients were followed up postoperatively through checkups at 1, 3, 6 months and one year. There was no postoperative mortality due to the interventions.

Conclusion. Major surgical interventions in the abdominal sphere performed in emergency are accompanied by an acceptable morbidity and mortality, slightly increased compared to those performed in a scheduled regime. However, such interventions must be performed in surgical services specialized in such operations and the surgical team must have increased experience in major abdominal surgeries, both from the point of view of multiorgan resections and vascular surgery.

Tumor cytoreduction plus HIPEC a feasible therapeutic method. How we can reduce postoperative morbidity and mortality

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Aim. Peritoneal carcinomatosis of different histopathological origin, from primary ones such as mesotheliomas, to those of colorectal, ovarian, appendicular, and gastric origin, has always been a therapeutic challenge, due to the advanced stage of the neoplastic

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disease.

Tumor cytoreduction (CR) and hyperthermic intraperitoneal chemotherapy (HIPEC) present postoperative complications related to both the need for extensive resections, cytotoxic effect of the chemotherapy and the effects of intraoperative hyperthermia. The importance of meticulous preoperative assessment of the patient, individualized therapy, multidisciplinary team of which experienced surgical team in anatomical dissections and vascular surgery are essential in terms of decreasing postoperative morbidity and mortality.

Methods. The present work aims to prospectively analyze immediate postoperative complications as well as postoperative mortality at 30 days, occurring in 37 patients, patients histopathological diagnosed with peritoneal carcinomatosis. The patients were hospitalized in the Surgery Clinic III Cluj-Napoca and the surgical interventions were performed by the same surgical team.

Results. From the point of view of the histopathological diagnosis of the primary tumor from the 37 patients with peritoneal carcinomatosis: 28 were of ovarian origin, 5 colorectal, 3 peritoneal pseudomyxomas of appendicular origin, 1 peritoneal pseudomyxoma of ovarian origin.

The presence of postoperative complications, according to the Clavien-Dindo classification, was 5.4% in grade I (gastric stasis, transient leukopenia), 2.7% in grade II (abundant ascites), 0% in grade III and IV and 2.7% in grade V (respiratory failure followed by death 15 days postoperatively). Postoperative mortality at 30 days was 2.7% (1 case).

Conclusion. Cytoreductive surgery followed by hyperthermic intraperitoneal chemotherapy is a complex procedure, accompanied by an acceptable rate of postoperative complications and death. The reduction in the occurrence rate of these complications being possible through a multidisciplinary perioperative management, a careful selection of patients and a surgical team with experience in major abdominal surgery, both from the point of view of dissections in anatomical planes, multiorgan resections and vascular surgery.

Medical rehabilitation in respiratory diseases

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Introduction. Respiratory rehabilitation is a medical intervention which implies the improvement of physical and psychological aspects of patients with respiratory diseases. The main goals of respiratory rehabilitation are to relieve respiratory symptoms, better effort tolerance and better quality of life.

Methods. Using PubMed and ResearchGate platform, we selected a number of 130 scientific articles regarding the physiopathology of respiratory diseases, effects of kinetotherapy and physiotherapy in different respiratory pathologies and the effects of natural physical factors on the respiratory system.

Results. Beside the classical treatment which consists of drug medication, kinetotherapy is widely used to improve the outcomes in patients with different types of respiratory diseases. But respiratory rehabilitation is not only about kinetotherapy. Massage, electrotherapy, hydrothermotherapy, balneotherapy and inhalations with mineral waters and plants infusions are all part of the respiratory rehabilitation.

Conclusion. A correct and complete plan of respiratory rehabilitation is built around the needs and the comorbidities of the patient and uses all the tools above.

Fatal outcomes after fall-related head injuries: a forensic evaluation of contributing factors

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Introduction. Fall-related cranio-cerebral injuries represent a major cause of accidental death, especially in elderly or vulnerable individuals, with significant forensic and clinical relevance. This study aimed to describe the main demographic, environmental, and clinical factors associated with fatal cranio-cerebral trauma resulting from accidental falls examined at the Cluj-Napoca Institute of Legal Medicine.

Methods. We performed a retrospective analysis of all autopsied fall-related cranio-cerebral injuries over a ten-year period. Only deaths due to accidental falls were included, regardless of the presence or absence of skull fractures. Demographic data, accident circumstances, medical interventions, and survival parameters were reviewed descriptively.

Results. Most victims were men of advanced age, often with comorbidities and alcohol involvement. Falls from height were associated with a higher risk of severe outcomes than same-level falls. Skull fractures, particularly those involving the base and frontal regions, were linked to reduced survival. The absence of cranial imaging or surgical intervention was associated with fatal evolution. Victims from rural areas experienced poorer outcomes, possibly reflecting delayed medical access.

Conclusion. Accidental fall-related cranio-cerebral injuries remain a major cause of preventable mortality. Early neuroimaging, timely surgical management, and improved emergency access in rural settings are essential to reduce lethality.

Spontaneous aortic dissections with fatal outcome: a forensic autopsy perspective

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Introduction. Aortic dissection is one of the most severe cardiovascular emergencies, often leading to sudden death and posing significant challenges in forensic diagnosis. This study aimed to outline the demographic, clinical, and morphological features of spontaneous aortic dissections with fatal outcome examined at the Cluj-Napoca Institute of Legal Medicine.

Methods. We conducted a retrospective observational analysis of all autopsied cases of non-traumatic aortic rupture over a ten-year period. Only spontaneous dissections confirmed at autopsy and unrelated to violent or iatrogenic causes were included. Demographic characteristics, anatomical location, associated cardiovascular lesions, medical interventions, and short-term survival were evaluated descriptively.

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Results. Most victims were men in their sixth decade of life, frequently presenting with severe atherosclerosis and, in nearly half of the cases, pre-existing aortic aneurysms. Cardiac tamponade was a common mechanism of death. A minority of patients received medical care or resuscitation prior to death, and only few achieved minimal post-event survival. No significant sex- or residence-related differences were found. The likelihood of short survival was higher in cases where resuscitation was attempted, while abdominal aortic involvement was associated with immediate fatality.

Conclusion. Fatal aortic dissections remain a rare but critical cause of sudden non-violent death, characterized by limited opportunities for survival and a high prevalence of chronic vascular pathology. Forensic evaluation continues to play an essential role in identifying their true incidence and pathophysiological context.

Suicide in the forensic setting: patterns, circumstances, and lethality factors

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Introduction. Suicide remains a major public health and forensic concern, reflecting the interaction of psychological, environmental, and social determinants. Understanding its patterns within a regional medico-legal framework can improve prevention strategies.

Methods. A retrospective observational analysis was conducted on all autopsy-confirmed suicides examined at the Cluj-Napoca Institute of Legal Medicine between 2014 and 2024. Sociodemographic, contextual, and toxicological data were analyzed using descriptive and comparative statistics to explore group differences by sex, age, residence, alcohol use, and site of death.

Results. The proportion of suicides among all autopsies showed a progressive decrease throughout the study period. Men represented the majority of victims, most often middle-aged, while women were slightly older and predominantly urban. Two-thirds of suicides occurred at home, or usually within the victim's locality of residence. Hanging was the leading method, followed by falls and voluntary intoxications. Alcohol consumption was significantly more frequent among men and associated with higher lethality and younger age. Survival beyond the event was rare, mainly in intoxication or fall-related cases. Seasonal variation was observed, with a higher incidence in warm months.

Conclusion. The study highlights stable demographic and situational patterns of suicide in Northwestern Romania, underlining the predominance of male victims, the domestic environment, and alcohol consumption as recurrent risk factors. The identification of these recurrent risk profiles may assist in developing targeted preventive approaches and community-level interventions.

Early rehabilitation in the intensive care unit: a case report of recovery and return to functional independence

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Introduction. Critically ill patients in intensive care units present a challenge for medical rehabilitation. Patients may experience intensive care unit-acquired myopathy, pressure ulcers and pulmonary problems; therefore, it is essential to start musculoskeletal and respiratory physiotherapy interventions within the initial 72 hours, in accordance with intensive care unit rehabilitation standards. We present this case to demonstrate the importance of starting procedures as quickly as possible and the necessity of combining all kinetic approaches.

Case description. A 58-year-old female patient was transferred to the ICU of Pneumology Hospital Leon Daniello Cluj-Napoca from an external institution, diagnosed with septic shock of indeterminate origin, severe ARDS following bilateral diffuse alveolar hemorrhage, acute respiratory failure necessitating mechanical ventilation, bronchopneumonia, thrombocytopenia and post-hemorrhagic anemia.

The patient was initially intubated with an endotracheal tube (ETT), mechanically ventilated and was administered IV sedation, with necessity of multiple ETT suctioning due to abundant secretions. . After the assessment of the patient, the rehabilitation program started within the first 48 hours of admission to the Intensive Care Unit. In the early stages passive mobilizations of all four extremities, chest physiotherapy and bronchial drainage positions were initiated, with beneficial effects on the mucus clearance. Electromuscular stimulation is incorporated into the passive physiotherapy sessions.

Due to the improvement of respiratory parameters, sedative infusions were stopped and the weaning from mechanical ventilation was initiated. Following clinical reevaluation, the patient has a muscle strength rating of 1 in all four limbs on the MRC scale and had no reaction to stimulation. A brain MRI exam was performed and indicated spastic tetraplegia resulting from severe widespread hypoxia. Difficulties in the process of weaning from the ventilator led to the placement of a tracheostomy tube. In this phase the patient was transferred from bed to chair and NMES therapy continues. A stationary bicycle facilitates both passive and active movement. Strength training was done using elastic bands with different resistances.

Upon the restoration of muscle strength in both the limbs and trunk the patient began the walking recovery with the help of a walker. The tracheostomy decannulation was successfully perfomed and after one month and three weeks, the patient was freed from our care, ambulating with the assistance of a walking frame and capable of independently executing activities of daily living (ADLs).

Conclusion. Both respiratory and musculoskeletal rehabilitation techniques are crucial for patient recovery. In order to promote a level of independence that is beneficial to social reintegration, physiotherapy should to be recognized as an essential part of intensive care unit management.

Antimicrobial resistance trends among non-*Pseudomonas*, non-*Acinetobacter nonfermenting* Gram-negative bacilli from clinical specimens

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Introduction. Nonfermenting Gram-negative bacilli other than *Pseudomonas aeruginosa* and *Acinetobacter baumannii* represent an increasingly recognized group of opportunistic pathogens. These organisms, such as *Stenotrophomonas maltophilia*, *Burkholderia cepacia* complex, *Sphingomonas paucimobilis*, and *Achromobacter xylosoxidans* are often associated with infections in immunocompromised hosts or patients with indwelling medical devices. Their intrinsic multidrug resistance poses significant therapeutic challenges.

Methods. A total of 64 nonfermenting Gram-negative isolates (excluding *Pseudomonas* and Acinetobacter) were analyzed between January and June 2025 in the Medical Analysis Laboratory of the "Prof. Dr. Octavian Fodor" Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca. Isolates were recovered from: respiratory secretions (22 isolates; 34.4%), blood cultures (14 isolates; 21.9%), wound exudates (13 isolates; 20.3%), urine samples (9 isolates; 14.1%), and catheter or drainage fluids (6 isolates; 9.3%). Bacterial identification was performed using the VITEK® MS automated mass spectrometry system, and antimicrobial susceptibility testing with the VITEK® 2 system, interpreted according to EUCAST 2025 criteria.

Results. Species distribution: *Stenotrophomonas maltophilia* (25 isolates; 39.1%), *Burkholderia cepacia* complex (18 isolates; 28.1%), *Achromobacter xylosoxidans* (12 isolates; 18.8%), *Sphingomonas paucimobilis* (9 isolates; 14.0%).

Antimicrobial susceptibility:

- *S. maltophilia* showed high susceptibility to Trimethoprim/Sulfamethoxazole (95%) and Levofloxacin (82%).
- *B. cepacia* complex exhibited variable susceptibility to Ceftazidime (60%) and Meropenem (52%), with intrinsic resistance to Colistin.
- *A. xylosoxidans* retained moderate susceptibility to Piperacillin/Tazobactam (72%) and Meropenem (65%).
- *S. paucimobilis* showed the most favorable profile, with >85% susceptibility to Ciprofloxacin and Tigecycline.

Most isolates displayed multidrug resistance, but none were classified a s pan-resistant.

Conclusion. Nonfermenting Gram-negative bacilli other than *Pseudomonas* and Acinetobacter constitute a heterogeneous yet clinically significant group of pathogens. The persistence of high susceptibility to Trimethoprim/Sulfamethoxazole, Levofloxacin, and selected β-lactams provides valuable therapeutic options. The increasing frequency of S. maltophilia and B. cepacia complex underscores the need for continuous local surveillance, accurate identification by mass spectrometry, and rational antimicrobial stewardship to prevent further resistance development.

Cumulative antimicrobial susceptibility profile of *Acinetobacter baumannii* clinical isolates

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Introduction. *Acinetobacter baumannii* is a major nosocomial pathogen whose ability to accumulate multidrug resistance (MDR) and persist in hospital environments makes it particularly difficult to manage. Continuous monitoring through cumulative antibiograms is critical for guiding empirical therapy and infection control strategies.

Methods. Between January and June 2025, 138 clinical isolates of *Acinetobacter baumannii* were analyzed at the Prof. Dr. Octavian Fodor Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca. Samples originated from respiratory secretions (41.3%), blood cultures (20.3%), wound/surgical site infections (18.1%), urine (13.0%), and catheter/drainage fluids (7.3%). Identification was performed by automated mass spectrometry, and susceptibility testing by VITEK® 2, interpreted according to EUCAST 2025 standards.

Results. MDR was present in 82% of isolates and XDR in 14%; no pan-resistant strains were found. Susceptibility rates were: Colistin 94%, Tigecycline 81%, Amikacin 42%, Carbapenems 11%, Ciprofloxacin 9%, Piperacillin/Tazobactam 6%, and <5% for Cefepime/Ceftazidime. Carbapenem resistance was predominantly associated with intensive care unit samples. A minority (6%) showed intermediate susceptibility to Cefiderocol.

Conclusion. Cumulative antibiogram data confirm A. baumannii as a highly resistant nosocomial pathogen with limited therapeutic options. While Colistin and Tigecycline remain the most active agents, rising resistance to Carbapenems and Amikacin underscores the urgent need for antimicrobial stewardship and strict infection control measures. Continuous surveillance is essential to support evidence-based empirical therapy and institutional infection prevention efforts.

Time to detection of blood cultures by pathogen

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Introduction. The time to detection (TTD) of blood cultures is a key indicator for assessing the dynamics of bloodstream infections and the performance of automated microbiological systems. Monitoring TTD assists in distinguishing true pathogens from contaminants and supports prompt therapeutic decisions.

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Methods. A total of 33 bacterial isolates obtained from blood cultures processed at the IRGH Prof. Dr. O.Fodor Cluj-Napoca Laboratory between June and October 2025 were analyzed using the BACT/ALERT® VIRTUO automated system. Detection time was recorded in days, and only clinically significant isolates were included.

Results. The overall TTD ranged from 0.18 to 3.39 days, with a mean of 0.76 days and a median of 0.49 days.

• Rapid detection (≤0.5 days): *Enterobacter cloacae* (complex and subspecies – 0.22 days), *Escherichia coli* (0.18–0.73), *Klebsiella pneumoniae* (0.22–1.59*),* *Raoultella planticola* (0.44), *Morganella morganii* (0.51), *Proteus mirabilis* (0.53).

• Moderate detection (0.7–1 day): *Staphylococcus epidermidis* (0.77), *Enterococcus faecalis* (0.74), *Pseudomonas aeruginosa* (0.74), *Salmonella enterica* (0.96).

• Slow detection (>1 day): *Streptococcus parasanguinis* (1.44), *Sphingomonas paucimobilis* and *Cronobacter sakazakii* (3.39 each).

Conclusion. Most pathogens become positive within the first 24 hours, particularly enteric Gram-negative bacteria (*E. coli*, *K. pneumoniae*, *Enterobacter spp*.). Slower-growing species such as *Sphingomonas paucimobilis* and Cronobacter sakazakii may require up to 72 hours. Knowledge of typical TTD values can improve interpretation of blood culture results and support timely clinical management.

Rule-in and rule-out performances of contemporary molecular panels for indeterminate thyroid nodules

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Introduction. The preoperative diagnosis of cytologically indeterminate thyroid nodules (ITNs) poses a significant clinical challenge, often leading to unnecessary diagnostic surgeries. Molecular tests have been developed to improve diagnostic accuracy. This study aimed to evaluate the diagnostic performance of novel molecular tests (Thyroseq v3, Afirma GSC) and microRNA-based assays compared to their prior iterations (Thyroseq v2, Afirma GEC), considering their „rule-out" and „rule-in" capabilities for malignancy. It further analyzed the impact of the NIFTP reclassification and Bethesda cytological subcategories on test performance.

Methods. A systematic review and meta-analysis were conducted following PRISMA guidelines. A search of PubMed, Scopus, and Web of Science identified studies evaluating molecular tests in patients with ITNs (Bethesda III, IV, V), using post-surgical histopathology as the reference standard. Data were extracted to calculate pooled sensitivity, specificity, likelihood ratios (PLR, NLR), and the area under the curve (AUC) using a bivariate random-effects model.

Results. The analysis included 40 studies, encompassing 7,831 nodules. Thyroseq v3 demonstrated the best overall performance (AUC 0.95), followed by Afirma GSC (AUC 0.90) and Thyroseq v2 (AUC 0.88). For ruling out malignancy (reflected by a low NLR), Thyroseq v3 (NLR 0.02) was superior. For ruling in malignancy (a high PLR), Thyroseq v2 (PLR 3.5) and Thyroseq v3 (PLR 2.8) outperformed Afirma GSC (PLR 1.9). The performance of Afirma GEC and Thyroseq v2 was negatively affected by NIFTP reclassification. Tests like ThyGenNEXT/ThyraMIR and RosettaGX showed promising preliminary results.

Conclusion. While no current molecular test is perfect, each has distinct strengths. The newer tests, Thyroseq v3 and Afirma GSC, show superior overall performance and excel at ruling out malignancy, surpassing previous versions. Paradoxically, Thyroseq v2 remains the most effective test for confirming cancer. The re-evaluation of NIFTP underscores the need for careful interpretation of molecular test results and the importance of ongoing test refinement.

A rare cause of brachial diparesis: cervical transverse myelitis with *haemophilus influenzae*

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Introduction. In the setting of both globalization and increasing use of immunosuppressive therapy, infectious myelopathies are an important cause of morbidity worldwide.

Methods. Determining the etiology of transverse myelitis can be challenging. Causative pathogens for infectious etiology include viruses, parasites, pyogenic and atypical bacteria, and fungi. Once adequate neuroimaging has ruled out a compressive etiology, and a lumbar puncture has demonstrated signs of inflammation within the cerebrospinal fluid, a workup of causes for an acute transverse myelitis must be undertaken.

Case presentation. A 79-year-old patient with history of recent pneumoniae presented in the Neurology Department for asymmetric motor deficit in both upper limbs. The disease had a sudden onset during the day, with bilateral hand paresthesia, followed by shoulder pain radiating to the upper limbs, and subsequently, asymmetric decrease in muscle strength in both upper limbs. Neurological examination on admission discovered the patient to have positive paresis tests in both upper limbs; bicipital and stylo-radial reflex absent; loss to pain and temperature dissociation in upper limbs.

Contrast MRI revealed signal alteration without contrast enhancement at C3–C6, involving up to 80% of the spinal cord cross-section at C4–C5 level — compatible with transverse myelitis. Multiplex PCR panel (CSF) - positive for *Haemophilus influenzae*. Following infectious disease consultation, antibiotic therapy with Cefort 2 g IV every 12 hours for 10 days was initiated.

Conclusion. This case highlights the difficulties in diagnosing individuals with acute or subacute cervical cord symptoms and the significance of prompt examination and treatment. A preliminary diagnosis based solely on clinical characteristics, MRI results, and basic CSF investigation is frequently the foundation for the crucial initial treatment.

Polycystic ovary syndrome: a possible cause of epilepsy

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Introduction. Polycystic ovary syndrome is one of the most common endocrine and metabolic disorders in premenopausal women. It is defined by a combination of signs and symptoms of androgen excess and ovarian dysfunction in the absence of other specific diagnoses. Polycystic ovary syndrome is frequently associated with abdominal adiposity, insulin resistance, obesity, metabolic disorders, and cardiovascular risk factors. Several hypotheses have been proposed regarding the link between polycystic ovary syndrome and epilepsy.

Methods. We report the case of a 45-year-old woman with known polycystic ovary syndrome, untreated at home, who presented with two generalized tonic–clonic seizures that occurred at night approximately two weeks before admission, accompanied by a traumatic tongue mark and a postictal altered general condition. Upon admission, neurological examination showed no pathological findings. Lumbar puncture with biochemical and cytological analysis of the cerebrospinal fluid revealed no abnormalities. Based on CSF studies, infectious, prionic, and autoimmune causes of seizures were excluded (anti–NMDA receptor, GAD II, anti–GABA-A and –GABA-B receptor, anti–LGI1, anti–MOG antibodies, protein 14.3.3, multiplex panel – all negative). Contrast-enhanced brain MRI revealed several nonspecific, demyelinating lesions in the superficial and deep white matter, without causal relation to the seizures. Electroencephalography (EEG) showed an awake pattern dominated by an alpha rhythm of 8.5–9 Hz, without epileptiform discharges or focal abnormalities. During follow-up under antiepileptic therapy, the patient remained seizure-free.

Results. This case describes a patient with known polycystic ovary syndrome who presented with generalized tonic–clonic seizures without any structural, infectious, or autoimmune cause. The favorable clinical course under antiepileptic treatment supports a reversible, functional mechanism possibly influenced by hormonal status. Although the manifestations of PCOS are predominantly metabolic and hormonal, recent studies have proposed several hypotheses concerning possible links between PCOS and neurological disorders, especially epilepsy. First, hypothalamic–pituitary–ovarian axis dysregulation in polycystic ovary syndrome may alter neuronal excitability, favoring seizure onset. Second, sex hormones play a crucial role in regulating neuronal excitability, with estrogens exerting proconvulsant effects and progesterone exerting inhibitory effects. The estrogen/progesterone imbalance characteristic of polycystic ovary syndrome, together with hyperandrogenism, may lower the seizure threshold. Experimental animal studies have shown that elevated testosterone reduces seizure threshold, an effect partially reversible after antiandrogenic therapy. Third, polycystic ovary syndrome is associated with metabolic and inflammatory changes; insulin resistance and low-grade inflammation may indirectly affect cerebral metabolism and neurotransmitter balance. In this case, the absence of other identifiable causes and the association with a hormonal profile consistent with PCOS support the hypothesis of a potential hormonal role in triggering epileptic seizures. The favorable outcome under antiepileptic therapy indicates a good prognosis; however, regular endocrinological monitoring and interdisciplinary collaboration between neurologist and endocrinologist are required.

Conclusion. This case highlights the importance of an integrated approach to patients with PCOS and neurological manifestations. The relationship between hormonal dysregulation and neuronal excitability requires further research, but current evidence suggests that endocrine dysfunctions may contribute to increased seizure susceptibility. Early identification and correction of hormonal imbalances may represent an important step in preventing or controlling epileptic seizures in patients with polycystic ovary syndrome.

Dietary interventions in irritable bowel syndrome

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Introduction. Irritable Bowel Syndrome (IBS) is one of the most complex and multifactorial gastrointestinal disorders, characterized by a strong interaction between gastrointestinal and extraintestinal symptoms. Recent evidence highlights the crucial role of nutrition in intestinal health and dietary therapy in IBS. Food components may either alleviate or trigger symptoms, while psychological factors strongly influence intestinal motility and visceral hypersensitivity. Emotional stress, disordered eating, and low physical activity aggravate symptoms, whereas proper coping strategies and nutritional management reduce their impact.

Methods. A cross-sectional online survey was conducted between May and July 2020 among individuals diagnosed with IBS. The questionnaire included 39 questions covering demographic data, disease characteristics, lifestyle, and dietary habits. Data were statistically processed using Microsoft Excel 2019.

Results. IBS predominantly affected young women (18–39 years) from urban areas. Common symptoms included abdominal pain, bloating, and irregular bowel habits. Major dietary triggers were lactose, fructose, and high-fat processed foods. Low-FODMAP interventions showed the greatest symptom improvement. Micronutrient deficiencies (iron, calcium, magnesium, vitamin D) were common due to restrictive diets. Emotional stress and irregular meals were significant aggravating factors.

Conclusions. IBS requires a holistic, multidisciplinary approach. Nutritional therapy, combined with psychological support and pharmacological treatment, can significantly reduce symptoms and improve quality of life. Although diet is not curative, correct application of first- and second-line dietary interventions provides substantial benefits and highlights the need for individualized patient care.

RESEARCH INSTITUTE

Neurotrophic-like activity of Cerebrolysin on astrocytes and microglia under oxygen-glucose deprivation

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Introduction. Ischemic stroke significantly affects population health, and current acute stage pharmacological interventions remain limited to recanalization therapy, underscoring the need for novel therapeutic strategies. Preclinical and clinical studies suggests that Cerebrolysin, a combination of peptides and amino acids extracted, exerts properties related to brain protection and recovery, like endogenous neurotrophic factors. This study aimed to document the functional effects of Cerebrolysin treatment on components of the neurovascular unit in a cellular stress model of ischemic stroke.

Methods. Functional assays were performed in two human brain astrocyte and microglia cell lines: one representing normoxia conditions with glucose-containing media, and the other conditions by glucose and oxygen deprivation. Cells were treated with different concentrations of Cerebrolysin for 24h, and various functional tests, including cell viability, cell confluence, cell cycle, inflammasome assay, and glutathione assay, were performed to evaluate the effect of Cerebrolysin. qRT-PCR profiling for different genes involved in several biological processes was performed.

Results and discussion. Cerebrolysin treatment compensates stress, induced by oxygen-glucose deprivation in the cells under different conditions and time points. Cells showed increased viability and confluence. Inflammasome, glutathione levels, and cell cycle phases were also modified. QRT-PCR analysis of the genes shows altered expression profiles in the treated cell lines.

Conclusion. Results corroborate the existing body of evidence on the biological agent. Findings should be confirmed in a more complex in vitro model of the neurovascular unit and the blood-brain barrier, including co-cultures studies and possibly in vascularized human brain organoids.

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Emerging roles of mRNA/miRNA/lncRNA networks in non-small cell lung cancer (NSCLC)

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Introduction. NSCLC progression is driven by coordinated dysregulation of mRNAs, miRNAs, and lncRNAs that disrupt key pathways controlling proliferation, apoptosis, and metastasis. We attempted to explore the role of (regulatory RNA interaction networks (RRINs) competing endogenous RNA networks (ceRNA networks).

Methods. *In silico* analysis for identification of differentially expressed miRNAs, lncRNAs and mRNAs and subsequent survival analysis of LUAD and LUSC TCGA datasets was performed. The interconection among these transcripts was emphasized.

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Correlation analysis of mRNA/miRNA/lncRNA pairs in lung cancer was performed. Validation of mRNA/miRNA/lncRNA expression using two independent cohorts of LUAD and LUSC patients, as well as lung cancer cell lines - A549, Calu6, H1703, SKMES1 - compared to BEAS2B- normal lung cell line was performed through qRT-PCR experiment.

Results. We identified top d ysregulated mRNA/miRNA/lncRNA transcripts in LUAD and LUSC TCGA datasets, while also performing a survival analysis. The expression pattern of the mRNA/miRNA/lncRNA in the TCGA datasets was confirmed in qRT-PCR experiments performed on LUAD and LUSC patient cohort, and the expression patterns were confirmed also in the lung cancer cell lines analyzed.

Conclusion. The identified 4 miRNA–3 mRNA–2 lncRNA network highlights a potential post-transcriptional regulatory axis implicated in NSCLC pathogenesis, particularly in apoptosis control. These findings open new directions for mechanistic exploration and *in vitro* validation of candidate regulatory interactions.

Acknowledgements. Validation of *in silico* bioinformatics workflows for targetable pathways in NSCLC using digital PCR methods – BIOMETER, 126TE from 01/09/2025 (PN-IV-P2-2.1-TE-2023-1158) and the Competitiveness Operational Program, 2014–2020, Clinical and economical impact of personalized targeted anti-microRNA therapies in reconverting lung cancer chemoresistance—CANTEMIR, no. 35/01.09.2016, MySMIS 103375.

Intracellular and secreted proteome profile in melanoma cells after targeted therapies with Vemurafenib and CAR-T

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Introduction. Resistance to therapy leads to a continuous development of targeted therapies, so the development of new diagnostic methods and identification of new therapeutic targets will create a favorable context for obtaining new therapeutic agents that inhibit tumor cells or will indicate the possibility of repositioning already well-known therapies. The objective of this project is to identify potential new therapeutic targets in skin melanoma and to characterize the response to targeted therapies with Vemurafenib and CAR T using state-of-the-art methods in the identification of intracellular and secreted proteins.

Methods. Melanoma cells were treated with Vemurafenib to determine the IC50 and the drug efficacy, and co-cultured with CAR-T cells targeting ROR1 for evaluating the effect. MTT assay assessed Vemurafenib toxicity, Flow cytometry methods were applied for testing the CAR-T cell efficacy on melanoma. The wound healing evaluated cells for 48h. Sample prep for amino acids evaluation, secretome and proteome profiling were prepared and stored.

Results. The coculture indicates a low efficacy of the targeted immunotherapy, suggesting that we need to adjust the CAR construct. Vemurafenib had a dose-dependent toxicity observed at 48h. Cell migration was significantly inhibited at 48h, and further testing is currently ongoing. The growth rate was inhibited at 48h exposure to Vemurafenib, and the cell count for amino acid evaluation, secretome and proteome

profiling was modified.

Conclusion. Vemurafenib inhibited cell growth and migration, induced changes in cell features, however the project is still ongoing, and molecular assessment needs to be performed to conclude the effectiveness of the therapy and to highlight changes in the metabolome, secretome and proteome profiles.

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Consistent PVT1 overexpression across tumor tissue and plasma-derived exosomes in clear cell renal cell carcinoma

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Introduction. Clear cell renal cell carcinoma (ccRCC) is currently lacking robust biomarkers for early detection, monitoring, and treatment. PVT1 is recurrently overexpressed in ccRCC tissue and may be exported via exosomes, enabling minimally invasive assessment. In this study, we evaluated PVT1 dysregulation in tumor tissue samples and plasma-derived exosomes (PDEs) from early and late-stage ccRCCs.

Methods. TCGA-KIRC (n=537) was used for preliminary analysis. The study included 45 ccRCC patients (paired TT/NT, plasma) and 45 healthy donors (plasma). PDEs were obtained with the Total Exosome Isolation Kit and characterized by NanoSight and TEM. Total RNA was extracted using TRIzol, exosomal RNA was isolated using the Norgen Kit, and both were quantified by NanoDrop. For total RNA, the cDNA was synthesized with the High-Capacity Kit and further analyzed by RT-qPCR (PoweUP SYBR, ViiA7). For exosomal RNA, the cDNA was synthesized using the QuantiTect Kit and further analyzed by digital PCR (QIAcuity EG, QIAcuity One system). Differential gene expression analysis was performed in GraphPad Prism 10.1.1 and RStudio (R 4.4.2).

Results. PEDs showed expected size distribution and morphology. In the TCGA-KIRC dataset, PVT1 ranked among the top dysregulated lncRNAs with significant upregulation across early, late, and combined stages. Its robust overexpression pattern was consistent in tumors and PEDs across all ccRCC stages.

Conclusion. PVT1 shows a conserved overexpressed pattern in ccRCC tumors and PDEs. These findings support its use as a biologically informative, minimally invasive biomarker, and motivate for larger studies to test its diagnostic and monitoring performance.

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Very small embryonic – like stem cells undergo enhanced differentiation into multipotent mesenchymal and hematopoietic progenitors following stimulation with human chorionic gonadotropin and granulocyte colony stimulating factor *in vivo* leading to improved survival after peripheral blood stem cell transplantation

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Introduction. Very Small Embryonic – like (LIN-CD45-SCA-1+) stem cells (VSELs) – are stem cell precursors with origins in the epiblast. They have a tight germline kinship and a high developmental potency toward hematopoietic and mesenchymal lineages, maintaining postnatal tissue homeostasis. Here we provide indirect evidence that VSELs induce in numbers and further differentiate into primitive HSCs and MSCs which positively impacts PBCST survival in a murine model.

Methods. A single dose of pegylated G-CSF with and without HCG was administered in rats followed by a complete blood count at 7 days post- administration. The treatment was further administered in mice and flow-citometry was used to characterize the peripheral blood cell populations 5 days after treatment. Male donor mice (n=20) were pretreated with a single dose of either peg-G-CSF alone (group A, n=10) or HCG + peg-G-CSF (group B, n=10), 5 days prior to PBMC harvest. PBMCs were immediately transplanted to the equivalent number of Busulfan mieloablated female mice by intravenous tail injection and OS was assessed in both recipient groups.

Results. A statistically signifficant increase in the number of monocytes and lymphocytes was seen in the in the combination arm compared to G-CSF alone, and this correlated with a 21% increase in CD29 and a 9.4% increase in CD34. The median OS in the group of recipients transplanted with peg-G-CSF mobilized PBMCs (group A) was 81 days. In the recipients transplanted with HCG+ peg-G-CSF mobilized PBMCs (group B) the median OS was 225 days. We noted a change in numbers of in SCA-1 (+ 0.7%) while CD45 decreased (-1%) in the HCG + G-CSF arm. This suggests that it was SCA-1 + CD45- VSELs that actually induced in numbers.

Conclusion. The pharmacological stimulation of endogenous VSELs in the onco-hematological setting could provide a paradigm shift from symptom-based management of oncological toxicities to stem cell-based endogenous regeneration.

Pan-cancer view of miR-155 in cancer: a bioinformatic approach

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Introduction. MicroRNA-155 (miR-155) is a key non-coding RNA known to regulate immune responses, inflammation, and oncogenic signaling. Although extensively studied in individual tumor types, its regulatory mechanisms and clinical significance across cancers are still not fully understood. We explored a pan-cancer perspective aiming to identify shared and cancer-specific roles of miR-155.

Methods. A pan-cancer analysis using datasets was performed using dbDEMC, with a focus on differential expression analyses between tumors and normal tissues and blood for tumor versus healthy controls. Pathway enrichment analyses and correlation with the overall survival rate were done for this transcript.

Results. miR-155 was significantly overexpressed in most of the cancer types (brain cancer, breast cancer, colorectal cancer, endometrial cancer, kidney cancer, lung cancer, ovarian cancer, pancreatic cancer). The association between miR-155 expression and overall survival varies across cancers, with overexpression linked to a favorable prognosis in some tumor types and an unfavorable prognosis in others, as shown by data from miRTarBase. This highlights the presence of cancer type–specific regulatory networks governing its function. Gene enrichment analysis revealed that this transcript influences multiple cancer hallmarks through its extensive network of gene targets and signaling pathways, particularly those related to drug resistance.

Conclusion. These findings indicate that miR-155 exerts both oncogenic and tumor-suppressive effects depending on the cellular and molecular context, emphasizing the importance of cancer type–specific regulatory networks in determining its clinical impact.

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Consolidation of flow cytometric immunophenotyping as a powerful method in the diagnostic work of HIV-associated Hodgkin's Lymphoma

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Introduction. Hodgkin lymphoma (HL) is prevalent worldwide and typically presents symptoms like sudden pain, swelling, and weight loss. Classical HL (cHL) is largely treatable with modern risk- adapted and response-based therapy. The present report aims to present the diagnostic work-up with an emphasis on flow cytometry in patients with HIV-associated lymphoma.

Methods. Three clinical cases of HIV patients, including HIV-related cHL, diagnosed by flow cytometry, are presented to illustrate the abundance of clonal B-cell populations across different HIV-associated lymphomas. The specific antibody panel

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design may help practitioners in disseminating among resembling subtypes of HIV-associated lymphomas.

Results. We identified neoplastic Hodgkin and Reed-Sternberg (HRS) cells that typically show weak or absent B-cell markers (CD19, CD20, CD79a), but are positive for CD30 and often CD15, and express PAX5 dimly. HRS cells are usually negative for CD45. Flow cytometry can identify these cells by their large size, high side scatter, and unique immunophenotype, but detection is challenging due to their scarcity and fragility. HIV-associated cHL is characterized by a high level of depletion of CD4+ T cells while the CD8+ T cells and CD163+ macrophage become relatively higher in the tumor microenvironment, resulting in an inverted or very low CD4:CD8 ratio. In contrast we found the characteristic T-cell-rich background with an elevated CD4:CD8 ratio in cHL immunocompetent patients.

Conclusion. FC detection of cHL can be performed rapidly and effectively, adding diagnostic value to small biopsy samples. FC is a method that has the potential to reduce invasive excisional procedures, high costs, and an extended time to treatment.

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Using targeted compound screening for the investigation of actionable vulnerabilities in lung squamous carcinoma

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Introduction. Lung squamous carcinoma (LUSC), a subtype of non-small cell lung cancer (NSCLC), remains difficult to treat due to limited actionable targets and resistance to standard therapies. Compounds acting on angiogenesis, cell cycle regulation, and DNA damage and repair (DDR) pathways represent promising therapeutic strategies. This study employed transcriptomic profiling of LUSC cell lines to identify cytotoxic compounds and characterize their cellular and molecular mechanisms.

Methods. Gene expression profiling was performed on two untreated LUSC cell lines (H1703 and SK-MES1) using microarray technology after RNA extraction. Microarray data were compared with TCGA datasets from LUSC patients, identifying 233 commonly altered genes across dysregulated pathways. Based on these findings, 27 compounds from an Immuno-Oncology Compound Library were screened on both cell lines, yielding five active compounds. Cytotoxicity was quantified to determine IC_{50} values. Functional assays, including cell cycle and apoptosis analysis on Nexcelom's Celigo platform, and RT-qPCR on downstream effectors, were used to assess pathway modulation.

Results. Two compounds—ENMD-2076 and bosutinib—showed the most significant effects. Both compounds caused sub G0/G1 accumulation in either both or just one cell line, indicating apoptosis and growth arrest. Bosutinib inhibited migration likely via ACK1 inhibition, and ENMD-2076 likely through MMP9 downregulation and EMT suppression. Increased caspase activity confirmed pronounced apoptosis, particularly with ENMD-2076.

Conclusion. Bosutinib and ENMD-2076 display distinct yet complementary anticancer mechanisms in LUSC. Bosutinib primarily inhibits migration, while

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ENMD-2076 induces cell cycle arrest and apoptosis, suggesting synergistic therapeutic potential in LUSC.

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Systematic evaluation of urine sample preparation methods for label-free MS-based proteomics

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Introduction. Urinary proteomics offers a non-invasive approach for biomarker discovery. However, the low protein concentration and high salt content of urine challenges proteome recovery and digestion efficiency. This study compares in-solution digestion with the single-pot solid-phase enhanced sample preparation (SP3) method to evaluate their impact on protein recovery, digestion efficiency, and urinary proteome coverage.

Methods. A pooled urine sample from 44 healthy volunteers was used for protocol optimization. 900 µL aliquots were concentrated using 3 kDa Amicon® filters and subjected to three extraction methods: trichloroacetic acid precipitation with a 60 min incubation time (TCA60), methanol–chloroform precipitation (MeOH-Chl) and buffer exchange (BE). Aditionally, three different lysis buffers were used: 0.1% Rapigest® prepared in 50 mM ammonium bicarbonate (R), 8M urea/2M thiourea (UT) and 8M urea in 50mM Tris-HCl (UTris). Protein concentration was determined by Bradford assay prior to in-solution (inSol) and on-bead digestion (SP3) using trypsin. Peptides were analyzed by nanoLC-HDMSE, and protein identification was performed in Progenesis QIP v.4.2.

Results. Both buffer and extraction method significantly influenced protein yield, with the highest recovery observed for BE-R and MeOH-UTris conditions. SP3 digestion achieved superior and more consistent cleavage efficiency (76.3%) compared to inSol (69.5%). While inSol identified more proteins in the low–mid molecular weight range, SP3 provided a more uniform distribution across MW categories. Moreover, SP3 reduced the presence of contaminants such as serum albumin and hemoglobin, while maintaining good detection of urinary biomarkers including uromodulin and osteopontin.

Conclusion. SP3 is a reproducible strategy for urinary proteomics, offering improved digestion efficiency, balanced protein recovery, and reduced contaminants compared to inSol digestion.

Integrative miRNA and protein expression profiling reveals regulatory networks driving melanoma progression

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Introduction. Malignant melanoma is an aggressive skin cancer characterized by high metastatic potential and poor prognosis. MicroRNAs (miRNAs), small non-coding regulators of gene expression, have emerged as key modulators of cancer initiation and progression, with potential applications as diagnostic and prognostic biomarkers.

Methods. We performed comprehensive miRNA expression profiling to distinguish melanoma from benign nevi using microarray analysis of formalin-fixed, paraffin-embedded (FFPE) samples. Differentially expressed miRNAs were identified and subjected to hierarchical clustering and pathway enrichment analyses to explore their biological significance. A subset of miRNAs (miR-20b-5p, miR-21-3p, miR-21-5p, miR-25-3p, miR-29b-3p, miR-93-5p, and miR-222-3p) was validated by quantitative RT-PCR in an independent cohort. In parallel, immunohistochemistry (IHC) was performed on serial FFPE sections to assess the expression of key melanoma-associated proteins, including MITF, BRAF^V600E, and p53, and to correlate their expression with miRNA profiles.

Results. Microarray profiling revealed a distinct miRNA signature that discriminated melanoma from nevi. qRT-PCR validation confirmed the dysregulation of selected miRNAs. IHC analysis demonstrated variable expression of MITF, BRAF^V600E, and p53, with significant correlations between their expression levels and those of specific miRNAs, suggesting potential regulatory relationships. Dysregulated miRNAs target genes involved in MAPK and PI3K/AKT signaling pathways.

Conclusions. This integrative analysis of miRNA and protein expression highlights a molecular network underlying melanoma pathogenesis. The identified miRNAs, together with their associated protein markers, may serve as promising diagnostic biomarkers and therapeutic targets. These findings provide insights into the mechanistic roles of miRNA–protein interactions in melanoma progression.

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In vitro and *in vivo* targeting the carcinoembryonic antigen ROR1 with specific CAR-T cells in MCL and other pathologies

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Introduction. ROR1 functions as a receptor for the Wnt family of proteins and plays many functions in cellular processes, including cell migration, differentiation and growth during the process of embryonic development. In healthy adults, ROR1 is found at minimal levels, but in mantle cell lymphoma (MCL) and other types of malignancies, ROR1 expression is markedly elevated. This study assesses the relative possible application of anti-ROR1 CAR-T cells in MCL by the measurement of the activity of CAR T therapy.

Methods. The CAR construct was developed and subcloned into lentivirus vector by Creative biolabs. The samples were analyzed by FACS CANTO II using anti ROR1-APC conjugated antibodies and eGFP signal. After 72h of incubation, the CD25 and CD69 expressions were determined by Flow Cytometry. LDH activity was determined using LDH PicoProbe assay. For cytokine measurements, ELISA assays were used. For the *in vivo* models, NSG/S mice, 6–8-week-old, inoculated with MCL cells Luc2+ and evaluated by IVIS.

Results. Many cell lines expressed ROR1 in different ratios (MDA-MB-231 as solid tumor model, was used as a positive control for ROR1 expression), with Z138 cell line as more than 95% positive cells. The testing on Z138 – MCL showed a time-dependent inhibitory effect of our anti ROR1 CAR T cells, with an increased LDH activity and cytokine release in all groups. However, the efficacy was limited in all cell lines tested.

Conclusion. Our CAR construct has low efficacy, an d th e CAR-T ce lls need adjustments for an increased antitumor activity against ROR1 positive cells.

Acknowledgements. Grant no 760278/26.03.2024,"Creating a Research Group of Excellence to Develop Cell and Immune Therapy Technology to Target the Tumor Microenvironment, CF106/31.07.2024," funded by the Ministry of Education of Romania and the European Union's Next Generation EU program and National Recovery and Resilience Plan.

D-Amino acids as emerging biomarkers in chronic kidney disease: insights from LC-IM-MS analysis

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Introduction. D-amino acids, once considered biologically insignificant, are more and more investigated as biomarkers in chronic kidney disease (CKD), their implications in renal metabolism, or contribution to disease progression. This study aims at better understanding their role in pathogenesis through profiling both D- and L-amino acids in plasma samples.

Methods. This case-control study consisted in D- and L-amino acids profiling

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in 195 plasma samples, 127 collected from CKD patients, while 68 were collected from healthy controls. Analysis was carried out by LC-IM-MS, using a Waters I-Class liquid chromatograph coupled with a Synapt G2-Si high-resolution mass spectrometer. Chiral resolution was achieved indirectly, by employing chiral derivatization of the amino acids using S-NIFE, all derivatives being subsequently separated on a phenyl-hexyl stationary phase.

Results. Compared to control, profiling of D- and L- amino acids revealed that CKD patients have significantly increased of D-Ala, D-Lys, D-Ser, D-Pro, D-Arg, D-Phe, D-Ile, while L-Asn, L-Met, L-Ser and L-Thr were recorded as significantly decreased. Of these, the most important role in differentiating between the two groups was attributed to D-Ala, D-Lys and D-Pro, while D-Ser recorded a strong positive correlation with CKD staging.

Conclusion. The altered D- and L-amino acid profiles observed in CKD patients highlight significant metabolic disturbances associated with disease progression. Elevated D-Ala, D-Lys, and D-Pro, alongside D-Ser's correlation with CKD stage, suggest their potential as biomarkers for diagnosis and monitoring.

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Differential response to acute treatment with tamoxifen in invasive lobular and ductal carcinomas

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Introduction. Invasive lobular carcinoma (ILC) is an estrogen-dependent breast cancer, with increasing incidence worldwide. Despite its unique biological and molecular features, ILC still presents no specifically targeted therapy and patients with ILC undergo similar therapeutical strategies as those with invasive ductal carcinoma (IDC), that include ER inhibitors, such as tamoxifen. However, ILC patients treated with tamoxifen develop late disease relapses, underlining the onset of resistance mechanisms and, therefore, a clear need of further investigations on treatments effects and therapy improvement. The objective of this study is to assess the response of ILC and IDC cell models to acute treatment with tamoxifen and to uncover new pathways potentially related to cell survival.

Methods. ILC and IDC cells were treated with doses of tamoxifen for 24 and 48 h to determine dose-dependent cytotoxicity. Cell apoptosis at 24 and 48 h was assessed by qPCR and flow cytometry. Also, the modulation of cell death-related pathways was investigated at gene and protein levels.

Results. Tamoxifen presented a dose-dependent toxicity in both cell models used in the experimental setup. However, treatment for 24 and 48 h modulated death-related pathways differently in ILC and IDC cells. Tamoxifen increased inflammation in both cell types, with TGF-β being increased only in ILC cells. In parallel, oxidative stress response was induced exclusively in IDC cells.

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Conclusion. ILC cells and IDC cells respond differently to tamoxifen. Acute treatment leads to dose-dependent cell death in both cell models; however, in ILC cells, it concomitantly induces inflammation and increases TGF-β levels, which have been demonstrated to play a role in cell survival. Further studies on chronic effect and resistance onset are needed.

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Crizotinib induces drug resistance mechanisms in triple-negative breast cancer cells

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Introduction. Globally, breast cancer is the most common malignancy and the second leading cause of cancer-related mortality among women. Triple-negative breast cancer (TNBC) represents a particularly aggressive subtype characterized by poor prognosis, a survival rate of less than two years, and a low response rate to conventional therapies. Therapeutic resistance remains a major challenge in clinical oncology. This study aimed to investigate the anti-cancer mechanism of crizotinib in paclitaxel-resistant TNBC cell models.

Methods. Experiments were conducted on TNBC cell lines (Hs578T) and their paclitaxel-resistant counterparts (Hs578T/Pax). The effect of crizotinib treatment was evaluated at 48 hours post-treatment at cellular and molecular levels.

Results. Crizotinib inhibited the viability of TNBC cells in a dose-dependent manner, suggesting activation of cell death pathways. Transcriptomic analysis revealed distinct gene expression profiles associated with drug resistance and identified molecular targets modulated by crizotinib. However, the limited therapeutic effect observed in resistant cells appears to be linked to the activation of specific drug resistance genes, particular in Hs578T/Pax.

Conclusion. Crizotinib exhibits anti-cancer activity in paclitaxel-resistant TNBC cells by modulating pathways involved in cell death. Nevertheless, its limited efficacy may be attributed to the upregulation of drug resistance-associated genes. These findings highlight the complexity of therapeutic resistance mechanisms in TNBC and suggest that combination strategies targeting these resistance pathways may enhance the clinical potential of crizotinib.

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Biologically synthesized Silver Nanoparticles treatment decreases biofilm formation in *ex vivo* infectious endocarditis model – a pilot study

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Introduction. Infective endocarditis is a widely prevalent nosocomial infection worldwide. Staphylococcus aureus is a major cause, especially due to biofilm formation on the heart valves. This study aimed to investigate the antimicrobial and anti-biofilm effects of biologically synthesized AgNPs using Kombucha tea extract against *S. aureus* in both *in vitro* and in an *ex vivo* infectious endocarditis model on pig heart valves.

Methods. AgNPs were obtained by reducing $AgNO_3$ with fermented Kombucha tea extract and characterized by UV–VIS and TEM. Antimicrobial activity was tested on *S. aureus* using broth microdilution method to determine the MIC and MBC. Biofilm inhibition was quantified through crystal violet staining. Fresh pig aortic valves were inoculated with *S. aureus* and treated with AgNPs-K at various concentrations, both by pre-treatment and co-incubation. CFU counts and Gram-stained histology quantified bacterial adhesion and biofilm formation.

Results. UV–VIS showed peak absorbance at 415 nm and TEM confirmed the successful biosynthesis of small, spherical particles of 10–20 nm and stable AgNPs-K. The nanoparticles demonstrated strong bactericidal and biofilm-inhibiting activity against *S. aureus*, with significant biomass reduction observed even at low concentrations. In the *ex vivo* heart valve model, AgNPs-K reduced bacterial adhesion by over 99% at higher concentrations and complete inhibition of biofilm formation was observed compared to untreated controls.

Conclusion. Biologically synthesized AgNPs using Kombucha fermented tea showed potent antimicrobial and anti-biofilm properties against *S. aureus* in both *in vitro*, and *ex vivo* endocarditis model. These findings highlight their promising potential as adjunctive agents in preventing biofilm-associated infections, particularly in cardiovascular contexts where conventional antibiotics show limited efficacy.

Plasma proteomic profiling and weight-loss–associated signatures after sleeve gastrectomy

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Introduction. Bariatric surgery induces profound systemic changes beyond body-mass reduction. However, the molecular basis of inter-individual variability in postoperative outcomes remains incompletely defined.

Methods. Label-free quantitative MS-based proteomics was applied to plasma samples from 26 obese patients (OBZ), 15 postoperative patients after sleeve gastrectomy (fWP), and 20 normal-BMI controls. Differentially expressed proteins (DEPs) between groups were identified ($|\log_2 FC| \geq 0.26$, $p.adj \leq 0.05$) and functionally annotated using pathway enrichment tools. In addition, 14 paired OBZ–fWP patients were selected

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for correlation analysis between percentage of total weight loss (%TWL) and protein abundance to identify molecular markers associated with surgical response.

Results. Comparative profiling revealed over 100 DEPs between OBZ and fWP groups, highlighting extensive remodeling of metabolic, inflammatory, and structural pathways. Lower-expressed proteins in fWP including CRP, FETUB, THBS1, APOA2, PON1, indicate hepatic stress, coagulation, and inflammation attenuation while higher-expressed proteins such as APOA1, IGF2, PPBP, GFAP PREP suggests improved lipid handling, antioxidant defense, and tissue repair. Correlation analysis identified 21 proteins significantly associated with %TWL ($p < 0.05$). Higher %TWL correlated with GPX3, HP, MST1, C1QA, C9, APOH, PLEK, SERPIND1, PPBP, CST3, TTR, and APCS, while PON1, PCYOX1, and F7 showed negative associations. These findings delineate coordinated activation of antioxidant, immune-modulatory, and vascular homeostasis pathways in strong responders.

Conclusion. Plasma proteomics reveals a molecular trajectory from inflammation and metabolic dysregulation in obesity toward systemic normalization after sleeve gastrectomy. The degree of total weight loss mirrors a reproducible multi-protein signature of metabolic recovery, offering potential biomarkers for monitoring or predicting surgical success.

ITF3756 as a promising anticancer compound in anaplastic thyroid carcinoma

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Introduction. Anaplastic thyroid carcinoma (ATC) is a rare, highly aggressive thyroid malignancy with rapid proliferation, early metastasis, high mutational burden, and extreme therapy resistance. It has a median survival of under 6 months and remains underrepresented in clinical trials. In this study, we aim to identify and characterize new treatment candidates with potential efficacy against ATC.

Methods. Transcriptomic profiling was performed using microarray technique to compare gene expression patterns between ATC cell lines and human thyroid epithelial cells (HPTE). Targeted screening was performed using selected compounds from the Small Molecule Immuno-Oncology Compound Library (Selleckchem). Functional validation assays included apoptosis detection, mitochondrial membrane potential assessment, cell cycle analysis, and gene expression profiling via RT-qPCR. Characterization of immune interactions between stimulated THP-1 monocytes and ATC cells in co-culture is now ongoing.

Results. Differential expression analysis identified 2164 genes as upregulated and 2425 as downregulated in ATC cell lines compared to HPTE cells. ITF3756 compound was selected for further evaluation. Functional assays confirmed that ITF3756 induced apoptosis, caused mitochondrial depolarization, and triggered cell cycle arrest in ATC cells. RT-qPCR analysis revealed modulation of the NF-κB pathway-related genes expression.

Conclusion. Our study underscores the relevance of transcriptomic profiling in uncovering novel treatment opportunities for ATC and supports ITF3756 as a promising therapeutic candidate for further development in the treatment of this disease. Further investigation into its immunomodulatory potential is currently underway.

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DOCTORAL SCHOOL

Distribution and incidence of hydrocephalus after posterior fossa tumor resection in the pediatric age group

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Introduction. Posterior fossa tumors are the most common central nervous system neoplasm at the pediatric age. Hydrocephalus is a frequent complication following posterior fossa tumours resection, impacting both pediatric and adult patients. It contributes significantly to operative mortality and morbidity. Of children with posterior fossa tumors, 10–50% have persistent hydrocephalus after primary tumor resection alone, and as such identifying predictive actors is essential for enhancing patient care and optimizing post-surgical follow-up strategies.

Methods. A retrospective, single-center single-surgeon study was conducted involving all patients with a posterior fossa tumor diagnosis, age range 0-30 years-old, hospitalized during the period of 2014-2024 at the Neurosurgical Department in Cluj-Napoca. The analysis assessed various preoperative and postoperative factors such as ventricular volume, tumor size and location relative to the fourth ventricle, clinical presentation, age at surgery, histology, presence of pseudomeningocele or infection.

Results. Our cohort's hydrocephalus incidence and age/histology distribution aligned with literature. Statistically significant predictors of hydrocephalus included larger tumor size, younger age at surgery, postoperative complications, and specific histologies.

Conclusion. Our findings confirm that tumor size, age, and histology are key predictors of postoperative hydrocephalus. These insights can guide risk stratification, patient counseling, and follow-up strategies, potentially improving outcomes. Future research should validate these predictors in larger cohorts and explore additional risk factors and variable interactions.

Insights on systemic inflammatory response index in patients with cholangiocarcinoma

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Introduction. Cholangiocarcinoma (CCA) is a primary tumor of the bile ducts with a global incidence of 6 cases per 100,000 inhabitants. Classified anatomically as intrahepatic (iCCA), perihilar (pCCA), and distal (dCCA), it is often diagnosed at late stages. The diagnostic process can be challenging and prone to errors. Systemic Inflammatory Response Index (SIRI), a metric derived from lymphocyte, neutrophil, and monocyte counts, serves as an indicator of systemic inflammation and has shown potential in the evaluation of cancer patients. Our study aimed to analyze SIRI's potential use in CCA patients.

Methods. Adult patients admitted at one Romanian hospital between January 1, 2018, and December 31, 2024, with a confirmed histopathological diagnosis of CCA,

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regardless of tumor site, were included in the study. Patients with gallbladder, ampulla of Vater, or with uncertain primary origin were excluded. Demographic and clinical data were retrospectively collected.

Results. Of the 393 patients enrolled, 59.8% were male. The median age was 67 years for males and 65 years for females ($p = 0.049$). The cohort comprised of 35.1% of patients with iCCA, 33.8% with pCCA and the remainder with dCCA. Systemic Inflammatory Response Index (SIRI), one of the lymphocyte-related ratios, demonstrated higher values in patients with metastases (median= 2.96) compared to those without metastases (median = 1.88) ($p < 0.001$). Furthermore, SIRI values exhibit increased value with worsening tumor differentiation, from a median of 1.83 in well-differentiated tumors to 2.8 in poorly differentiated ones ($p = 0.038$).

Conclusions. Systemic Inflammatory Response Index demonstrated higher values in patients with metastatic disease and poorly differentiated tumors. The SIRI may be valuable in the evaluation of patients with CCA; however, further studies are necessary to establish and validate its clinical utility.

Optimising the electrochemical detection of bacteria using AI-assisted approaches

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Introduction. The increasing antimicrobial resistance crisis urges the development of new strategies to overcome it. One of these methods is represented by early and efficient detection, utilising novel and rapid approaches, like portable sensors. Although the development of sensing technologies offers promising results for point-of-care diagnostics, their application remains limited to laboratory settings, as direct analysis of real samples without pretreatment remains challenging to achieve.

Methods. An AI-assisted electrochemical sensor was developed to classify target signals and reduce interferences from complex biological matrices using machine learning (ML) algorithms. The electrochemical behaviour of bacterial markers from *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Escherichia coli* was evaluated on carbon electrodes in commercial human serum. The ML models were applied to the raw data collected from the electrochemical tests to enhance sensitivity and improve classification accuracy.

Results. Considering the significant matrix effect and the influence of electrochemical signals, the ML model managed to analyse and identify the main characteristics that discriminate between the three bacterial siderophores and a Decision Tree Classifier algorithm was established as an additional resource for the rapid detection of pathogens.

Conclusion. This work highlights the integration of ML with electrochemical sensing for the simultaneous detection of three bacterial species. Compared to conventional diagnostic methods, the proposed system enables rapid identification of all three pathogens. With larger datasets and the inclusion of alternative classification algorithms, this approach shows strong potential for developing more accurate models for biomarker detection in complex biological matrices.

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Cardiovascular-kidney-metabolic dysfunction in heart failure patients requiring implantable defibrillators in primary prevention of sudden cardiac death

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Introduction. Sudden cardiac death (SCD) occurs frequently in patients with heart failure (HF) with reduced ejection fraction. Prevention of SCD with internal cardioverter-defibrillators (ICD) or cardiac resynchronization therapy with defibrillators (CRT-D) is recommended in patients with low ejection fraction (EF) despite optimal medical therapy (OMT). We aimed to assess prevalence and impact of cardiovascular-kidney-metabolic dysfunction in patients undergoing ICD and CRT-D implantation in the Cardiology Department of the Clinical Rehabilitation Hospital.

Methods. We retrospectively collected data including age, sex, metabolic dysfunction [ischemic heart disease (IHD), diabetes mellitus (DM)], decreased kidney function, biochemical and echocardiographic parameters from 50 patients undergoing ICD or CRT-D implantation in primary prevention. Data was analyzed using the SPSS 20 software. We used contingency tables, Chi-square test, the Spearman correlation coefficient and linear regression to study possible associations between quantitative and qualitative parameters.

Results. Mean age at ICD/CRT-D implantation was 61.06 years old. Seventy-eight percent of patients were male. IHD was present in 54% of cases. Mean left ventricular EF was 26.8%. A third of patients had an estimated glomerular filtration rate below 60ml/min/1.73 m2 and a similar percentage had type 2 diabetes mellitus (34%). Female sex was positively correlated with a higher ejection fraction. There was a significant association between use of angiotensin converting enzyme inhibitors or sartans and a lower EF, which was not seen for sacubitril/valsartan. There was no association between presence of diabetes mellitus and significant kidney dysfunction.

Conclusions. Metabolic and kidney dysfunction were highly prevalent in the studied population, independently of each other. Future studies should investigate their contribution to progression of HF and need for implantable devices.

Inflammatory immune score as a predictor of clinical outcomes in first episode psychosis

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Introduction. First-episode psychosis (FEP) represents a critical space for intervention, during which early identification of prognostic factors may significantly influence long term outcomes. Increasing evidence indicates that peripheral immune activation contributes to the pathophysiology of psychosis through neuroinflammatory mechanisms. Several serum biomarkers: pro-inflammatory cytokines (IL-6, TNF-α,

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IL-1β, IFN-γ, IL-17), chemokines (MCP-1/CCL2, IL-8), acute-phase proteins (CRP), and hematological inflammatory indices (NLR, PLR, MLR) are associated with symptom severity, response to antipsychotic treatment, and illness course. However, no standardized model currently integrates these biomarkers into a clinical prognostic tool. The aim of this study is to develop and validate a composite immunoinflammatory score, calculated using standardized (z-score) serum levels of selected biomarkers.

Methods. The project follows a prospective cohort design and includes patients hospitalized with first-episode psychosis at the County Emergency Clinical Hospital Cluj-Napoca, who will be clinically monitored over 24 months. Serum samples will be analyzed for IL-6, TNF-α, IL-1β, IFN-γ, IL-17, CRP, and MCP-1. The inflammatory score will be correlated with clinical outcomes including remission, length of hospitalization, therapeutic response, and relapse rates.

Results. We hypothesize that a high inflammatory score at baseline predicts poorer outcomes and increased relapse risk. Furthermore, simple, routine hematological markers (NLR, PLR, MLR) may partially substitute the cytokine panel, providing high clinical applicability and reduced cost.

Conclusions. This project proposes the identification of an "inflammatory clinical subtype within FEP, characterized by greater symptom burden and higher risk of poor prognosis, aiming to integrate accessible peripheral biomarkers into clinical decision-making. By linking immune dysregulation to treatment outcomes, this score has the potential to support personalized early intervention strategies and improve prognosis in first-episode psychosis.

Docetaxel and gemcitabine modulate cellular effects and long non-coding RNA profiles in non-small cell lung cancer

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Introduction. Lung cancer is the leading cause of cancer-related death worldwide, with non-small cell lung cancer (NSCLC) accounting for about 85% of cases. Chemotherapy remains the mainstay for a specific setting in metastatic NSCLC with low PD-L1 expression and poor performance status. Gemcitabine (GEM) and docetaxel (DOC) are used as single agents, yet their effects on long non-coding RNAs (lncRNAs) are currently not entirely defined. This study aimed to characterize the cellular actions of GEM and DOC and their influence on specific lncRNAs relevant to NSCLC biology.

Methods. We profiled GEM and DOC as monotherapies across LUAD (A549, CALU6) and LUSC (H520, H1703) cell lines. Cells were treated at IC50-based concentrations (GEM 10 μM, DOC 20 μM) for 48 h. Cellular outcomes included apoptosis, migration (scratch assay), cell cycle distribution, and autophagy. In parallel, MALAT1, NEAT1, and HOTAIR expression was quantified by qRT-PCR and mapped to canonical apoptotic and autophagy effectors to infer regulatory directionality.

Results. GEM and DOC reduced viability and induced apoptosis, which is consistent with their pharmacodynamic effects - GEM acts as a nucleoside analogue, and DOC as an anti-mitotic drug. They inhibited migration and produced phase-specific cell cycle arrest (DOC mainly G2/M; GEM variably S or Sub-G0/G1). Autophagy increased with GEM in CALU6 and with both drugs in H520 and H1703. MALAT1 decreased with

GEM in CALU6 and increased with DOC in H520/H1703; NEAT1 increased with GEM in A549 and DOC in H1703; HOTAIR decreased with both drugs in A549 but increased with GEM in CALU6.

Conclusions. Gemcitabine and docetaxel presented consistent cytotoxic effects across NSCLC *in vitro* models, inducing apoptosis, autophagy, and cell cycle changes aligned with their pharmacologic actions. Their differential modulation of MALAT1, NEAT1, and HOTAIR links chemotherapy-induced stress responses to lncRNA dynamics, supporting their value as potential indicators of treatment response.

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Comparison of the inflammatory syndrome in elderly patients with COVID-19 vs. influenza A

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Introduction. The course of COVID-19 infection is influenced by the inflammatory response, and cytokine storm episodes reported during the Delta variant period were associated with poor prognosis. The aim of this study was to evaluate the inflammatory profile in elderly patients with COVID-19 (Omicron variant) compared with patients with Influenza A.

Methods. This prospective study was conducted at the Cluj-Napoca Clinical Hospital of Infectious Diseases (March 2023 – March 2024) and included patients >60 years, hospitalized, with confirmed infection (RT-PCR or antigen test) and severe respiratory impairment. The proinflammatory cascade was assessed by measuring Interleukin-6 on day 1 and day 5 of hospitalization using the Luminex technique. Clinical and biological parameters and mortality were recorded.

Results. A total of 83 patients were included (39 COVID-19 and 44 Influenza A). Clinical characteristics, Charlson Comorbidity Index and mortality were similar between the two groups. Interleukin-6 on day 1 was significantly higher in the COVID-19 group (p=0.009), suggesting a more significant inflammation at the level of the pulmonary parenchyma in this group.

Conclusions. Although the Omicron variant is generally perceived as having a more attenuated inflammatory profile, patients with COVID-19 in this study showed a more pronounced inflammatory response compared with patients with Influenza A. In contrast, mortality, age and Charlson Comorbidity Index were similar between groups, indicating comparable overall clinical severity. These results require validation in larger cohorts.

In vitro, *in vivo* and *in silico* evaluation of some *Betula* Sp. extracts

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The aim of the present study was to evaluate the hepatoprotective activity of some extracts obtained from the buds and leaves of *Betula pubescens* Ehrh. and Betula pendula Roth., attributed to their secondary metabolites, using *in silico, in vitro* and *in vivo* assays.

Secondary metabolites were identified and quantified by spectrophotometric and LC-MS methods. Antiproliferative methods assessed *in vitro* cell viability on hepatic adenocarcinoma cell lines. *In vivo*, hepatoprotective activity was tested in mice with experimentally induced hepatotoxicity by CCl4. Major metabolites of tested extracts such as: betulinic acid, salicylic acid, chlorogenic acid, cryptochlorogenic acid, gallic acid, ferulic acid, isoquercitrin, hyperoside, tilianin, quercitrin, luteolin-7-O-glucoside, apigenin were subjected to *in silico* predictions using DFT/B3LYP algorithm to evaluate the main molecular descriptors of interest for explaining pharmacological mechanisms as important premises for molecular docking testing. Assessment of their oral bioavailability as a function of the predicted values of topological surface area and water-octanol partition coefficient was conducted and compared with previous studies. The antiproliferative effect was found to be dose-dependent and strongly correlated with the chemical composition of the extracts.

Administration of extracts in mice highlighted a significant attenuation of liver damage, reducing serum transaminase activity and mitigating cholestatic injury. Oxidative stress parameters were also improved. Liver histology showed ameliorated vascular congestion, multifocal necrosis, microvacuolar steatosis and mononuclear infiltrates, with frequent mitotic figures and signs of cellular regeneration, indicating partial hepatoprotection.

These findings suggest that the hepatoprotective effects of tested extracts are mediated through anti-inflammatory and antioxidative mechanisms, highlighting their therapeutic potential in managing toxic liver injuries.

From bile to bedside: the clinical relevance of biliary microbiology in pancreatoduodenectomy patients

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Introduction. Postoperative infections remain a major concern after pancreatoduodenectomy, often linked to biliary contamination occurring before surgery. Evaluating the microbiological profile of bile samples helps identify the most frequent pathogens and guide targeted antimicrobial strategies.

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Methods. This retrospective study analyzed bile samples collected between 2022 and 2024. Data on preoperative biliary drainage (endoscopic, surgical, percutaneous, or none) and microbiological results were reviewed. Cultures were classified as monomicrobial or polymicrobial, isolates were identified and antimicrobial susceptibility testing was performed.

Results. Endoscopic drainage was the most frequent preoperative procedure (55 in 2022, 46 in 2023, 42 in 2024), while 37, 26, and 25 patients, respectively, had no drainage. A total of 172 positive cultures were analyzed: 68 (2022), 56 (2023), and 48 (2024). Monomicrobial growth predominated (108; 62.8%) over polymicrobial (64; 37.2%). The main isolates were *E. faecalis* (65), *E. faecium* (51), and *E. coli* (67), followed by *Klebsiella spp*. (54) and *Enterobacter spp*. (33). *Candida spp.* was identified in 41 samples, while *Pseudomonas aeruginosa* and *Proteus spp*. were less frequent. Other *Enterococcus* species accounted for 29 isolates.

Conclusions. Biliary colonization is common in pancreatoduodenectomy, predominantly involving *Enterococcus*, *Enterobacterales*, and *Candida*. The microbial spectrum remained relatively stable across the three years studied. Endoscopic drainage was the main factor associated with positive bile cultures. Routine microbiological assessment of bile may help optimize perioperative antimicrobial management and reduce postoperative infectious complications.

From literature to laboratory: building the basis for a translational project on SSRIs and genetic variability

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Introduction. Selective serotonin reuptake inhibitors (SSRIs) are the primary pharmacotherapeutic antidepressant agents. The extent of drug exposure influences both therapeutic efficacy and adverse reactions. Several genes such as CYP2C19, CYP2D6 or CYP2B6 contribute to SSRIs metabolism and influence the therapeutic response of each patient. Therefore, therapeutic drug monitoring (TDM) serves as a tool to evaluate and correlate plasma concentration of each drug to patient therapeutic outcome, possible adverse effects and personal gene variability.

Methods. A literature search was performed using PubMed and Web of Science databases selecting articles from 2015 to 2025 with keywords including therapeutic drug monitoring, CYP2C19, CYP2D6, SSRIs, depressive disorder and anxiety disorders. We investigated the implications of CYP2C19, CYP2D6 and CYP2B6 polymorphisms on plasma concentration of sertraline or escitalopram and their therapeutic response. Ten relevant articles were included for analysis.

Results. CYP2D6 genetic variation is important for the individual differences in escitalopram pharmacokinetics. In medical setting, testing both CYP2C19 and CYP2D6 genotypes ensures a more accurate prediction of optimal drug dosing than CYP2C19 testing alone. CYP2C19 genotype and age may have an impact on dose-adjusted escitalopram levels, especially on elderly patients who are CYP2C19 poor metabolizers (PMs). CYP2C19 genotype–guided dosing can influence escitalopram treatment outcomes. PMs and ultrarapid metabolizers (UMs) may benefit the most from CYP2C19-guided escitalopram dosing.

Conclusion. TDM in correlation with patient's genetic variations can be utilized to adapt or change SSRIs therapy. Combined pharmacokinetics and pharmacogenomics offers insight into antidepressant outcomes, although other genetic, clinical, and environmental factors also play a role. Ongoing research is necessary to ensure the development of personalized psychiatric treatment.

Is penicillin still the gold standard? An unexpected resistance profile of *Streptococcus Agalactiae* in a university hospital in Cluj-Napoca

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Introduction. Streptococcus agalactiae (Group B Streptococcus, GBS) is a leading cause of invasive neonatal infections, such as sepsis and meningitis. Intrapartum antibiotic prophylaxis (IAP) with Penicillin G is considered the standard of care to prevent vertical transmission. However, epidemiological data and antibiotic susceptibility profiles for GBS are scarce in the Transylvania region of Romania. This study aimed to determine the local prevalence of GBS in obstetric patients and to characterize the antimicrobial resistance profiles of the isolated strains.

Methods. A retrospective, observational study was conducted at the Cluj County Emergency Clinical Hospital, in Cluj-Napoca, Romania. We analysed 376 cervical secretion samples collected between January 2021 and December 2022. GBS-positive cultures were isolated, and antimicrobial susceptibility testing (AST) was performed on an automated Vitek 2 Compact system, using the AST-ST03 reagent card.

Results. GBS was identified in 15.15% of the analysed samples. The implementation of a national screening protocol in November 2021 significantly improved detection, accounting for 93% of all identified positive cases identified. We identified unexpectedly high resistance rates to first-line antibiotics: 22% resistance to Penicillin and 18% resistance to Ampicillin. This finding contrasts with other national studies (which reported 100% sensitivity to these first-line antibiotics). We also identified high resistance rates to second-line antibiotics: 40% resistance to Erythromycin and 24% resistance to Clindamycin. These rates were higher than or comparable to recent national reports (23.7% and 25%, respectively).

Conclusions. Increasing resistance to Penicillin (22%) and Ampicillin (18%) challenges the empirical use of guideline-based prophylaxis in our region. Antimicrobial susceptibility testing should be considered for all GBS-positive cultures to guide appropriate intrapartum antibiotic prophylaxis (IAP), especially in patients reporting penicillin allergy, thereby preventing prophylaxis failure.

Electrochemical detection of bacterial biofilm

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Introduction. Bacterial biofilm is a structured bacterial population covered by an extracellular matrix made out of polymeric substances produced by the bacterial cells. Its identification is important, as bacteria can become up to 1000 times more resistant to antibiotics and detergents, ensuring their survival on both abiotic and biotic surfaces from healthcare and food industries. An important molecule involved in all the steps of biofilm formation is cyclic di-guanosine monophosphate (cdGMP).

Methods. All the used substances were of analytical purity. The electrochemical measurements were made using the Autolab potentiostat and the Nova software. The electrodes used were purchased from Dropsens and Micrux. Cyclic voltammetry (CV) was used for determining the best surface for detection, while differential pulse voltammetry (DPV) was used for quantifying cdGMP concentrations. Interference studies were carried out by using molecules that are frequently present in the biofilm matrix. Real life analysis were conducted by analyzing laboratory-cultivated biofilms samples from three distinct bacterial species and by analyzing a commercial fish sample spiked with cdGMP.

Results. The best electrochemical signal for cdGMP (anodic peak at around 850 mV) was registered by using commercially modified SPE with carbon nanotubes (CNT-SPE) at pH 4 in acetate buffer. The method showed linearity in the range of 25 nM – 1 µM, with a limit of detection of 15 nM. The electrochemical sensor was selective for cdGMP even in the presence of the interferents. Furthermore, the real life analysis of biofilms revealed a strong correlation between the density of biofilm and the concentrations of cdGMP detected by the sensor. When tested on the food sample, it was able to provide qualitative insights into the biofilm contamination.

Conclusion. The fast, selective and sensitive detection of bacterial biofilm was performed by correlating cdGMP concentration with biofilm production.

Canalicular cholestasis is linked with a higher hepatic venous portal gradient in patients with alcohol-related liver disease

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Introduction. The link between portal hypertension (PHT), assessed by the hepatic venous portal gradient (HVPG), and histological cholestasis has not yet been studied. We aimed to evaluate whether HVPG is higher in patients with histologically proven cholestasis. Secondly, we analyzed the interrelation between canalicular cholestasis, systemic inflammation markers, and infections.

Methods. We retrospectively reevaluated the histology specimens of 90 patients with alcohol-related liver disease between 2016 and 2020 and rescored them using the SALVE scoring/grading system. Serum from the biobank was used for ELISA tests for cytokeratin18 (CK18), heat shock protein 90 (Hsp90), toll-like receptor 4 (TLR4), tumor

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necrosis factor alpha (TNFα), and lipopolysaccharide (LPS). We analyzed the correlation between HVPG, systemic inflammation, infection, and histological cholestasis.

Results. Of the 90 enrolled patients, 81 went through transjugular liver biopsy (TJLB) and HVPG measurements. The gender ratio was 24 (29.6%) female to 57 (70.4%) male. Median HVPG was 20 mmHg (4.94 SD, 95%CI). HVPG correlated with canalicular cholestasis, but not with the ductular type. There was a significant difference in the mean HVPG value between patients without canalicular cholestasis (M=19.14; SD=4.79) and those with canalicular cholestasis (M=21.61; SD=4.84; t(80)=2.31, p=0.023). The systemic inflammation markers CK18, Hsp90, TLR4, TNFα, and LPS did not correlate with cholestasis in our cohort. Patients who had canalicular cholestasis on histology had a higher probability of being infected (Pearson Chi square p=0.041) than those with the ductular type of cholestasis (p=0.611).

Conclusion. The hepatic venous portal gradient is correlated with histological cholestasis, and particularly the canalicular type. Cholestasis was found to be an independent predictor of infection in these patients, although, usually, infections and sepsis are the cause of cholestasis.

Rino-cerebro-orbital mucormycosis – a devastating fungal invasion: a case report

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Introduction. Rhino-orbito-cerebral mucormycosis is a rare but rapidly progressive and potentially fatal fungal infection that mainly affects immunocompromised individuals. The disease spreads from the paranasal sinuses to the orbit and brain through vascular and neural pathways, causing extensive tissue necrosis, thrombosis, and severe neurological complications.

Methods. We report the case of a 50-year-old woman with ethmoidal rhinosinusitis due to mucormycosis and orbital extension. Her medical history included operated right breast carcinoma treated with radio- and chemotherapy and insulin-dependent type II diabetes mellitus. The disease had an abrupt onset with visual disturbances, left eyelid ptosis, ophthalmoplegia, exophthalmos, and frontal headache. Imaging revealed thickened mucosa of the left paranasal sinuses, orbital fat infiltration, and left ophthalmic artery occlusion. The patient underwent functional endoscopic sinus surgery (FESS) with debridement. Histopathology confirmed acute necrotizing inflammation suggestive of Mucorales infection, and antifungal treatment with Cresemba was initiated.

Results. Despite early antifungal therapy and sinonasal debridement, the infection extended to the anterior cranial fossa, requiring multidisciplinary reintervention (ENT and neurosurgery) for endoscopic nasal debridement, excision of necrotic-infected tissue, and meticulous cleaning of the frontal and ethmoidal sinuses, and removal of necrotic medial orbital tissue through a left frontal supraorbital approach. Postoperatively, the patient showed favorable evolution under systemic antifungal therapy, broad-spectrum antibiotics, and strict glycemic control.

Conclusions. Early diagnosis, aggressive surgical debridement, and prompt antifungal therapy are crucial for survival. Multidisciplinary management remains essential to control disease progression and improve outcomes in this life-threatening opportunistic infection.

Adrenal gland tumors: comorbidities, quirks, and unexpected outcomes

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Introduction. Analyzing hormone secretion and differentiating between benign and malignant adrenal masses is essential for an accurate diagnosis. As objectives, the intention is to identify metabolomic markers for adrenal tumors.

Methods. A prospective study, undertaken between February 2020 and October 2025, included 78 patients with adrenal adenomas (AA), divided into two groups: group A (functional AA) and group B (non-functional AA). Of these, 75 patients underwent surgery.

Results. Fifty-two women and 26 men with AA were enrolled, aged between 19 and 78 years (average age 52.87 years). Group A included 64 patients (hyperaldosteronism (n=17), cortisol-secreting AA (n=21), pheochromocytomas (n=24), reninoma (n=1), and testosterone hypersecretion (n=1)). Group B included 14 patients (myelolipoma (n=4), adenoma (n=4), oncocytoma (n=1), hemangioma (n=1), adrenal cysts (n=3), and carcinoma (n=1)). In the functional AA group, the predominant comorbidities were cardiovascular diseases (hypertension, ischemic heart disease, and valvulopathies), followed by metabolic diseases (obesity, diabetes, dyslipidemia). The mean blood pressure (BP) in group A was 151.51/90.56 mmHg. High blood pressure was found in patients with hyperaldosteronism, averaging 166.58/65.64 mmHg, and in those with pheochromocytomas, averaging 148.66/89.70 mmHg. Adrenal tumors > 4 cm were present in group B and in patients with pheochromocytoma. Some cases have created dilemmas regarding hormonal diagnosis.

Conclusions. Cardiovascular and metabolic disorders can sometimes hide the presence of a secreting adrenal tumor, and it is essential to exclude a secondary endocrine cause. Complete adherence to the endocrine diagnostic algorithm is crucial. For possible or malignant tumors, surgical excision is advisable, while imaging characteristics and tumor size should influence the management of benign lesions. Multidisciplinary teamwork is essential in the management of particular cases.

A comparative evaluation of 18F-FES PET/CTl and 18F-FDG PET/CT scans in breast cancer patients

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Introduction. Estrogen Receptor-Targeted Positron Emission Tomography Imaging with 16α-18F-Fluoro-17β-Fluoroestradiol (FES-PET) represents a new option for breast cancer (BC) patients. This study aimed to compare the clinical impact of using

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FES-PET and fluorodeoxyglucose F18 (FDG-PET) in selected cases.

Methods. Patients with a confirmed BC who underwent FDG and FES-PET imaging in the Nuclear Medicine Department of Centre Leon Berard from October 2022 to July 2025 were included. Clinical data were retrospectively collected. The results and impact of both investigations were analysed using descriptive statistics.

Results. Thirty-four patients matched the inclusion criteria. The median age at the time of FES PET was 65 (range 36-84). The most frequent types were lobular cancer (N=20; 58.8%) and ductal cancer (N=13; 38.2%). Hormone receptor positivity was documented at diagnosis in 31 patients (94.1%); most had HER2-negative tumors (N=29; 85.3%) and grade 2 SBR (N=24; 70.6%). Nine patients (26.5%) were metastatic at diagnosis. Twenty-six (76.5%) patients received surgery for their primary breast tumors, almost half (N=12, 46.2%) being treated with mastectomy, and most of them had axillary lymph node dissection (N=21, 80.8%). Fifteen (44.1%) patients received adjuvant chemotherapy, 20 (58.8%) received adjuvant hormonal therapy, and 13 (38.2%) received postoperative radiation therapy. There were 38 FES-PET scans, matched with FDG-PET scans, in 34 patients. The median interval between diagnosis and FES-PET was 5.5 years (0-29), and the main indications were initial staging (N=6; 15.8%), restaging (N=14; 36.8%), and ER detection (N=19; 50%). Thirty-five (92.1%) of the 38 FES-PET had differences in tracer uptake intensity and/or distribution, compared to the FDG-PET. In 26 cases (68.4%), the FES-PET result influenced the redefinition of disease extent and/or the treatment decision.

Conclusion. FES-PET evaluation can provide a significantly different result in selected breast cancer patients. The investigation had an impact on patients' clinical management in the majority of the cases.

Transcriptomic profiling of angiogenesis in clear cell renal cell carcinoma

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Introduction. Clear cell renal cell carcinoma (ccRCC) is the most common and aggressive of renal cancers, driven by VHL/HIF-mediated angiogenesis. Yet, the stage-specific transcriptomic architecture of angiogenesis and its biomarker utility remain unclear. Here, we profile the angiogenesis-related transcripts in early and late ccRCC cases to nominate biomarkers for early detection, risk stratification, and targeted therapy.

Methods. Fresh-frozen tumoral and adjacent non-tumoral tissue samples (N=73) were collected from early and late ccRCC patients. RNA isolation was performed using the TriReagent protocol from Sigma-Aldrich. For the PCR Array, cDNA synthesis was performed with the RT2 First Strand Kit, and we used the PAHS-024Z PCR Array kit to investigate angiogenesis-related gene expression alterations across early, late, and all stages of ccRCC. For RT-qPCR validation, cDNA was obtained with the High-Capacity cDNA Reverse Transcription Kit, and selected gene expression analysis was conducted with the PowerUp SYBR Green Master Mix for qPCR. Results were analyzed at Qiagen's GeneGlobe, using GraphPad Prism 10.6.1 (ΔΔCt method), and RStudio (R 4.4.2).

Results. PCR-array profiling of angiogenesis genes revealed distinct, stage-specific signatures in ccRCC. RT-qPCR validation confirms these findings.

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Conclusions. Stage-specific angiogenesis signatures converge on core pro-angiogenic circuits (VEGF/HIF, ANGPT/TIE–Notch, and S1P) consistent with ccRCC biology. Early-stage upregulation of ANGPT2, NOTCH4, and S1PR1 implicates vessel remodeling and tip–stalk control, whereas late-stage VEGFA enrichment suggests hypoxia-amplified VEGF signaling. Validation on a larger ccRCC cohort is ongoing.

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Effect of the restorative material on the mechanical performance of endodontic crowns

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Introduction. This study aimed to evaluate how material type affects the mechanical properties of endocrown restorations.

Methods. This *in vitro* study was conducted on 25 radicular models (n=5) restored with endocrowns made from five different materials: Gr1: monolithic polyetheretherketone (PEEK); Gr2: PEEK with full composite covering (PEEK-FC); Gr3: lithium disilicate ceramic (LD); Gr4: monolithic composite (C); Gr5: PEEK with buccal composite veneers (PEEK-BC). 3D-printed radicular models were created using a standard first mandibular molar (Frasaco, GMBH) to simulate severe crown damage. Endocrown restorations were obtained through milling. Cementation was performed with Variolink DC, following the manufacturer's recommendations for each material. The periodontal ligament was simulated with a layer of condensation silicone impression material. Thermomechanical aging was conducted (5–55 °C, 5000 cycles, 30 s dwell time); as a result, G5 was excluded due to composite veneering debonding. A mechanical fatigue load test was then performed on the remaining specimens, with a 100 N preload at 200, 400, and 600 N for 10,000 cycles at each force level. Axial compression fracture strength was tested by applying vertical load to the central fossa of the occlusal surface at a compression speed of 2 mm/min. Data analysis was carried out using the Kruskal-Wallis test.

Results. The mean compressive load for each group is as follows: G1: 2899.91N; G2: 770.98N; G3: 2112.26N; G4: 1257.29N. The results ($p=0.004$) indicate a significant difference between the groups ($p<0.05$).

Conclusions. The monolithic PEEK endocrowns (G1) showed superior results compared to all other groups. The veneered PEEK group (G5) experienced multiple failures, indicating poor bond strength between the two materials. The fully covered PEEK group (G2) had the lowest values among all groups, suggesting that layering PEEK negatively affects its mechanical properties.

Artificial intelligence agents for hospital management decision support: a multi-agent architecture study protocol

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Our research project leverages generative agent artificial intelligence (AI) to develop a novel multi-agent system architecture for hospital administration. The system is designed to integrate structured and unstructured hospital data, providing conversational, contextualized, and adaptive decision support for hospital administrative management staff.

An AI agent is a software system capable of learning and adapting, which extracts data from the external environment, interprets data, and makes decisions autonomously to achieve certain objectives. Currently, AI agents in hospitals are used for isolated tasks such as budgeting, bed management, operating room optimization, resource management, and patient flow management. Our project aims to move beyond these limited applications by developing a comprehensive, modular framework composed of multiple specialized AI agents with distinct roles, including import and interoperability, data quality, descriptive analysis, forecasting, anomaly detection, comparisons, decision, contextualization, and communication.

The project involves analyzing managers' needs, developing the agents and system architecture, conducting comparative validation for data analysis, and performing case studies with human validation for decision-making.

The originality of the proposed solution lies in its focus on organization-wide operational efficiency, as well as in the deep contextualization of analysis and decision-making. The „contextualization layer" enhances both analytical and decision-making processes, increasing confidence and explainability for administrative decisions.

The role of the nurse in antimicrobial stewardship

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Introduction. The unjustified and excessive use of antibiotics has ultimately led to the alarming increase in bacterial resistance. Currently, antimicrobial resistance is a priority issue for all healthcare systems and it's considered to be the main threat for public health all around the world and requires a multidisciplinary approach.

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Stewardship policies involve a series of coordinated interventions aimed to improve the use of antimicrobials. The purpose of implementing these programs is found in favorable clinical outcomes. This study was conducted with the aim of identifying the role of the nurse within these interventions and assessing its importance.

Methods. To identify the role intended for the nurses and the value of its implementation, a specific search strategy was used in the specialized literature using the PICO technique (P- problem, I- intervention, C- what is compared to, O- objective). In this study: P- antimicrobial resistance, I- antimicrobial stewardship, C- role of the nurse, O- improving the use of antimicrobials. The most important information was extracted from three databases: PubMed, Cambridge University Press and Clarivate and a synthesis was subsequently compiled.

Results. In several of the studies identified in the literature, procedures through which nurses can contribute to this process have been highlighted in detail. These procedures include: correct collection of biological samples, administration of medication, patient monitoring, compliance with nosocomial infection prevention measures and medical education provided to patients. The importance of the role that nurses play is decisive, due to their involvement 'at the patient's bedside'.

Conclusion. The involvement of nurses becomes imperative, with the aim of accelerating the beneficial effects of the antimicrobial stewardship program.

The oral-gut microbiome relationship in periodontitis patients. A literature review

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Introduction. Periodontitis is an infectious and inflammatory disease caused by dysbiosis of subgingival bacteria, resulting in progressive alveolar bone loss around teeth. Periodontopathogens and other bacteria specific to the oral cavity may translocate through the digestive system, thus causing dysbiosis. The scope of this review is to assess the recent literature on the oral-gut connection in the context of periodontal disease.

Methods. A systematic database search was performed using preestablished search strategies. The searches were conducted in three databases. A total of 578 articles were screened for eligibility. Two authors agreed on the selection process. 11 studies were considered eligible and included in the review.

Results. The gut microbiome is found to be similar to the oral microbiome in periodontitis patients. Gut microbial shifts may drive systemic inflammation and metabolic dysfunction. Tooth loss and gum disease are associated with lower bacterial alpha diversity. In contrast, the presence of natural teeth might prevent oral-gut transmission. Changes in gut microbiota significantly correlated with improvements in the periodontal status after non-surgical periodontal therapy in some studies. Other studies suggested that periodontal treatment may not be highly effective at improving gut dysbiosis.

Conclusions. Systemic inflammation caused by periodontal disease and the presence of periodontal pathogenic bacteria should be considered as risk factors for gastrointestinal dysbiosis and dysfunction. Therefore, in addition to oral care and periodontal disease control, the importance of targeted therapy for the gut microbiome is highlighted.

Innovative biochar-based platform for green and direct antibiotic detection for biomedical and environmental applications

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Introduction. Antimicrobial resistance is a global issue driven by misuse of antibiotics and surveillance across healthcare and food industry by using robust methods is mandatory. Electrochemical approaches could address the issue due to their ease-of-use, low cost, high sensitivity and selectivity and stability. Incorporating biochar (BCK), a carbon rich material can enhance the performance of the sensor due to its electrocatalytic effect. This study aimed to develop a BCK-based approach for direct and sensitive detection of antibiotics in complex real samples.

Methods. The sensor was developed by embedding the BCK onto the surface of carbon-screen-printed electrodes using polyethyleneimine (PEI). Spent coffee-derived BCK was produced by pyrolysis at 850°C under an anaerobic atmosphere and activated using KOH and CO_2. Both BCK as a solid powder and the electrode surface functionalized with BCK and PEI based composite film were characterized using microscopic, spectrometric, and electrochemical methods. The fingerprint of the target was obtained by the direct detection via differential pulse voltammetry (DPV) using solutions of various concentrations and different scan rate and pH values of the electrolytic media.

Results. The highest current signal for the electrochemical transformation of the antibiotic was achieved with the polymeric composite film. The analytical performance of the sensor was evaluated and its selectivity for the target was tested in simulating complex real samples.

Conclusions. The optimized sensor's enhanced performance demonstrates its potential for portable, decentralized detection with applications in diagnostics, environmental monitoring, and food safety.

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Identification and functional evaluation of novel therapeutic candidates in anaplastic thyroid carcinoma

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Introduction. Anaplastic thyroid carcinoma (ATC) remains one of the most lethal endocrine tumors. It is a rare and aggressive malignancy with limited treatment options and poor prognosis. Due to its high mutational burden and resistance to conventional therapies, there is an urgent need for new targeted strategies.

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Methods. Transcriptomic profiling was performed to compare gene expression between ATC cell lines (C643, CAL-62) and normal thyroid epithelial cells (HPTE). Differentially expressed genes guided the selection of compounds from the Small Molecule Immuno-Oncology Compound Library (Selleckchem). The cytotoxic potential of selected compounds was assessed via viability assay, while functional validation included analyses of apoptosis, mitochondrial depolarization, cell cycle distribution, and cell migration. Ongoing experiments assess the effects of selected compounds across additional thyroid carcinoma models (TPC1, FTC133, BCPAP, and 8305C).

Results. Microarray analysis revealed 2164 upregulated and 2425 downregulated genes in ATC cells. 17 compounds targeting key dysregulated pathways represented by differentially expressed genes were prioritized for screening. ITF3756 and fludarabine phosphate demonstrated the most pronounced cytotoxic and pro-apoptotic effects, inducing mitochondrial depolarization and cell cycle arrest.

Conclusion. Our findings highlight ITF3756 and fludarabine phosphate as promising candidates for ATC therapy. Further transcriptomic and functional validation may elucidate their underlying molecular mechanisms and therapeutic potential.

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Understanding Down syndrome in 2025: a 120-case cohort perspective

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Introduction. Down syndrome (DS) or trisomy 21 is the most frequent chromosomal disorder and the leading genetic cause of intellectual disability; associates a wide spectrum of health challenges throughout life. While many conditions are congenital, others emerge progressively, as gene overexpression and downstream molecular pathways influence the development and function of nearly every system. This study aimed to evaluate the clinical and paraclinical features of a Romanian pediatric DS cohort, to refine understanding the phenotype variability and improve case management.

Methods. Data were collected from 120 genetically confirmed DS patients evaluated at the Emergency Hospital for Children, Cluj-Napoca from 2022 to 2025, including growth trajectories versus international standards, parental age at conception, associated comorbidities and complications, and available paraclinical investigations.

Results. In this cohort, 51,66% were male and 32% were under two years old. Mean maternal and paternal ages were 35.30 and 38.15 years, respectively. Cardiovascular anomalies were common (63.33%), followed by endocrine disorders (44.16%). Immune dysregulation occurred in 37.5%, dyslipidemia or glucose abnormalities in 33.92%, and leukemia and myelodysplasia each in 3.33%. Underweight status was noted in 33.33% and overweight in 16.66%. Our cohort showed comorbidities similar to international data and highlighted a high prevalence of metabolic and immune dysfunctions. Shared features with progeroid syndromes—growth delay, alopecia, immune and metabolic disturbances—suggest a common premature-aging mechanism. Perspectives include

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developing targeted interventions that address the effects of trisomic gene dosage on different pathways.

Conclusion. Children with DS have multisystem involvement requiring individualized monitoring. Multidisciplinary care, tailored screening, and national growth and paraclinical reference charts are essential for better outcomes.

Development of liposome–AuNP nanohybrids for co-delivery of daunorubicin and cytarabine

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Introduction. Liposomes are widely used in clinical drug delivery due to their biocompatibility, capacity to encapsulate both hydrophobic and hydrophilic drugs, and ability to enhance the bioavailability of therapeutic agents. The functionalization of lipidic nanostructures with metal nanoparticles (NPs) to produce hybrid systems that combine the advantages of both classes can improve their therapeutic efficacy while also enabling multimodal bioimaging applications. The combination of Cytarabine, a nucleoside analog interfering with DNA synthesis, and daunorubicin, an anthracycline that intercalates DNA and inhibits topoisomerase II, represents the current gold-standard regimen for AML treatment. However, conventional administration of these agents is often limited by their poor selectivity. To overcome the limitations, our study aims to synthesize PEGylated AuNPS, conjugate them covalently with daunorubicin, and functionalize cytarabine-loaded liposomes with these drug-linked AuNPs.

Methods. Microwave-assisted synthesis was used to produce uniform, reproducible gold nanoparticles suitable for further modification. UV–Vis and TEM were done to confirm particle shape and size distribution. AuNPs were PEGylated to improve biocompatibility and stability and to provide carboxyl groups for later coupling. EDC/NHS chemistry was used to covalently attach daunorubicin to the AuNP surface. Moreover, liposomes were synthesized and characterized using TEM, NTA and Zeta potential.

Results. We obtained AuNPswith a plasmon peak around ~520 nm, suitable for PEGylation and covalent conjugation with daunorubicin. In parallel, we prepared nanoscale cytarabine-loaded liposomes with a narrow size distribution and stable Zeta potential, compatible with PEG-AuNP coupling for nanohybrid assembly.

Conclusion. We established a reproducible workflow for PEGylated AuNP–liposome nanohybrids, providing a solid basis for *in vitro*/*in vivo* testing of synergistic daunorubicin–cytarabine action.

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Monocyte profile and persistent inflammation post-COVID-19: a literature review

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Introduction. A persistent proinflammatory profile of circulating monocytes has been associated with the development of certain comorbidities, such as impaired renal function or pulmonary fibrosis. The expression of activation markers, as well as changes in monocyte subset proportions, has also been reported during the convalescent period following SARS-CoV-2 infection. The aim of this study was to synthesize the available literature regarding the association between the expression of these markers and Long-COVID syndrome.

Methods. We conducted a systematic search of the PubMed, Scopus, and Embase databases between January 1, 2020, and July 1, 2025, using a predefined list of monocyte activation markers. Original studies on human subjects published in English that evaluated at least one marker of interest were included. Systematic reviews, case reports, *in vitro* or animal studies, and studies addressing other pathologies were excluded. Two independent reviewers performed study selection and data extraction, and discrepancies were resolved by a third reviewer.

Results. A total of 526 abstracts were screened, of which 23 studies met the eligibility criteria and were analyzed in full text, resulting in six articles included in the review. Most publications focused on the expression of activation markers during the acute phase of the disease. CD169 (Siglec-1) was the only biomarker reported to remain elevated in monocyte subsets three months post-infection.

Conclusion. Available evidence supports the involvement of monocytes in the acute phase of COVID-19. However, there are limited data regarding the association between persistent monocyte activation and Long-COVID. Further studies are needed to clarify their role in chronic inflammation during the post-acute phase of infection.

Simplifying complexity: rzCheck™ for efficient tracking of resident performance and procedures

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Introduction. A consistent and structured approach to training and evaluating medical residents is essential for cultivating skilled and reliable physicians. Although Romania's residency program operates under standardized guidelines, their application in daily practice is often hindered by the complexity of the evaluation system and the significant time investment required for comprehensive assessments. Our aim was to design a mobile-friendly digital platform to optimize the evaluation and management process for medical residents.

Methods. The proposed application integrates a daily activity checklist and a personal logbook, enabling residents to record surgical procedures performed throughout

their training. A dedicated software development team was involved in its creation. The system utilizes a cloud-based database to provide secure, universal access to resident, surgical, and patient data, safeguarded by Firebase authentication. The Residency Coordinator can review and oversee all information entered by residents.

Results. We developed rzCheck™, a freely accessible mobile application designed for urology residents and trainers. It allows for systematic tracking of daily clinical activities and surgical performance. The daily checklist is structured around five key areas: (1) reviewing patients before morning rounds and communicating overnight updates to the supervising physician; (2) completing preoperative checklists and documenting intraoperative responsibilities; (3) managing postoperative follow-up and preparing discharge paperwork; (4) engaging in dedicated self-study; and (5) practicing surgical skills using simulators. This system enables residents to record their roles in each intervention and receive structured feedback from mentors.

Conclusions. The application offers a streamlined, structured framework for evaluating residents' progress, minimizing administrative workload while supporting consistent feedback and skill development. By promoting standardization and transparency in training assessment, the application contributes to improved educational outcomes and the formation of highly competent urologists.

Primary signet-ring cell carcinoma of the paranasal sinuses: a rare localization

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Introduction. Primary signet-ring cell mucinous carcinoma of the sinonasal tract is an exceptionally rare malignancy, often mistaken for metastatic disease from the gastrointestinal tract or breast.

Case presentation. A 60-year-old man with long-term occupational exposure to wood dust presented with progressive, severe left-sided headaches, without nasal obstruction or epistaxis.

Results. Endoscopic and imaging evaluation revealed a left sinonasal mass with limited orbital invasion. Histopathology showed mucin lakes containing signet-ring carcinoma cells, with CK7, CK20, and SATB2 positivity supporting a primary sinonasal origin. Gastrointestinal investigations ruled out a secondary tumor.

Management and Conclusion. The patient underwent chemotherapy using docetaxel, cisplatin, and fluorouracil (DCF regimen), but sadly passed away after completing only three sessions. This case is significant because it highlights the need to consider rare, malignant sinonasal tumors - even the exceptionally rare signet-ring cell type - in patients presenting with persistent headaches who have a history of occupational wood dust exposure, particularly when typical symptoms like nasal obstruction are absent.

Pitfalls and surprises in small-biopsy diagnostics: what 154 cases taught us about immunohistochemistry and communication

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Introduction. Interpretation of small biopsies often relies on focused immunohistochemistry (IHC) panels and partial clinical or imaging data. Both technical and communication gaps may generate diagnostic uncertainty or unexpected findings. The presentation highlights diagnostic pitfalls and surprises observed in daily small-biopsy practice, emphasizing the role of interdisciplinary collaboration.

Methods. From a 154-case audit of tumors diagnosed by consecutive ultrasound-guided (US-guided) core biopsies (2022–2024), which were reviewed for IHC adequacy, use of lineage-specific markers, and concordance with the pathological diagnosis, nine illustrative cases were extracted: four showing IHC-related limitations and five demonstrating communication-related pitfalls or unexpected outcomes. Each vignette summarizes context, key stains, and the main lesson.

Results. IHC pitfalls (4 cases) included incomplete lineage panels (e.g., breast metastasis without GATA3, renal oncocytic neoplasm without PAX8, urothelial carcinoma without GATA3) and occasional overreliance on CK7/CK20 tandem staining. Communication failures and surprises (5 cases) involved missing or misleading clinical information: a metastatic breast carcinoma presented as malignancy of unknown origin (MUO), a bone metastasis with unreported clinical suspicion of a lung primary, a "healed lung carcinoma and a bladder tumor later showing metastatic neuroendocrine tumor (NET), and an MUO that proved to be gastrointestinal stromal tumor (GIST).

Conclusions. Both IHC strategy and clinician-pathologist communication critically influence diagnostic accuracy in small biopsies. Recognizing these pitfalls - and the occasional surprises - helps reduce unnecessary stains, strengthens interdisciplinary dialogue, and prevents diagnostic drift.

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A novel cyanoacrylate/polylactic acid composite for topical hemostasis: development and *in vivo* validation

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Introduction. This research addresses the critical need for effective hemorrhage control by developing and testing an innovative composite hemostatic material. The project's originality lies in the design of a novel patch that integrates a cyanoacrylate (CA) tissue adhesive with a biodegradable polylactic acid (PLA) substrate, a combination not previously described in scientific literature.

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Methods. The material was created using an advanced technological process. A fibrous PLA substrate was fabricated via electrospinning, with a 10% polymer concentration identified as optimal. A key innovation was the use of sulfur dioxide (SO2) gas to inhibit premature polymerization of the CA adhesive, significantly extending the patch's shelf life and stability. This method also provides a controlled setting time of several seconds, allowing surgeons crucial intraoperative malleability for precise placement.

Results. *In vivo* testing on a rat liver laceration model compared the CA+PLA patch against electrocautery and the standard TachoSil® patch. The results demonstrated superior acute hemostatic performance for the new material. It achieved hemostasis significantly faster, with a median time of 94 seconds, compared to 256 seconds for electrocautery and 120 seconds for TachoSil®, leading to reduced blood loss. However, long-term biocompatibility assessments revealed significant disadvantages. The CA+PLA patch induced a more pronounced chronic foreign body reaction, resulting in high rates of collagenous fibrosis (79% of cases) and late abscess formation (28.6%), complications not seen with TachoSil®.

Conclusion. The research successfully developed a high-performance hemostatic patch with exceptional efficacy in rapidly controlling bleeding. While its acute performance is superior, its long-term integration is compromised by adverse tissue reactions, indicating that further research is essential to optimize its composition for improved chronic biocompatibility.

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PAT-driven quality control of 3D printed medicines

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Introduction. There has been a rapid advancement in pharmaceutical 3D printing over the past decade. However, quality control of 3D printed dosage forms and the quality control of the process is still not established, highlighting the need for rapid, non-destructive Process Analytical Technology (PAT) tools, such as Near-Infrared (NIR) spectroscopy (1,2). This study aimed to develop propranolol hydrochloride loaded printlets prepared by Hot Melt Extrusion (HME) coupled with Fused Deposition Modelling (FDM) and predict the drug concentration by NIR spectroscopy, as a PAT tool.

Methods. A Design of Experiments (DoE) approach was used to build the calibration set, with two factors: propranolol hydrochloride across 5 levels of concentration (80-120%) and mannitol at three levels (13.5-15-16.5%). Cylindrical printlets (7x4 mm, 85% infill) were printed from each filament, and both sides were analysed by NIR spectroscopy in transmission and reflectance. The calibration models were created using the Orthogonal Partial Least Squares (OPLS) regression model, in which spectral information was correlated with the theoretical drug content in each printlet. To improve the models' linearity and predictability, in both cases, SNV and Offset spectral preprocessing were applied.

Results. Both models presented a good linearity (R2>0.98) and good predictability (Q2>0.97), with low Root Mean Square Error Estimation (RMSEE <0.3). The model was validated by internal cross-validation and external validation as well. To confirm the predicted concentrations, HPLC analysis was used as a reference method.

Conclusion. The results demonstrated the feasibility of NIR as a rapid and non-destructive PAT tool for the drug concentration assessment from printlets.

Formulation development of lipid and hybrid nanosystems for targeted delivery of sorafenib in hepatocellular carcinoma

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Introduction. Hepatocellular carcinoma (HCC) is a highly prevalent and aggressive cancer, often diagnosed at advanced stages, which limits therapeutic options and contributes to its poor clinical prognosis. Conventional chemotherapy is constrained by major drawbacks, including low efficacy and severe side effects. In order to mitigate these disadvantages, the study aims to develop and comparatively evaluate two different types of nanosystems – cationic PEGylated liposomes and polymer-lipid hybrid nanoparticles (NPs) – intended for the targeted delivery of sorafenib (SOR), the first-line chemotherapeutic agent for advanced HCC.

Methods. Both nanosystems included a PEGylated phospholipid (DSPE-PEG2000) and a cationic lipid (DOTAP), which were added alongside a phosphatidylcholine derivative (DPPC) in the liposomes and zein in the hybrid NPs. The preparation methods were thin-lipid film hydration and nanoprecipitation, respectively, followed by purification through centrifugation. The nanosystems were characterized in terms of size, polydispersity index and Zeta potential using a Nano Zetasizer device, and in terms of drug concentration (µg/mL) and encapsulation efficiency by HPLC. Preliminary *in vitro* cell viability assays were conducted on HepG2 cells line using the Alamar Blue assay.

Results. For both types of nanosystems, the formulation studies showed a correlation between their characteristics and the formulation parameters. The cell viability assays demonstrated low toxicity for the unloaded nanosystems and a concentration-dependent increase in cell death for SOR-loaded formulations.

Conclusions. The developed formulations featured satisfactory physico-chemical properties, meeting the criteria for successful targeted delivery and offering new perspectives for HCC therapy. Furthermore, the nanosystems' design allows functionalization with active targeting agents, such as aptamers, to enhance their selectivity and therapeutic efficacy.

Molecular recognition strategy for early detection of hepatocellular carcinoma

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Introduction. Early detection of hepatocellular carcinoma (HCC) remains challenging, as current diagnostics often lack sensitivity in early stages. Golgi protein-73 (GP-73), a transmembrane glycoprotein overexpressed in HCC, shows higher sensitivity and selectivity than alpha-fetoprotein. According to the 2022 GLOBOCAN report, HCC is the eighth most diagnosed cancer and the third leading cause of cancer deaths worldwide, with deaths expected to reach 1.52 million by 2050. Aptamers, short, single-stranded nucleic acids with high affinity and selectivity, offer promising alternatives to antibodies. They are selected via SELEX, enabling identification of high-affinity binders for diagnostics.

Methods. GP-73 was immobilized on magnetic beads functionalized with carboxyl or tosyl groups to optimize SELEX. Negative selection and counter-selection steps were included to enhance specificity and reduce nonspecific binding. DNA sequences bound to GP-73 were amplified by PCR, with amplification yield and purity assessed by fluorescence quantification and agarose gel electrophoresis.

Results. Bradford assay showed better protein immobilization on tosyl-functionalized beads than on carboxyl-functionalized ones and initial selection rounds led to gradual enrichment of sequences with potential GP-73 affinity.

Conclusion. The selection process will continue, and sequences from the round with the highest affinity will be cloned and sequenced. Further studies will analyze aptamer structures and their interaction with GP-73. The ultimate goal is to develop an electrochemical aptasensor to complement current HCC screening methods.

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The first pediatric robotic-assisted urologic surgery program in Romania - our insights

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Introduction. Minimally invasive surgery has emerged as effective alternative to open surgery for the most complex cases, offering enhanced visualization, improved dexterity, and precision in intracorporeal suturing. These advantages are particularly relevant in pediatric patients, where anatomical constraints can be challenging.

Methods. Starting in April 2025, a national charity program for robotic pediatric interventions was developed at Medicover Hospital in collaboration with Iuliu Haţieganu

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University of Medicine and Pharmacy Cluj-Napoca. Until October 2025, 10 urologic surgical procedures were carried out on children aged 4 to 18. We hereby present our initial experience.

Results. Out of the 10 cases, there were 3 radical nephrectomies for nephroblastoma and 7 non-oncological procedures: one robotic repair of a complex urinary fistula, one varicocelectomy and 5 pyeloplasties for ureteropelvic junction obstruction. There were no major peri-operative complications. The mean operative time was 4 h 16 min, blood loss was minimal, bowel movements resumed from day 1 in all cases, there was minimal need for analgesics and the mean hospitalization time was 3 days (1-4 days). The surgical resection margins in nephroblastoma cases were all negative.

Conclusions. Robotic-assisted surgery is a safe and effective minimally invasive option for managing pediatric urology cases. It achieves similar or better surgical outcomes when compared to the standard of care while offering reduced morbidity and postoperative pain, shorter hospital stay and excellent cosmetic results.

Compound screening for the identification of therapeutic candidates in lung squamous carcinoma

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Introduction. Lung squamous carcinoma (LUSC), a subtype of non-small cell lung cancer (NSCLC), remains difficult to treat due to limited actionable targets and high resistance to conventional therapies. Targeting pathways such as angiogenesis, cell cycle regulation, and DNA damage and repair (DDR) offers promising therapeutic opportunities. This study aimed to identify potential therapeutic compounds through targeted screening in LUSC cell lines, supported by transcriptomic and bioinformatic analyses.

Methods. Gene expression profiling of two untreated LUSC cell lines (H1703 and SK-MES1) was performed using microarray technology after RNA extraction. The resulting data were compared with TCGA LUSC datasets, revealing 233 commonly dysregulated genes across multiple pathways. Based on these results, 27 compounds from a commercially available compound library were selected for *in vitro* screening. Cytotoxicity was assessed at three time points using a luminescence-based viability assay to determine IC50 values. Compounds with reproducible cytotoxic effects in both lines were selected for further functional characterization.

Results. Five compounds showed consistent cytotoxicity across all timepoints (24, 48 and 72h) in both cell lines, with two displaying pronounced and sustained reductions in viability. The overall response patterns suggest that these compounds may target distinct molecular pathways, producing complementary antiproliferative effects.

Conclusion. The screening process effectively narrowed a broad compound panel to a small group with reproducible cytotoxic activity in LUSC models. Functional tests, including cell cycle analysis, apoptosis assay, scratch assay, and RT-qPCR, will be done on downstream pathway effectors of the selected compounds for the investigation of functional pathway modulation.

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Outcomes of type 2 diabetes mellitus vs. non-diabetic patients after TAVI – a small study in a single center

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Introduction. Transcatheter aortic valve implantation (TAVI), a minimally invasive procedure first implemented for inoperable patients with severe aortic stenosis is nowadays more frequently performed. As type 2 diabetes mellitus (T2DM) affects a significant amount of patients undergoing TAVI, there are several questions that arise regarding patient and interventional characteristics, complications, and mortality.

Methods. This study included 34 patients diagnosed with aortic stenosis admitted to the Niculae Stăncioiu Heart Institute in Cluj-Napoca between 07.01.2021 and 12.04.2021 for TAVI. The data collected included patient demographics, comorbidities, echocardiographic parameters, interventional characteristics, complications, hospitalization, death, and follow-up, obtained from the hospital's informational system. Time-to-event details were obtained through contact with family members. The study aimed to assess the differences in outcomes between diabetic and non-diabetic patients that underwent TAVI.

Results. 41.18% of patients had a diagnosis of T2DM, and no statistical differences were observed in terms of comorbidities or post-TAVI complications compared to non-diabetic patients. Echocardiography demonstrated no significant differences except for lower post-TAVI mean maximum gradients in T2DM patients ($p=0.005$). Overall results post-TAVI show a significant reduction in peak aortic velocity ($p<0.001$) and mean aortic gradient ($p<0.001$). The mean follow-up was 3.36 +/- 1.916 months, and T2DM patients had tendencies of higher mean TAPSE (19.71 +/- 3.904 vs. 18.13 +/- 2.532) and lower mean ejection fraction (46.50% +/- 12.519 vs. 55.92% +/- 11.874) compared to non-diabetic patients. Death occurred in 38.24% of all cases, without significant differences between the two groups ($p=0.719$).

Conclusion. No differences in terms of patient characteristics, complications, and mortality were observed between T2DM and non-diabetic patients treated with TAVI.

From bone quality to fracture stability - the role of the second metacarpal index

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Introduction. Distal radius fractures (DRFs) are typically the first event in the sequence of fragility fractures. Despite their widespread occurrence the treatment strategy for DRFs remains a matter of debate. The second metacarpal index (IMC2) is a novel radiographic parameter that has been shown to correlate with DEXA T-scores, making it a reliable tool for assessing osteoporosis. Given the critical role of bone quality in determining fracture stability, it has been hypothesized that IMC2 may also serve as a predictor of instability in DRFs. Therefore, the aim of this study was to evaluate the

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predictive value of MCI2 for fracture instability.

Methods. A retrospective study encompassing all patients diagnosed with a DRF and conservatively treated between January 2023 and May 2025. Radiographic data, including IMC2, volar and radial inclination, and ulnar variance, were extracted from radiographs obtained at three time points: pre- and post-reduction and at 6 weeks follow-up. Univariate and multivariate linear regression analyses were applied. Receiver operating characteristic (ROC) curve analysis was employed on the best performing model to establish the optimal IMC2 threshold capable of predicting clinically significant secondary displacement

Results. Our analysis revealed an association between the IMC2 and variations (Δ) in radial inclination ($p < 0.001$), volar inclination ($p<0.001$), and ulnar variance ($p<0.001$) in univariate regression analysis. In multivariate regression analysis the IMC2 is an independent predictor of both Δ volar inclination ($p<0.001$) and Δ radial inclination ($p=0.004$). ROC analysis identified an IMC2 threshold of 41.25%, which accurately predicted a loss of volar inclination greater than 10°.

Conclusions. The results of this study highlight the value of the IMC2 as a simple, objective, and reproducible parameter for assessing DRFs instability and guiding treatment decision.

Outcomes of pulmonary artery intimal sarcoma surgery and oncological management – a 10 years single-center experience

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Introduction. Pulmonary artery intimal sarcoma (PAIS) is an extremely rare neoplasm with a poor prognosis due to late diagnosis. Pulmonary endarterectomy (PE) is the optimal surgical intervention for the resection of this tumour. The use of a multimodal treatment (surgery +chemotherapy) could significantly influence overall survival compared to chemotherapy alone.

Methods. A monocentric, retrospective, and observational study was conducted at the Marie Lannelongue Hospital, Paris, including all patients with PAIS who underwent PE between 2014 and 2024.

Results. During this period, 37 patients were diagnosed with and underwent surgery for pulmonary intimal sarcoma (PIS). The majority were men, with a mean age of 63 years. The symptoms presented were typical of pulmonary thromboembolism or chronic thromboembolic pulmonary disease. Based on clinical presentation and imaging (PET scan), pulmonary artery intimal sarcoma was suspected. Pathological examination diagnosed 33 patients with high-grade sarcoma and 4 with intermediate grade. 16% died within the first 90 days postoperatively, and among those discharged, 70% received adjuvant chemotherapy, which improved survival ($p < 0.05$). 33.3% presented with metastatic disease at the time of surgery, which was associated with a higher one-year mortality rate ($p < 0.05$). No reinterventions for recurrence were performed in any case.

Conclusions. Pulmonary endarterectomy is a surgical intervention with the potential to prolong survival in patients with pulmonary artery intimal sarcoma. The results are significantly improved when combined with adjuvant chemotherapy. The prognosis for this rare disease remains poor.

The impact of invasive fungal infections in patients admitted to the intensive care unit of a tertiary infectious diseases hospital

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Introduction. Population ageing, growing accessibility of advanced medical interventions (organ transplantation, immunosuppressive therapies) and prolonged intensive care hospitalizations with invasive procedures increase the incidence and mortality of invasive fungal infections (IFI). In response, the World Health Organization issued a report outlining recommendations for developing strategies focused on the early identification of at-risk patients, preventive measures, and timely etiological treatment. Within this framework, the present study aimed to identify the most common etiological agents of IFI in patients admitted to intensive care units.

Methods. In this retrospective cross-sectional study, all patients admitted to the Intensive Care (IC) department of the Clinical Hospital of Infectious Diseases from Cluj-Napoca in 2024 were included. The electronic health records of the patients were assessed, and all cases of IFI, either at admission or during hospitalization, were included. Patients with superficial fungal infections (oral candidiasis, urogenital infections) were excluded. The data from the electronic health records were collected and analyzed with Microsoft Excel (Microsoft Corporation, U.S.A.).

Results. During 2024, 20 cases of IFI have been identified in the IC department, with an incidence of 8.91% and a mortality of 50%. The mean hospitalization period for these patients was 29.11 days. The most prevalent etiology in the cohort was *Candida spp*. (11 cases of candidemia and one case of polymicrobial empyema), with *Candida Auris* being the most frequent (isx cases). Also, there were five cases of *Pneumocystis jirovecii* pneumonia, two cases of invasive pulmonary aspergillosis, and one case of disseminated *cryptococcosis*.

Conclusions. This study highlights the significance of understanding the predominant local etiological agents of IFI and their related risk factors to design tailored strategies for infection prevention and empirical treatment choice.

CT-US FUSION biopsy for renal masses – preliminary experience

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Introduction. Accurate diagnosis of renal tumors is essential for determining the appropriate treatment strategy. Traditional biopsy methods are limited by challenges in targeting small or anterior located lesions, which can affect diagnostic yield and patient safety. The Real-time Virtual Sonography (RVS) system allows image-fusion of real-time live ultrasound (US) with pre-operative contrast-enhanced CT, integrating the anatomical imaging capabilities of CT with the real-time guidance of ultrasound. The objective was to assess the feasibility and safety of this new technique for targeting renal masses.

Methods. In February 2025, we performed two CT-US fusion biopsies of renal masses. The first case was a 77 years old male patient with metastatic melanoma and

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concurrent 34mm left renal mass. The oncological committee recommended renal mass biopsy in order to establish the best treatment regimen. The second case was an 82 years old male patient, with 59mm right renal mass and three concurrent neoplasia and a previous negative renal mass biopsy, for whom systemic treatment was planned.

Results. Both biopsies were performed in local anesthesia. The first patient was positioned prone, whereas the second in lateral decubitus. RVS system facilitated targeting the contrast-enhanced lesion, as it improved visualization of important anatomical landmarks. The CT-US synchronization was performed using the antero-posterior axis of the kidney at the level of the maximum diameter of the tumor. The duration time of fusion imaging was 15 min and the total time of the procedure was 45 min. There were no perioperative complications. Renal cell carcinoma was confirmed in both cases with 5/5 and 4/5 cores positive.

Conclusions. CT-US fusion kidney mass biopsy is a feasible technique, representing an important advancement in renal diagnostics, offering enhanced precision and improved safety profiles. As it continues to gain acceptance in clinical practice, further research is warranted to standardize protocols and explore its application in various clinical scenarios.

Left atrial strain as a predictor of atrial fibrosis in patients undergoing atrial fibrillation ablation

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Introduction. Atrial fibrosis plays a key role in the pathophysiology of atrial fibrillation (AF), contributing to electrical and mechanical remodeling and influencing ablation outcomes. Voltage mapping during catheter ablation is the reference method for detecting fibrosis, but noninvasive markers are needed. Left atrial (LA) strain assessed by speckle-tracking echocardiography may reflect atrial compliance and fibrosis. The study aimed to assess the relationship between LA strain parameters and atrial fibrosis identified by voltage mapping in patients undergoing AF ablation.

Methods. Patients with AF were prospectively enrolled. Correlations were assessed using Pearson coefficients.

Results. Twenty-eight AF patients (67.9% male, mean age 64 ± 7.9 years) were evaluated. Paroxysmal AF was present in 39.3%, persistent in 60.7%. Mean LA diameter was 45 ± 7.2 mm, mean LA volume 84.9 ± 29.4 mL, reservoir strain 18.6 ± 10.9%, and contraction strain 7.6 ± 6.7%. During ablation, LA fibrosis (low-voltage areas <0.5 mV) was found in 10 patients (35.7%), with a mean area of 4.1 ± 8.5 cm². Lower reservoir strain correlated with lower contraction strain ($R = 0.44$, $p = 0.02$), higher LA volume ($R = 0.68$, $p < 0.001$), and larger fibrotic area ($R = 0.59$, $p = 0.01$). Contraction strain also correlated with LA volume ($R = 0.68$, $p < 0.001$) and fibrosis extent ($R = 0.48$, $p = 0.08$). Patients with fibrosis had significantly reduced LA strain values.

Conclusion. Left atrial strain, particularly reservoir strain, is closely associated with atrial fibrosis detected by voltage mapping. Echocardiographic assessment of LA strain may serve as a simple, noninvasive marker of structural remodeling, potentially guiding patient selection and risk stratification before AF ablation.

3D printing of furosemide pediatric formulations - a comparison between FDM and SSE blister filling

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Introduction. Oral dosage forms for children present a challenge for pharmaceutical formulators. Palatability, a minimal number of excipients, the requirement for precise and flexible doses, and excipient safety are critical. 3D printing has become a rapidly expanding area of study in the pharmaceutical field. Among the most widely used methods are fused deposition modeling (FDM) and semi-solid extrusion (SSE). The aim of this study was to evaluate the feasibility of manufacturing oral paediatric formulations with doses ranging from 3 to 50 mg/unit, by comparing two different 3D printing techniques: FDM and SSE blister filling (SSE-BF).

Methods. In terms of materials, furosemide, as active pharmaceutical ingredient, poly(vinyl) alcohol and mannitol as excipients for hot melt extrusion (HME) and FDM, and Techna 20 as excipient for SSE-BF, were used.

Results. All of the optimized dosage forms had an immediate release. The FDM dosage forms had a slower release of around 80% after 40 or 60 minutes, while the troches had a rapid release, 100% in only 20 minutes. A suitable weight uniformity and content of furosemide was identified, and the SSE 3D printer made the weight measurement more convenient with an in-process balance.

Conclusions. In conclusion, the advantage of FDM is that it can print dosage forms with various infills, and numerous designs, but the process is more laborious, and time-consuming. On the other hand, for SSE blister filling, more palatable excipients can be utilized, in this case, Techna 20 with a natural sweetener and Bitter-Bloc technology, and a wider dose range can be reached.

Noonan syndrome and related RASopathies: clinical patterns and evolving treatment approaches

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Introduction. Noonan syndrome (NS) is a genetic disorder within the RASopathy spectrum, caused mainly by pathogenic variants in genes regulating the RAS/MAPK signaling pathway. Advances in molecular medicine have enabled both hormonal and targeted therapeutic approaches, with promising outcomes in selected patients.

Methods. This study analyzed 34 pediatric patients diagnosed with NS and related RASopathies, evaluated in the 1st Pediatric Clinic, with comparative analysis based on recent literature from the past five years.

Results. In our cohort, 76.47% of patients presented short stature, while the

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most frequent feature combination—short stature with pulmonary stenosis—occurred in 16 cases (47.05%). Of the 26 patients with height below the 3rd percentile, two did not exhibit growth hormone (GH) deficiency, and five patients received GH therapy, achieving a median growth of 5.6 cm/year. Separately, four of the twenty patients diagnosed with cardiac conditions underwent surgical interventions

Discussion. Our results confirm that short stature and pulmonary stenosis are the most frequent features in NS, consistent with recent literature. The good response to GH therapy supports its role in managing growth delay, though outcomes vary by genotype. Additionally, recent studies highlight targeted therapies—MEK, mTOR, and tyrosine kinase inhibitors—as promising options for severe or refractory complications, potentially leading to stabilization or even remission of critical manifestations such as hypertrophic cardiomyopathy, refractory chylothorax, and lymphangiectasia, sometimes achieving near-complete remission.

Conclusions. Short stature and cardiac defects are key features of NS. GH therapy improves growth, while emerging targeted treatments show promise for severe complications. Genotype-based, personalized management is essential to optimize outcomes.

Life-threatening complications of portal vein thrombosis in children

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Introduction. Portal cavernoma is a network of tortuous vessels that develops in the portal vein, secondary to a local chronic thrombotic event, to compensate for the hepatofugal flow. Extrahepatic portal vein thrombosis (PVT), although rare in children, is the most common cause of portal hypertension (PHT) in non-cirrhotic liver pathology. Upper gastrointestinal bleeding (UGIB), splenomegaly, and thrombocytopenia may be the disease's initial presentation. 80% of the children with PVT develop UGIB, with a mortality of 8 to 10% at the first episode, subsequently increasing to 20%. Liver function is initially normal, but may be affected secondary to the cholangiopathy.

Case series. We present two cases followed up in our clinic, who developed severe complications secondary to PVT. Both patients had umbilical venous catheterization in the neonatal period as a predisposing factor, with neonatal sepsis being present in only one case. The first patient (13 years old), diagnosed at the age of one, with an occluded surgical splenorenal shunt, presents multiple episodes of UGIB, for which interventional endoscopy was initially attempted. Still, despite repeated transfusions and inotropic support, she evolved into hemorrhagic shock and cardiorespiratory arrest. The second patient (16 years old, diagnosed at 8 years old), in whom variceal banding was not sufficient to stop UGIB, which is why a rescue transjugular intrahepatic portosystemic shunt was attempted, followed by an emergency splenectomy.

Conclusions. Portal hypertension secondary to PVT develops over time, and esophageal varices and hypersplenism can lead to serious, unpredictable complications. The management of UGIB requires a multidisciplinary team in a specialized center to decrease mortality.

Keratoconus treatment by double procedure: a case of an implant of asymmetric intracorneal segments and cross-linking

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Introduction. We aimed to present the combined corneal reshaping and stretching technique using a double procedure: corneal segment implantation, followed by collagen cross-linking and one-year follow-up results.

Case presentation. We present a case of a 17-year-old patient diagnosed with keratoconus in both eyes, with decreased visual acuity in the right eye. To stop the progression of the disease and to improve the visual acuity, the implantation of the intracorneal rings and the crosslinking "epi-off" procedure was performed in the same session in the right eye. At one month, the visual acuity (VA) at the right eye was 0.2 nc, at 3 months, VA was 0.5nc, and at 6 months, VA was 0.8 nc. After 12 months, VA at the right eye was 0.8nc.

Conclusions. Cross-linking performed in the same session enhances the action of segments. A combination of intrastromal implants with collagen cross-linking treatment improves both refraction and visual acuity. The procedure is safe, but the predictability is less accurate. The effect of this combination is more pronounced after the first 6 months but takes effect slowly over the next 2-3 years.

The peripheral effect of microbiome-derived metabolite TMAO and *E. coli* lipopolysaccharide in Parkinson's disease animal models – implications of MPTP acute and semi-acute induced models on liver, kidney, heart, and the intestine

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Introduction. Parkinson's disease (PD) animal experimentation is central in understanding the disease. The two main models used to explore it in animal models being transgenic and toxic. This study focuses on the peripheral effect of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), and the interactions with trimethylamine N-oxide (TMAO) and *E. coli* lipopolysaccharide (LPS).

Methods. 148 male 6-8 weeks-old CD1 mice were used (G=25±5g), divided into 2 experiments, the first - subacute regimen (n=46) and the second - acute regimen (n=102). For the first experiment, 30 mg/kg of MPTP was administered for 5 days intraperitoneally (i.p.) for half of the mice, while the other received saline i.p., and the intervention consisted of administering TMAO orally at an atherosclerotic dose of 40 mg/kg for 50 days, while the non-TMAO groups received distilled water. For the second experiment, the MPTP regimen was 4 doses of 25 mg/kg i.p., 2 hours apart, for half of

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the mice, while the others received saline i.p. The intervention consisted of the same TMAO dose (40 mg/kg) that was combined or not, depending on the group, with LPS at a dysbiosis dose (0.18 μg/kg) administered for 50 days.

Results. The results showed a redox imbalance (RI) in multiple organs induced both by the interventions and by the disease model. Thus, the combination of TMAO and LPS enhanced the oxidative stress triggered by MPTP in the heart ($p<0.05$), intestine ($p<0.05$), and liver ($p<0.05$) and amplified the hepatic level of IL1β. A synergistic effect was noticed on RI in kidney and liver homogenates. TMAO increased IL6 levels in the liver and kidneys ($p<0.05$) while LPS influenced only the RI in the kidney ($p<0.05$).

Conclusions. Dysbiosis with increased TMAO and LPS could be a possible confounding variable for studies that use one of the most studied PD models, the MPTP toxin, with possible further implications due to the involvement of renal and hepatic RI and inflammation in the development of PD.

The use of CURODONT™ REPAIR in the management of incipient carious lesions – an evidence-based analysis

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Introduction. Curodont Repair is an innovative product based on self-assembling peptide technology, offering a modern, minimally invasive option for treating early carious lesions. This study aims to synthesize current scientific evidence on the efficacy and clinical applicability of Curodont Repair, based on publications in the specialized literature.

Methods. Clinical studies, systematic reviews, and case reports published between 2015 and 2025 in international databases (PubMed, Scopus, Cochrane Library) were analyzed.

Results. The data indicates a higher remineralization rate of enamel lesions treated with Curodont Repair than with conventional non-invasive methods, such as fluoride treatment. Additionally, good clinical tolerance and a favorable safety profile were observed.

Conclusion. The analysis emphasizes the potential of Curodont Repair as a key part of modern approaches for preventing and minimally invasive treating early caries. However, more long-term studies are needed to fully confirm these results.

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Attitudes and practices regarding volunteering among medical graduates from Romania

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Introduction. The public health sector is one of the areas that is most in need of volunteer engagement. Medical students can contribute to public health initiatives, community awareness campaigns, administrative assistance, and disaster response operations. Research shows that extracurricular engagement reduces burnout, enhances stress management, and develops leadership, teaching, and interpersonal skills, such as communication and empathy. Additionally, volunteering improves academic performance. This study aimed to explore medical graduates' perspectives on the importance of volunteering and the key factors that influence their participation in voluntary activities: personal, community, and educational. It also seeks to identify volunteering and research-related behaviors, compare motivational factors between Romanian and international graduates, and assess trends in participation across cohorts from 2021–2023.

Methods. A cross-sectional study was conducted between 2021 and 2023 among medical graduates of the Iuliu Haţieganu University of Medicine and Pharmacy (IHUMP), Cluj-Napoca, Romania.

Results. The findings revealed that most graduates acknowledged the importance of volunteering. The main motivators include personal fulfillment, opportunities for social interaction, enhancement of clinical competencies, and contribution to community well-being. Over 70% of respondents reported volunteering, with statistically significant differences between Romanian and international graduates.

Conclusion. This study suggests that strengthening educational and cultural approaches could further promote volunteer engagement among medical students. The findings provide valuable guidance for educators, policymakers, and future graduates, supporting a more integrated strategy to enrich medical education and encourage active participation in community service.

Laparoscopic partial nephrectomy - our center's experience over the last 10 years

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Introduction. Renal cell carcinoma (RCC) ranks as the sixth most common malignancy in men and the eighth most common in women. However, in clinical practice, the vast majority of RCC patients remain asymptomatic even in the late stages. For clinically localized RCC, previous studies have demonstrated that partial nephrectomy (PN) is superior to radical nephrectomy (RN) due to its advantages in preserving overall kidney function and reducing the risk of metabolic and cardiovascular complications. For tumors measuring 4–7 cm in maximum diameter (T1b tumors), PN can be performed in specialized centers on selected patients.

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Methods. We conducted a retrospective descriptive analysis of laparoscopic partial nephrectomies performed at the Municipal Hospital, Cluj-Napoca, over the past 10 years, from October 2015 to September 2025, totaling 235 patients.

Results. A total of 235 patients underwent laparoscopic partial nephrectomy at our center. Among them, 136 were male and 99 were female. Regarding the anatomical distribution of renal tumors, 127 tumors were located in the left kidney. One hundred seventy-three of the tumors were classified as cT1a (less than 4 cm diameter), with a mean diameter of 33.26 mm; the smallest tumor measured 10 mm and the largest 125mm. Tumor location varied, with 84 tumors located in the upper pole, 76 in the midrenal region, 75 in the lower pole. One hundred eighteen procedures were performed using a retroperitoneal approach, and the mean operating time was 184 minutes, with an average ischemia time of 19.43 minutes. Fifty-three procedures were made in 0 ischemia time. The majority of tumors were clear cell carcinomas of the papillary subtype, accounting for 138 cases, while 41 tumors were benign, including 21 oncocytomas. Positive resection margins were found in four cases. Most complications were classified as Clavien grade 1 or 2; however, two patients required radical nephrectomy due to ureteral injury and fistula, and in two cases a ureteral stent was placed for urinoma. The average hospital stay was 9.6 days.

Conclusions. Laparoscopic partial nephrectomy has proven to be a safe and effective surgical approach for the treatment of renal tumors in appropriately selected patients. Our experience with 235 cases demonstrates favorable perioperative outcomes, with minimal complications and good oncological control. The majority of tumors treated were small renal masses (cT1a), predominantly clear cell carcinoma of the papillary subtype, and the procedure was successfully performed using both retroperitoneal and transperitoneal approaches.

The link between umbilical blood biomarkers and ADHD risk - a systematic review

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Introduction. Attention-Deficit/Hyperactivity Disorder (ADHD) is a multifaceted neurodevelopmental condition shaped by genetic, environmental, and perinatal factors. Emerging research shows that metabolic markers found in umbilical cord blood may reflect intrauterine exposure and newborn metabolic status, offering potential predictive value for identifying infants at higher neurodevelopmental risk. Given this background, the study aimed to explore the association between measurable changes in cord blood metabolites and subsequent ADHD risk.

Methods. A systematic review of the literature was conducted using the PubMed, Web of Science, and EMBASE databases in order to identify studies measuring metabolic indicators in umbilical cord blood at birth, which also assessed ADHD-related symptoms in early childhood using standardized assessment tools.

Results. A total of 9 studies met all inclusion criteria. The heterogeneity of metabolic pathways and metabolites assessed across these studies restricted us from performing statistical analyses. The qualitative assessment did, however, suggest a potential link between changes in lipid metabolites and a higher subsequent risk of ADHD. Furthermore, a few authors noted a positive correlation between elevated

branched-chain amino acids (BCAAs) and developing ADHD in early childhood. Regarding vitamin D, no association was found.

Conclusions. Although cord blood–derived biomarkers measured at birth show promise as a predictive tool for ADHD risk and could enhance the understanding of its pathophysiology, current data remains insufficient to draw definitive conclusions.

Designing a new label-free aptasensor for *Campylobacter jejuni* detection

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Introduction. *Campylobacter jejuni* is the principal cause of the zoonotic disease campylobacteriosis, which is one of the most frequently reported foodborne illnesses worldwide. Although the origin of *Campylobacter* infection is the gastrointestinal system, neurological complications have also been reported following C. jejuni infection. This pathology has become a socio-economic concern in recent years. Conventional detection methods, such as those based on cell culture, are widely used, but they present several drawbacks: analysis often takes days, and the process is laborious. Due to these limitations, this study presents a label-free aptasensor for the selective and sensitive detection of C. jejuni.

Methods. In this study, carbon screen-printed electrodes (SPEs) were functionalized with gold nanoparticles. Subsequently, the immobilization of the aptamer (functionalized at the 3'-end with a thiol group) was performed, followed by a blocking step with 3-mercaptohexanol to prevent non-specific adsorption of the target. The aptasensor was then incubated with different concentrations of C. jejuni suspensions and electrochemically tested.

Results. The resulting aptasensor exhibits a wide linear range between 17.3 – 865 CFU/mL, a limit of detection (LOD) and limit of quantification (LOQ) of 17.3 CFU/mL.

Conclusion. Overall, a label-free aptasensor was successfully designed for the selective and sensitive detection of C. jejuni in culture samples, with promising results for its implementation as an alternative rapid test for bacterial assessment.

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Cognitive dysfunction screening in inflammatory bowel disease patients

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Introduction. Inflammatory bowel diseases (IBD), including mainly ulcerative colitis (UC) and Crohn's disease (CD), have been associated with cognitive and psychological changes, probably caused by gut microbiome disruption and systemic inflammation.

Methods. This prospective case-control study aimed to evaluate cognitive performance and biomarkers (homocysteine, serum amyloid A, brain-derived neurotrophic factor, and S100B protein) in IBD patients.

Results. A total of 90 individuals (34 UC, 21 CD, and 35 controls) were assessed using the Montreal Cognitive Assessment (MoCA), the Memory Impairment Index (MIS), and biomarker analysis. MoCA and MIS testing showed significant differences between UC, CD, and the controls, with lower scores observed in IBD groups ($p = 0.003$, $p = 0.015$). Regarding trail-making tests, digit symbol substitution tests, and forward and backward digit spans, no significant changes were observed, thus IBD patients performed worse compared to controls. No functional deficits were observed in daily activities. Biomarker analysis revealed lower brain-derived neurotrophic factor and higher serum amyloid A levels in IBD patients, correlated to MOCA and MIS scores. There were no significant differences in psychological distress between IBD patients and the controls. Subtle cognitive declines were noted across all groups during the 1-year follow-up, without any statistical significance when groups were compared.

Conclusions. In conclusion, IBD patients reported lower cognitive scores compared to the controls, while no differences in depression and anxiety scores were observed. Higher BDNF levels correlated with better cognitive functioning, while higher serum amyloid A correlated with lower cognitive functioning.

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More surfactant doses, less complications for extreme prematurity? A tertiary center experience in Romania

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Introduction. The administration of surfactant represents the key therapy in the prognostic of extreme prematurity affected by RDS. The aim of our study was to evaluate the impact of increased number of surfactant doses administration and its role in the appearance of complications in neonates under 28 gestational weeks.

Methods. We conducted a retrospective cohort study of 118 infants from 2022-2024, in I-st NICU, CECH Cluj, a III-rd level unit. Infants were grouped based on the number of surfactant doses received: noD (dose)- D0- 20 cases with BW=990 g and GA= 27.5 WG, one

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dose D1 - 46 subjects with BW= 985g and GA= 27 WG, or two (doses) D2 - 52 subjects, BW= 740 g and GA = 25 WG. First dose administrated: 200mg and respectively 100 mg/kg/dose, according to European Guidelines for the Management of RDS 2022).

Results. 100% subjects needed resuscitation in the delivery room. The APGAR score at 1 min was: 7(D0), 5 (D1), 3.5 (D2) ($p<0.001$). The number of doses was correlated with the severity of RDS and GA of the groups. No factor significantly involved in determining extreme prematurity has been identified. The dynamics of oxygen requirements remain statistically significant ($p<0.001$) in days 1,7, 28 of life, independent of the number of doses. Duration of respiratory support showed differences, with increased values in D2 group: 13 days, $p< 0.001$. The incidence of complications of prematurity was the highest in D2 group: LPV - 19.23% ($p= 0.03$) late onset sepsis - 82.69% ($p=0.006$), BPD: 84.62% ($p=0.001$) and ROP - 61.54% ($p= 0.001$). Inflammatory syndrome in 1st day of life was negative in all subgroups. In a separate multiple linear regression model, late-onset sepsis ($p <0.001$) and PDA ($p <0.036$) were independently associated with higher oxygen requirements, while higher gestational age was linked to lower oxygen exposure. The death rate was not influenced by the number of doses administered ($p=0.38$).

Conclusion. These findings suggest that while surfactant dosing reflects the initial severity of respiratory distress, long-term outcomes are more strongly influenced by infection and systemic complications.

Treatment of patients with moderately to highly exudating non-healing wounds using Resposorb Silicone border: a single center observational study

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Introduction. The aim of this study was to obtain data regarding the use of Resposorb Silicone Border in the treatment of patients with non-healing wounds with moderate to high exudate.

Methods. This study was a single-center observational study. The patients included in the study were selected according to whether they required the use of Resposorb Silicone Border. They were chosen in order to manage moderately to highly exuding non-healing wounds.

Results. The primary aim of this study was the evaluation of exudation management in patients with chronic non healing wounds. We assessed a 100% response regarding this particular aspect. Resposorb Silicone Border improved the wound edge and perilesional skin in over 90% of the cases, also promoting wound contraction. The pain related to the exudate and perilesional skin condition decreased with at least two points on visual analogue pain assessment scale. The dressing was changed every two or three days, but there was a shift to extended wear time, as the exudate control and wound contraction appeared.

Conclusions. Resposorb Silicone Border dressing was successfully used in managing wounds with low healing tendency, with moderate to high exudate. We obtained a beneficial impact on the wound edge, wound bed and perilesional skin. The healing response was positive and progressive.

Influence of cigarette smoke and heated tobacco product aerosols on biofilm formation by airway bacteria

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Introduction. Biofilms play an important role in chronic and recurrent respiratory infections by protecting microbes from antibiotics and the immune system. Cigarette smoke has been shown to promote biofilm formation by several airway pathogens, indicating that tobacco exposure can influence bacterial physiology. Heated tobacco products (HTPs), marketed as reduced-risk alternatives, also release combustion-derived constituents, but their microbiological effects remain poorly characterized. This study compared the impact of cigarette smoke extract (CSE) and HTP aerosol extracts on biofilm formation and metabolic activity of major respiratory pathogens.

Methods. Reference strains of *Staphylococcus aureus, Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Streptococcus pneumoniae,* and non-typeable *Haemophilus influenzae* were grown as biofilms in 96-well tissue-treated plates for 24 h (48 h for *S. aureus* and *P. aeruginosa*). Extracts from Marlboro Red™ cigarettes, iQOS™ Terea™ Turquoise (ILUMA™), and glo™ neo™ Azure (HyperPro™) were prepared in bacterial growth media. Biofilm biomass was quantified using crystal violet staining, and metabolic activity of planktonic and biofilm cells was measured by MTT reduction. Epifluorescence imaging (SYTO 9, WGA-AF594, Texas Red–ConA) assessed biofilm matrix composition.

Results. At 24 h, CSE significantly reduced *H. in uenzae* biofilm biomass compared with iQOS™, glo™, and control. After 48 h, CSE increased biofilm density in *S. aureus* and *P. aeruginosa*. CSE also enhanced metabolic activity in *K. pneumoniae* and *S. aureus*. HTP extracts produced limited or inconsistent changes. Microscopy confirmed thinner *H. influenzae* biofilms under CSE exposure and denser, matrix-rich *S. aureus* and *P. aeruginosa* biofilms.

Conclusions. Cigarette smoke extract exerted stronger and more consistent effects on biofilm formation and metabolism than HTP extracts, likely due to higher levels of combustion-derived constituents. In contrast, HTP aerosols had limited biofilm-modulating effects in this in vitro model. These findings suggest that combustion-related components are key drivers of biofilm promotion and warrant further studies.

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Direct antitumoral effect of zoledronic acid and the potential synergistic effect of dexamethasone

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Introduction. As part of our doctoral thesis, we investigated the direct effects of zoledronic acid and dexamethasone on various tumor cell cultures. Cytoxicity, single agent and combined administration, migration studies, colony formation studies, morphology, cell cycle, and cell death were investigated.

Methods. Cell cultures of lung, prostate, and breast cancer were investigated – cell lines were purchased from American Type Culture Collection (ATCC). Cell viability assays and IC50 determinations for Zoledronic acid and Dexamethasone were performed. Similarly, the potential synergistic effect was investigated.

Results. A synergistic effect is observed in the lung and prostate groups, whereas an opposite apparent impact is observed in the breast group. Regarding cell migration, the combination has a greater inhibitory effect on lung colonies and a lesser effect on breast colonies compared to zoledronic acid alone.

Conclusion. These results may have an impact on how we administer zoledronic acid, with a potential benefit of adding dexamethasone as standard pre-medication before administration of ZOL. Further studies are needed in this area.

The efficacy and safety of intra-meatal application of tadalafil cream versus oral administration: results from a randomized, two-administration route, cross-over clinical trial

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Introduction. Tadalafil cream, a topically administered phosphodiesterase-5 inhibitor (PDE5), presents a potential alternative to oral PDE5 inhibitors like tadalafil for the treatment of erectile dysfunction (ED). This study evaluated the non-inferiority and potential superiority of tadalafil cream compared to oral tadalafil.

Methods. This randomized controlled trial employed a cross-over design with two treatment periods of two weeks each, separated by a one-week washout phase. Thirty-five male participants aged 18-75 with diagnosed ED (International Index of Erectile Function-Erectile function: IIEF-EF score < 26) were randomized to receive either tadalafil cream or oral tadalafil. Tadalafil cream was applied topically,

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while tadalafil was taken orally. The primary endpoint was IIEF-EF, and secondary endpoints were measured using the International Index of Erectile Function (IIEF) domain scores. Adverse events and treatment preferences were also assessed.

Results. Tadalafil cream showed a higher increase in sexual function across all IIEF domains compared to oral tadalafil. The lower bounds of the confidence interval [improvement: final-baseline scores between tadalafil cream and oral tadalafil 0.72 (95% CI -2.72-4.15)] were above the non-inferiority margin of -3.22, confirming tadalafil cream's non-inferiority in the erectile function domain. In the intercourse satisfaction domain, tadalafil cream was superior to oral tadalafil. At the end of the trial, 88.57% of participants preferred tadalafil cream (95% CI 73.26%-96.79%), a result significantly above the non-inferiority margin that indicated superiority ($p < 0.001$). No systemic adverse events were reported for tadalafil cream, and significant differences in dizziness, headache, nasal congestion, and erythema were observed between the two treatments.

Conclusions. Tadalafil cream is a safe and effective treatment for erectile dysfunction, demonstrating non-inferiority and potential superiority over oral tadalafil, with a high patient preference. Its topical administration offers a promising alternative for patients, particularly those with cardiovascular diseases where oral PDE5 inhibitors are contraindicated or less well tolerated.

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A scoping review of agent-based modelling of nosocomial COVID-19 transmission

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Introduction. Application of Agent-based modelling (ABM) to understanding hospital-acquired infections (HAIs), particularly in the context of COVID-19, remains limited. To address this gap, we aimed to map the existing literature on the use of ABM for simulating and managing the transmission of SARS-CoV-2 within healthcare settings.

Methods. We conducted a systematic search on Web of Science, Scopus, IEEE Explore, and PubMed, on 29 Aug 2025. The search strategy targeted original studies published in English within the last decade that involved agent-based models of hospital-acquired COVID-19.

Results. We identified nine articles that fulfilled our criteria. Most models were custom-built and utilized a discrete-time SIR (Susceptible-Infected-Recovered) model, enabling specific (e.g., day-by-day) estimation of transmission parameters. Three studies modeled a hospital, five simulated generic ones, and one examined a region and its hospitals. The primary agents were patients and healthcare workers (HCWs). Key findings on intervention effectiveness included: a) universal masking, patient testing, and HCW isolation were consistently effective at reducing nosocomial

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COVID-19; b) de-escalation of controls revealed that removing multiple control measures simultaneously exponentially increased infection risk; c) N95 masks for HCW were found to be more cost-effective than surgical masks. Modeling of transmission dynamics highlighted that HCW-HCW interactions were a primary route of spread, and higher-transmissibility variants increased transmission, especially from pre-symptomatic individuals.

Conclusions. Agent-based modeling can differentiate between multiple infection control measures, even when they co-occur, giving valuable insight into managing nosocomial COVID-19. However, the field would benefit from the consistent application of existing ABM reporting guidelines and a greater incorporation of primary data to enhance model validity and utility.

Implementation and evaluation of a school-based smoking and e-cigarette use prevention program among adolescents in rural Romania

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Objectives. This study focuses on prevention of smoking and electronic cigarette use and has three objectives. Firstly, it evaluates the exposure to health education in schools, focusing on the frequency and content of smoking prevention lessons. Secondly, explores students' perceptions and feedback on the smoking and e-cigarette prevention program they attended, and finally, assesses teachers' view on health education in rural schools, and their evaluation of the smoking and electronic cigarette prevention initiative.

Methods. A longitudinal study was conducted in schools from rural Romania. Students were assigned to control and experimental groups. Students in experimental group participated in a school-based prevention program consisting of 5 smoking prevention lessons delivered face to face by teachers and peer leaders and two lessons about prevention of e-cigarette use delivered as online presentations by the research team. Data were collected at baseline (T1-October 2019-November 2019, 748 students), followed by the implementation of the program in the experimental group (January-March 2020, and December 2020-January 2021, 452 students) and post-intervention (T2-January 2021-March 2021, 264 pupils). 240 children participated in both assessments.

Results. Regarding to students in both assessments, 57.3% students in experimental group and 38.9% in the control group at T1 were not exposed to any smoking prevention lesson. At T2, in the experimental group, the number of lessons increased. While at T1 in the experimental group, only health effects of smoking were discussed by more than a quarter, at T2, common subjects discussed also included refusing cigarettes (44.7%), smoking addiction (39.3%), peer pressure (32%). Both students and teachers appreciated positively the program, its content and materials. All teachers found school-based educational programs useful and necessary, though 61.9% said their school lacks a health education subject in the curriculum.

Conclusion. This study underlines that a structured and interactive approach using multimedia tools in health education programs targeting adolescents can be useful in smoking prevention.

Predictors of suicidal and non-suicidal self-injurious behaviors in adolescents admitted for emergency psychiatric care before and after the COVID-19 pandemic

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Introduction. Adolescent self-harm and suicidal behaviors represent a growing challenge in pediatric psychiatric emergencies, further intensified by the social and emotional disruptions of the COVID-19 pandemic. This study explored the risk and protective factors associated with suicidal behaviors (SB) and non-suicidal self-injury (NSSI) among adolescents presenting to a pediatric psychiatry emergency unit before (2019) and after (2022) the pandemic.

Methods. Data from 341 patients aged 6–18 years were analyzed using both logistic regression and random forest modeling to capture convergent and complementary predictors.

Results. Across analyses, prior suicidal ideation (OR = 68.4, $p < 0.001$) and depression (OR = 6.8, $p < 0.001$) consistently emerged as the strongest predictors of suicidal behavior. Additional risk factors included parental absence due to migration (OR = 11.4, $p = 0.020$) and female sex, while school-related conflicts acted as a protective factor (OR range = 0.12-0.33). For NSSI, a history of self-harm (OR = 52.4, $p < 0.001$) and a higher number of psychiatric comorbidities (OR = 1.7, $p = 0.003$) markedly increased risk. Interestingly, conduct disorder showed a protective association (OR = 0.18, $p < 0.001$) — a finding not previously described in the literature. Although the two analytic approaches showed substantial overlap, the random forest models additionally highlighted the importance of borderline personality traits and academic performance as relevant predictors. Post-pandemic increases were observed in depression, suicidal ideation, and exposure to negative life events.

Conclusions. Our results emphasize the complex interplay between emotional vulnerability, psychiatric comorbidity, and contextual stressors. Integrating traditional regression and machine learning approaches offers a more nuanced understanding of adolescent self-harm, supporting early identification and tailored interventions in clinical settings.

Renal protective effects of SGLT2 inhibitors beyond tubuloglomerular feedback: podocyte protection

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Introduction. Sodium-glucose cotransporter 2 inhibitors (SGLT2i) have become a cornerstone therapy for slowing chronic kidney disease (CKD) progression and reducing cardiovascular risk in both diabetic and non-diabetic patients. Beyond modulating tubuloglomerular feedback, SGLT2i exhibit pleiotropic effects, including direct podocyte protection. Podocyturia indicates podocyte injury and detachment,

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reflected by urinary nephrin, podocin, and podocalyxin—key proteins for glomerular filtration barrier integrity. Their early urinary presence precedes microalbuminuria, suggesting their potential role as early biomarkers of renal injury.

Methods. Patients with chronic kidney disease from the Nephrology Clinic in Cluj-Napoca, eligible for SGLT2i therapy, were enrolled from July 2024. A total of 88 patients, both diabetic and non-diabetic were included. Blood and urine samples were collected at baseline, three, and six months, and routine laboratory tests for renal function evaluation were performed. Urinary nephrin, podocin and podocalyxin levels were quantified using ELISA technique.

Results. Significant positive correlations were found between the reduction in podocyte injury markers (podocin and podocalyxin) and the decrease in albuminuria. Multivariable regression analysis demonstrated that reductions in urinary podocalyxin were significantly associated with improvements in both eGFR and albuminuria, suggesting a close link between podocyte recovery and renal function preservation.

Conclusion. Podocalyxin emerged as the most sensitive biomarker, followed by podocin, in reflecting renal response to SGLT2i therapy. Their early decrease correlated with the initial dip and subsequent improvement in albuminuria, supporting their role as early indicators of podocyte recovery and renal protection in CKD.

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Assessing the link between stress and gut dysbiosis in depression

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Introduction. Major depressive disorder (MDD) represents a primary public health concern, with significant impact on quality of life and socio-economic burden. Growing evidence highlights the involvement of the gut-brain axis (GBA) in depression, through alterations in gut microbiota, increased intestinal permeability, and immune-neuroendocrine mechanisms. Psychological stress can alter gut microbiota composition, increase intestinal permeability, and promote lipopolysaccharide (LPS) translocation into the bloodstream, activating systemic inflammation and the hypothalamic-pituitary-adrenal (HPA) axis, thereby contributing to the onset and persistence of depressive symptoms.

Methods. The study included patients diagnosed with MDD and healthy controls. Psychiatric evaluation was conducted using the Hamilton Depression Rating Scale (HAM-D) and the Global Assessment of Functioning (GAF). Clinical, anthropometric, and routine laboratory data were collected, together with serum markers of intestinal permeability (zonulin, I-FABP, LBP), inflammation (CRP, IL-6, TNF-α), and cortisol. Serum analyses will be performed using ELISA techniques. Of 93 initially enrolled participants, 80 (50 patients and 30 controls) were included.

Results. Preliminary findings show increased C-reactive protein (CRP) levels in MDD patients compared with controls, suggesting an inflammatory process associated with depression. A higher proportion of patients also presented elevated cortisol levels, indicating HPA axis hyperactivation. These preliminary data support an

association between stress, inflammation, and depressive symptomatology.

Conclusions. Preliminary results confirm the link between stress, inflammation, and depression. The study contributes to a better understanding of the role of the GBA in MDD and may open new biologically-oriented therapeutic perspectives. Next steps include completion of ELISA analyses and detailed statistical data processing.

Interleukins – An effective diagnostic strategy in early-onset neonatal sepsis

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Introduction. Early and accurate diagnosis of neonatal sepsis remains a major challenge in clinical practice. Inflammatory biomarkers such as interleukins (ILs) may provide additional diagnostic and prognostic value alongside conventional markers like C-reactive protein (CRP) and procalcitonin (PCT).

Methods. This prospective study was conducted in our unit, between Jan 2024 and Dec 2024. A total of 66 neonates of both sexes, terms and preterms, with suspected early-onset sepsis. Data included clinical evaluation, perinatal history, documentation of sepsis-related signs and symptoms. Blood samples were collected on days 1, 3 and 6 of life. We determined serum levels of interleukins (IL-1, IL-6, IL-10, and IL-33), CRP and PCT. Laboratory analyses were performed using standardized immunoassay techniques. The neonates were divided into two groups: .

Results. A total of 66 neonates of both sexes, a case group (n = 33) consisting of infants with clinical and laboratory evidence of infection, and a control group (n = 33) of clinically well neonates were evaluated. All interleukins showed significantly higher mean values in the sepsis group compared to controls on day 1 ($p<0.001$). ROC analysis demonstrated strong discriminative ability for IL-1 (AUC = 0.88, sensitivity = 79%, specificity = 97%) and IL-33 (AUC = 0.99, sensitivity = 100%, specificity = 97%). IL-6 showed moderate performance (AUC = 0.70). IL-10 was higher in controls, reflecting its anti-inflammatory modulation (AUC = 0.80 for predicting non-septic status). Within-group analysis revealed limited day-to-day variation in ILs values among cases, but significant decreases were observed in controls. Correlation analysis indicated strong associations between PCT, PCR, and IL-6 in septic neonates ($p<0.05$).

Conclusion. IL-1 and IL-33 measured on the first day show excellent diagnostic accuracy for neonatal sepsis. Their combination with conventional biomarkers (CRP, PCT) may improve early identification and monitoring of the inflammatory response in newborns.

Pathogenesis of focal segmental glomerulosclerosis and minimal change disease: insights from glomerular proteomics

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Introduction. Podocyte injury is widely recognized as a central pathological feature in both focal segmental glomerulosclerosis (FSGS) and minimal change disease (MCD), conditions that share common manifestations such as foot process effacement and the development of proteinuria. Despite significant advances in understanding glomerular diseases, the precise molecular and cellular events that trigger podocyte damage remain elusive. In particular, the signaling pathways and pathogenic mechanisms responsible for cytoskeletal disorganization and structural alterations in podocytes are still only partially elucidated.

Methods. Our objective was to deepen the understanding of these molecular pathways by performing bottom-up proteomic profiling on laser-capture microdissected glomeruli obtained from patients with MCD and FSGS.

Results. Between the two groups forty-six differentially expressed proteins were identified, $p < 0.05$, fold change ≥ 1.2. Pathway analysis showed that 16 out of 46 proteins were associated with the immune system, with E2 ubiquitin-conjugating enzyme (UBE2K) and complement factor H-related protein-1 (CFHR1) yielding the highest fold change in FSGS compared to MCD. The two target proteins were further validated through immunohistochemistry, confirming the podocyte localization of UBE2K and endothelial staining of CFHR1. Other differentially expressed proteins were linked to pathways involved in the mechanisms involved in regulation of cytoskeleton structures and cell adhesion.

Conclusion. Our results indicate that dysregulation of the complement system may result from disturbances in the ubiquitin–proteasome system, ultimately driving cytoskeletal rearrangements and leading to foot process effacement in FSGS.

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Comparative analysis of artificial intelligence models in developing a rehabilitation plan for a complex post-stroke case

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Introduction. Artificial intelligence (AI) is increasingly used to support clinical reasoning and rehabilitation planning, yet its performance in complex post-stroke cases remains uncertain. Integrating multimorbidity, prevention, and functional outcomes into AI-generated recommendations is a key challenge for rehabilitation medicine. This study aimed to compare several large language models (LLMs) in developing rehabilitation strategies for a patient with multiple comorbidities after ischemic stroke.

Methods. A detailed post-stroke clinical profile, based on data from a prospective study (PMCID: PMC6400340), described a 68-year-old male with hypertension, diabetes mellitus, atrial fibrillation, and prior myocardial infarction, presenting with right hemiparesis and expressive aphasia (Barthel Index 45/100, mRS 4). The same standardized prompt was provided to three LLMs—GPT-5, Claude, and Gemini—requesting a structured rehabilitation plan including functional diagnosis, therapeutic goals, and preventive recommendations. Outputs were assessed qualitatively by three rehabilitation specialists using a 5-point Likert scale for accuracy, applicability, personalization, and clarity.

Results. All models produced clinically coherent rehabilitation plans. GPT-5 demonstrated the best structure and adherence to guidelines, Claude emphasized clarity and psychosocial elements, while Gemini integrated preventive and long-term management recommendations most effectively. Differences were noted in the level of functional reasoning and prioritization of therapy components.

Conclusion. AI-based models can assist clinicians in creating structured, preventive, and personalized rehabilitation plans for complex post-stroke patients. Model-specific variations highlight the need for standardization and validation before routine implementation in rehabilitation medicine.

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Tunable structure-activity relationships define divergent cellular responses in ceria-graphene nanocomposites

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Introduction. Graphene-based materials (GBNs) have emerged as promising candidates for diverse biomedical applications, but their clinical translation has been hindered by their inherent cytotoxicity.

Methods. We synthesized three distinct cerium-containing graphene nanocomposites using a single-step *in situ* electrochemical exfoliation process and

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investigated their structure-activity relationships in normal dermal fibroblasts (BJ) and hepatocarcinoma cells (HepG2).

Results. The properties of the resulting nanocomposites, including their morphology, cerium loading and the surface redox state (Ce^{3+}/Ce^{4+} ratio) were directly dictated by the employed synthesis parameters, such as the cerium salt precursor and its concentration. These distinct materials induced cell-specific responses, that ranged from selective cytotoxicity in HepG2 cells to a significant hormetic (stimulatory) effect in BJ fibroblasts.

Conclusion. Our findings indicate that by employing the *in situ* electrochemical exfoliation method, the hybrid graphene compounds might be further tailored for specific purposes, moving the narrative beyond the mere functionalization of the graphene in order to achieve biocompatibility.

Obesity, morphology, and the immune landscape in endometrial cancer

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Introduction. Obesity is a modifiable risk factor for endometrial cancer, influencing its incidence and biological behavior. Through metabolic, hormonal, and inflammatory pathways, excess adiposity could interfere with the tumor microenvironment and immune dynamics. Morphological evaluation of inflammation patterns may provide insight into obesity-related modulation of the immune microenvironment.

Methods. This study was conducted on a cohort comprising patients with histologically confirmed endometrial cancer treated between 2020 and 2024. Morphological and inflammatory features were reassessed on hematoxylin–eosin slides using semiquantitative scores for evaluating immune anti-tumor activity: invasive margin inflammation score (IMIS), tumor necrosis index (TNI), stromal tumor-infiltrating lymphocytes score (sTILs), and anti-tumor immune activity (ATA). Clinical variables, including age and body-mass index (BMI), were extracted from patient records and correlated with histological features. Statistical tests were performed using jamovi.

Results. The study included 76 cases. Age and obesity classes were predictors of histological grade ($p=0.027$), with higher age increasing ($p=0.021$, OR=1.06) and higher obesity classes decreasing the odds of higher-grade tumors ($p=0.033$). Obesity class also correlated with IMIS ($p=0.021$), ATA ($p=0.036$), and histological grade ($p=0.026$). IMIS and sTILs were both associated with tumor grade ($p=0.047$ and $p = 0.035$, respectively). ATA scores correlated with histological grade ($p<0.001$) and LVSI-positive tumors ($p=0.015$). TNI was associated with ATA ($p<0.001$, OR≈9.3) and inversely with sTILs ($p<0.001$), while ATA correlated with the presence of tumor

necrosis (p=0.010).

Conclusion. Obesity can influence the morphological and immune landscape of endometrial cancer, being associated with histological grade of differentiation and distinct inflammatory patterns. The results indicate an immune–morphological interplay within the tumor microenvironment in the context of obesity, with implications for further integrative evaluation of morpho-immune markers in endometrial cancer.

Beyond LVEF in DCM: insights from speckle-tracking echocardiography

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Introduction. In patients with dilated cardiomyopathy (DCM), eligibility for primary prevention implantable cardioverter-defibrillator (ICD) therapy relies predominantly on left ventricular ejection fraction (LVEF), despite its limited ability to fully capture myocardial dysfunction. Speckle-tracking echocardiography parameters, including global longitudinal strain (GLS), myocardial work (MW) indices, and mechanical dispersion (MD), offer complementary insights into contractile performance and temporal dyssynchrony, with potential to detect dysfunction beyond LVEF.

Methods. In this prospective study, 33 patients with non-ischemic DCM underwent speckle-tracking echocardiography. Patients were stratified by LVEF into <35% and ≥35% groups. GLS, myocardial work indices (GWI, GCW, GWE, GWW), and MD were evaluated in both groups. MD ≥70 ms was considered abnormal.

Results. Patients with LVEF <35% (n = 18) were older than those with LVEF ≥ 35% (60.1 ± 13.9 vs. 49.8 ± 15.3 years, p = 0.05), with similar sex distribution between groups (p = 0.69). The LVEF < 35% group showed significantly worse GLS, lower GWI, GWE, GCW, and higher MD and GWW (p < 0.05 for all). Although MD ≥70 ms was more frequent in patients with LVEF <35% (88.9%), 60% of those with LVEF ≥ 35% also exhibited elevated MD. While not statistically significant, this finding suggests relevant mechanical dyssynchrony in a notable proportion of patients despite mildly reduced or preserved LVEF.

Conclusion. Although altered MW indices and elevated MD align with advanced systolic dysfunction, a relevant subset of patients with LVEF ≥ 35% demonstrates increased MD suggesting subtle contractile heterogeneity not reflected by LVEF. Speckle-tracking parameters may therefore offer valuable insights for a more comprehensive evaluation of myocardial contractile performance in patients with DCM.

Shaping the future of medicine – European Union artificial intelligence act

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The European Union Artificial Intelligence Act (AIA), REGULATION 024/1689, published on 13 June 2024, establishes the legal framework to regulate artificial intelligence systems within the EU, aiming to ensure their safety, transparency, and respect for fundamental rights. AIA introduces harmonized rules for AI, addressing potential risks to health, safety, and fundamental rights. It outlines the responsibilities of member states and provides a timeline for implementation (https://artificialintelligenceact.eu/). The AIA defines an „AI system" as a machine-based system…designed to operate with varying levels of autonomy and…may exhibit adaptiveness after deployment. Such systems can operate with a degree of independence from human intervention and possess self-learning capabilities that enable them to evolve during use. Transparency, encompassing explainability and interpretability as critical technical requirements, is a fundamental principle, particularly for „high-risk" AI systems. The AIA classifies AI systems in medicine as high-risk technologies with the potential for serious harm, thereby imposing stringent standards for safety, transparency, and human oversight. Thus, medical AI systems must achieve a high level of accuracy and demonstrate resilience against errors, faults, and malicious cyberattacks that could compromise patient safety. While the primary focus of the AIA is on AI providers and deployers, it strongly emphasizes the need for „AI literacy." The regulation highlights the crucial importance of healthcare professionals understanding and effectively interacting with AI technologies. The convergence of the AI Act with existing medical device regulations (MDR/IVDR) establishes a new, integrated pathway to market conformity within the EU. The Authority for the Digitalization of Romania is designated as the national competent authority for AIA implementation. However, as of 8 November 2025, the Romanian AI Regulatory Sandbox remains undeveloped.

STUDENT SECTION – SCIENTIFIC START

Cystic fibrosis in a 70-year-old patient with tracheobronchomalacia?

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Introduction. Cystic fibrosis (CF) is considered a childhood disease. However, an increasing number of cases diagnosed in adulthood have been reported in the medical literature. The phenotype associated with an adult diagnosis is usually milder and tends to affect fewer organs at the time of outbreak. The diagnosis is based on identifying CF transmembrane receptor dysfunction together with characteristic clinical features of the disease.

Case Report. We report the case of a 70-year-old male patient known with COPD stage III GOLD, bronchiectasis, and tracheobronchomalacia. The patient presented with dyspnea, productive cough with muco-purulent sputum, and asthenia. On respiratory examination, an emphysematous chest appearance was noted, while auscultation revealed harsh vesicular breath sounds with prolonged expiration and bilateral basal crackles. Laboratory investigations showed the presence of an inflammatory syndrome and sputum examination revealed an infection with *Pseudomonas aeruginosa*. The patient has a history of *Pseudomonas aeruginosa* infection diagnosed four months ago and treated with Ceftazidime. The current recurrence of the infection raises concerns regarding the possibility of chronic bacterial colonization associated with the underlying bronchiectasis. Moreover, considering the patient's family history (a grandson diagnosed with CF) and the CT chest findings (bilateral bronchiectasis and tracheobronchomalacia), a diagnosis of late-onset CF was considered, and testing for the most common CFTR gene mutations was recommended.

Conclusion. The increasing incidence of CF is caused by a combination of factors, including the widespread availability of testing for CFTR mutations, and simpler diagnostic criteria. Although diagnosis in adults was once considered a medical curiosity or a missed childhood diagnosis, it is now understood that it often results from CFTR mutations with residual function, leading to both delayed onset and milder disease severity.

Aptasensor-based detection of DKK1 in liquid biopsies: integrating bioinformatics and clinical validation in pancreatic cancer

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Introduction. Dickkopf-1 (DKK1) is a soluble inhibitor of the Wnt/β-catenin pathway increasingly recognised as a promising cancer biomarker. Pancreatic ductal adenocarcinoma (PDAC) is commonly diagnosed late, with few circulating biomarkers and limited screening options. Sensitive detection of DKK1 could support earlier diagnosis. This study aims to develop and clinically evaluate the first electrochemical aptasensor for DKK1 detection in PDAC liquid biopsy.

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Methods. Preliminary work included a systematic review and a bioinformatics analysis of DKK1 expression in human cancers using TCGA/GTEx databases. Survival was assessed using Kaplan-Meier curves and log-rank tests. The experimental phase involves: (1) development and optimization of the aptasensor and (2) clinical validation in 30 PDAC patients and 30 controls. Ethics approval was obtained from the UMF Cluj-Napoca, Romania.

Results. DKK1 showed diagnostic or prognostic value across several cancer types. In PDAC, scarce data suggest higher accuracy than CA19-9, with detection limited to ELISA. Bioinformatics analysis confirmed significantly higher DKK1 expression in PDAC, with a significant prognostic impact. Based on preliminary experimental data, the optimal sensing platform was selected: a graphene oxide-based electrode modified with a biochar-polycysteine composite, and functionalised with a DKK1 specific aptamer. A preliminary calibration curve showed a progressive increase in signals with rising DKK1 concentrations in the 0.5–10 ng/mL range. Each step was characterised using electrochemical methods and scanning electron microscopy.

Conclusion. Preliminary findings support the feasibility of a sensitive electrochemical aptasensor for DKK1. Further optimization and clinical testing may enable a rapid, minimally invasive diagnostic tool for PDAC.

When imaging falls short: the added diagnostic value of endoscopic ultrasound-guided fine-needle aspiration

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Introduction: Endoscopic ultrasound-guided renal fine-needle aspiration (EUS-FNA) provides an alternative technique for tissue sampling of renal lesions, however few cases have been recorded thus far. The first reported case dates back to 2002, and until now, there is only one case series in the literature which includes 15 patients. Ultrasound-guided percutaneous renal biopsy (PRB) is the usual procedure for sampling renal lesions, however it may not be possible in some cases: anatomical restrictions such as obesity, elevated kidney placement, central or anterior mass, and skin-to-tumor distances more than 13 cm.

Case report: We are presenting the case of a 68 years old patient who was referred to our Department in order to be assessed for renal and suprarenal biopsy. Regarding his medical history, he was previously diagnosed with clear cell carcinoma, and underwent a right kidney nephrectomy tree years prior to this appointment. We performed the EUS examination which revealed two tumoral masses in the left kidney, a finding that was not anticipated, since the CT scan had revealed only a solitary lesion. After we visualized and chose the lesions, we performed EUS guided FNA on both the kidney and the suprarenal

gland. The samples collected were sent to the Pathology Department. Histopathological and immunohistochemical examination revealed that the renal specimen was compatible with a left renal metastasis of clear cell renal carcinoma. The second specimen revealed clusters of cells similar in appearance to those described in specimen 1, suggestive of left adrenal metastasis of clear cell renal carcinoma.

Conclusion: EUS-FNA is effective in cases when ultrasound or CT guidance is challenging, such as obesity and in scenarios with higher hazards. Moreover, EUS proved to be superior to CT imaging, as it succeed in identifying an additional tumor in the kidney

Management of refractory juvenile dermatomyositis with extensive calcinosis – a case report

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Introduction. Juvenile dermatomyositis (JDM) is a rare autoimmune inflammatory muscle disease in children, characterized by weakness of the proximal muscles and skin rashes such as heliotrope rash and Gottron's papules. Calcinosis, or calcium deposition in skin and muscles, is a major cause of morbidity.

Case report. We report the case of an 11-year-old boy whose symptoms began at age four with muscle and joint pain, heliotrope rash, and later Gottron's papules. Muscle enzymes were mildly elevated. Diagnosed with JDM in January 2019, he started prednisone, methotrexate, and hydroxychloroquine, but adherence and response were poor. By May 2019, persistent disease activity (Childhood Myositis Assessment Scale 11/52) and malnutrition prompted reevaluation in Madrid, revealing anti–signal recognition particle antibodies. Therapy was intensified with monthly intravenous immunoglobulin, high-dose corticosteroids, methotrexate, and rehabilitation, achieving partial improvement (score 39/52). Subcutaneous calcinosis appeared in July 2019 and worsened. Despite low-dose corticosteroids and methotrexate, relapse occurred between October 2019 and May 2020. On admission to Cluj-Napoca, Romania, he was cachectic, with painful diffuse calcinosis, muscle atrophy, and persistent rash. Laboratory tests showed normal creatine kinase, vitamin D deficiency, and high triglycerides. Whole-body magnetic resonance imaging demonstrated diffuse muscle edema and fibrotic subcutaneous nodules. In 2021, therapy escalation with baricitinib, monthly intravenous immunoglobulin, pamidronate, methotrexate, and corticosteroids led to improved strength, mobility, and pain control, partial regression of calcinosis, and 3-kg weight gain.

Conclusion. This case highlights the importance of early recognition and individualized, timely therapy in juvenile dermatomyositis with severe calcinosis.

The rollercoaster course of a severe necrotizing post-ERCP pancreatitis

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Introduction. Endoscopic retrograde cholangiopancreatography (ERCP) is routinely performed for the management of pancreatobiliary disorders, yet it carries a risk of adverse events. Among these, post-ERCP pancreatitis remains the most frequent and feared serious complication, with reported rates between 3.5% and 9.7%.

Case Report. A 57-year-old male recently diagnosed with a T3N0M0 pancreatic head ductal adenocarcinoma was admitted for ERCP with placement of an uncovered self-expandable metallic stent (SEMS) to relieve obstructive jaundice caused by tumor invasion of the common bile duct. The post-procedural course was complicated by severe post-ERCP pancreatitis, resulting in near-total pancreatic necrosis and large infected peripancreatic fluid collections. Two initial attempts at endoscopic drainage using double pigtail plastic stents failed, as the stents spontaneously dislodged and migrated distally through the gastrointestinal tract. A lumen-apposing metal stent (LAMS) was subsequently placed, enabling a step-up endoscopic management strategy with multiple sessions of direct endoscopic necrosectomy. During the prolonged hospitalization, a febrile episode prompted imaging that revealed new dilation of the biliary ducts secondary to occlusion of the previously placed SEMS. A repeat ERCP with stent-in-stent placement was therefore performed, resulting in clinical improvement. The patient gradually improved under combined endoscopic and antibiotic therapy, with normalization of amylase levels and resolution of infection. At discharge, he was afebrile, hemodynamically stable, and the necrotic collection was completely drained through the LAMS.

Conclusion. This case underscores the importance of early diagnosis and individualized endoscopic management in achieving favorable outcomes in complex post-ERCP pancreatic complications.

Beyond family history – MTOR mutation in a suspected retinoblastoma

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Introduction. Diagnosing pediatric neurodevelopmental disorders is difficult, as early symptoms are often nonspecific. The cause may be masked by a positive family history, suggesting an inherited defect. Retinoblastoma is a childhood ocular tumor associated with RB1 gene mutations, either hereditary or sporadic. In this case, the father's history of retinoblastoma, treated surgically in childhood without secondary neoplasms, indicated a possible RB1-related disorder in his daughter. Considering the child's phenotype, broader genetic testing was proposed.

Case Report. The patient is a 3-month-old girl with abnormal posture and movement. Born at 38 weeks by cesarean after mild pregnancy complications, her

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neonatal period showed slow adaptation, transient hypocalcemia, cholestasis treated with ursodeoxycholic acid, and accentuated jaundice. Neurological examination revealed developmental delay, hypotonia, spontaneous myoclonic jerks and mild facial dysmorphism (prominent glabella, slightly smaller left palpebral fissure). She had poor head control, weaker grasp and plantar reflexes on the left side and a tendency to fall leftward during traction. Due to her father's history, RB1 analysis was considered first. However, the complex phenotype suggested a more intricate cause, so whole-exome sequencing (WES) was performed. WES revealed no RB1 variants but identified a heterozygous MTOR c.6717G>C variant, predicted harmful. Located in the catalytic activation domain of mTOR, it has been reported in Smith-Kingsmore syndrome, within the mTORopathy spectrum. The variant was de novo, absent in both parents.

Conclusion. The case demonstrates how suspicion of ocular malignancy led to discovering a neurodevelopmental disorder caused by an MTOR mutation. Extended genetic testing enabled the correct diagnosis and allowed family counseling and risk calculations to be reformulated. WES should be applied cautiously, only with strong clinical indication and genetic counseling.

Severe atherosclerotic pad with ischemic ulcers - a multidisciplinary case

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Introduction. Peripheral Artery Disease (PAD) is a common manifestation of Systemic Atherosclerosis, characterized by progressive stenosis and occlusion of the peripheral arteries. In patients with Diabetes Mellitus (DM), it increases the risk of critical limb ischemia and chronic, non-healing ulcers.

Case report. A 56-year-old female patient presented left lower limb pain and multiple 2-week-old ulcerating lesions in the inguinal and intergluteal region. Medical history includes Paranoid Schizophrenia, stage IV PAD, Arterial Hypertension, newly diagnosed type 2 DM, obesity and heavy smoking.

On examination, the ulcerations exhibited malodorous fibrino-purulent deposits and necrotic margins on an erythematous background, with fistulous tracts opening to the surface. Cyanosis and ischemic necrosis of the left toes, and dystrophic nail changes in the right foot were also noted.

Laboratory investigations indicated hyperglycemia, elevated HbA1c, dyslipidemia and methicillin-sensitive *Staphylococcus aureus* (MSSA)-positive wound culture. CT angiography demonstrated significant stenosis of the right and complete thrombosis of the left Common Illiac Artery, with preserved distal perfusion.

Revascularization, targeted antibiotic therapy, glycemic optimization, and advanced wound care were initiated. Amputation of the necrotic fifth left toe was required, but the remaining lesions healed rapidly with functional improvement.

Conclusion. This case highlights an atypical presentation of PAD with inguinal and intergluteal involvement. Understanding the detailed arterial supply is essential, since the vessels supplying the inguinal region are typically spared in PAD, making ischemic ulcers in this area an uncommon finding.

The combination of T2DM, obesity, and chronic smoking precipitated critical limb ischemia and ulcer formation. Early multidisciplinary management enabled the remaining ulcers to heal rapidly, with marked functional recovery within a short timeframe.

Concurrent diaphragmatic and intercostal hernias

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Introduction. Diaphragmatic and intercostal hernias are rare thoracoabdominal defects that can result from trauma, chronic increased intrathoracic pressure, or congenital weakness of the thoracic wall.

Case report. A 75-year-old male presented at Baia Mare County Hospital with altered mental status, dyspnea, thoracic pain and painful coughs. Following examination, morbid obesity and extensive thoracic and abdominal ecchymosis were noted. PMH includes end-stage COPD, pulmonary hypertension, cor pulmonale and chronic heart failure. Abdomino-thoracic CT showed left diaphragmatic hernia (15 cm x 10 cm), left-sided posterior rib fractures and costochondral disjunction of ribs V VI and VII, left intercostal hernia in VI-VII intercostal space with lung atelectasis and mediastinal shift. Laboratory results include pathological values for multiple parameters - leukocytes (12.15 x $10^3/\mu L$), LDH-2 (497 U/L) and CRP (33.37 mg/L), proteinemia (3.8 g/dL)

Anterolateral thoracotomy in VI and VII left intercostal space is started, exhibiting live intestinal ansae, epiploon and intercostal muscle rupture; the left hemithorax was almost full by functioning abdominal viscera. The herniated content was retracted in the abdominal cavity; diaphragmaplasty was performed using double-layer surgical mesh substitution (Polymesh Inova). sutures were used for solidifying ribs to repair the intercostal hernia; pelvis, left thorax and subcutaneous drainages were also performed

Results. The postoperative course was complicated by progressive organ dysfunction and worsening laboratory markers. The patient required intensive care support. However, clinical deterioration continued, culminating in cardiac arrest. Resuscitation maneuvers were unsuccessful

Conclusion. The limited number of cases of concurrent intercostal and diaphragmatic hernias are usually caused by trauma. To our knowledge, the occurrence of it due to cough-induced thoracoabdominal stress is extremely rare, making this case unique.

Targeted delivery of regorafenib using aptamer-functionalized magnetic nanoparticles for hepatocellular carcinoma

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Introduction. Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer and among the leading causes of cancer-related mortality worldwide. Despite advances in therapeutic strategies such as systemic therapy with multikinase inhibitors, treatment remains limited by systemic toxicity and poor tumor selectivity. Therefore, the development of targeted drug delivery systems which improve the local bioavailability of chemotherapeutics while minimizing off-target effects is essential. Magnetic nanoparticles (MNPs) functionalized with aptamers represent a promising approach due to their magnetic guidance, biocompatibility, and molecular specificity toward tumor cell receptors.

Methods. In this study, we developed a regorafenib-loaded MNP/aptamer system

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specific to HCC cellular receptors. The functionalization and loading processes were monitored through UV-Vis spectrophotometry to assess aptamer attachment, regorafenib encapsulation, and the structural stability of the functionalized MNPs.

Results. The UV-Vis tests confirmed the successful conjugation of the aptamer onto the MNPs by a decreased absorbance near 260 nm, indicative of the supposed amide bond formation between activated carboxyl and terminal amino groups. Regorafenib loading was demonstrated by a decrease in absorbance in the supernatant and the presence of its specific absorption band in the final suspension. The aptamer maintained structural integrity over 24 hours at room temperature, supporting its stability under physiological conditions.

Conclusion. The obtained results show the feasibility of developing an aptamer-functionalized magnetic delivery platform for regorafenib targeting HCC cells.

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When protection becomes risk - direct oral anticoagulant treatment responsible for duodenal hematoma: case report

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Introduction. Duodenal hematomas are rare, but potentially life-threatening. Usually, they are the result of a traumatic injury of the abdomen. They can also occur following endoscopic procedures, associate with coagulation disorders, or they can be idiopathic. In this case report, we present a rare case of a giant duodenal hematoma caused by anticoagulant medication.

Case report. A 65-year-old female, with a history of hypertension, rheumatic mitral valve disease and persistent atrial fibrillation, under direct oral anticoagulant treatment, presented for a cardiologic assessment, prior to a possible surgery for a duodenal tumor of unknown nature. The patient lost weight significantly, complains of fatigue, dysphagia, nausea, vomiting and diffuse abdominal tenderness. Laboratory tests revealed hepatic cytolysis, cholestasis and increased pancreatic enzymes. The abdominal ultrasonography uncovered a 7.5 cm diameter hypoechoic structure in the D2 wall with a stratified aspect, suggesting a hematoma rather than a tumor, the initial suspicion. The duodenal lumen was collapsed and both the main pancreatic duct and common bile duct were dilated, explaining the test results. The anticoagulant therapy was discontinued and the patient's condition improved, but it was soon reinstated, considering the embolic risk of the mitral valve disease. An evaluation was scheduled one month later.

Two weeks later, the patient was readmitted for recurrence of nausea and vomiting. The assessment of the hematoma showed a slight growth, but eventually it completely remitted. Unfortunately, after three months of hospitalization, the patient succumbed to cardiorespiratory complications.

Conclusion. Considering the unspecific symptoms, the digestive wall hematoma is easily misdiagnosed leading to management errors. This case highlights the importance of the differential diagnosis of rare conditions such as duodenal hematomas and on the unexpected complications of anticoagulant therapy.

Typical vs. atypical hemolytic uremic syndrome– challenges in differential diagnosis: a case-based discussion

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Introduction. Hemolytic uremic syndrome (HUS) is characterized by the triad of microangiopathic hemolytic anemia, acute renal failure, and thrombocytopenia. HUS is classified as typical (diarrheal, caused by Shiga-like toxins) or atypical (non-diarrheal, due to complement pathway dysregulation, often genetic). It primarily affects children under five and is a leading cause of pediatric dialysis. Atypical HUS has a lower incidence but a higher mortality rate.

Case report. We report a 7-month-old girl who presented with persistent diarrhea initially treated as infectious enterocolitis. Despite appropriate therapy, she developed fever, anuria, ascites, and periorbital edema. Laboratory tests revealed leukocytosis, hemoglobin 9.4 g/dL, platelets 125,000/µL, creatinine 5.14 mg/dL, LDH 1225 U/L, and procalcitonin 1.08 ng/mL, suggestive of hemolytic uremic syndrome. Fluid and metabolic therapy failed to improve renal function, prompting initiation of peritoneal dialysis. Stool PCR for *Escherichia coli* STEC was negative, thus raising suspicion for atypical HUS. Following meningococcal vaccination, Eculizumab therapy was initiated. Complement studies showed mildly decreased ADAMTS13 activity and low C3 and C1q levels, excluding thrombotic thrombocytopenic purpura and confirming complement-mediated aHUS. The evolution under treatment was favorable: after three doses of Eculizumab, laboratory values improved significantly, with hemoglobin 11.8 g/dL, platelets 468,000/µL, and creatinine 0.57 mg/dL at discharge.

Conclusion. This case highlights the importance of differentiating between typical and atypical HUS, especially in the absence of confirmed enteric infection, and underlines the need for rapid recognition of complement-mediated forms. Early initiation of Eculizumab therapy is crucial to prevent severe renal complications and to improve long-term outcomes.

From shock to shield – enabling hypertension management through wasp venom immunotherapy

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Introduction. Hymenoptera stings are common causes of anaphylaxis, with no reliable biomarker predicting which sensitized individuals will develop systemic reactions. Venom immunotherapy (VIT) is an effective treatment providing long-term protection even after discontinuation. It induces peripheral tolerance through the slow release of allergens adsorbed onto aluminum hydroxide, increasing IgG4 blocking antibodies and reducing venom-specific IgE. By preventing anaphylaxis, VIT enables safe management of comorbidities, including beta-blocker therapy in hypertensive patients previously considered high-risk.

Case report. A 56-year-old hypertensive man with allergic reactions to wasp stings since childhood presented for specific allergen immunotherapy (Alutard SQ Vespula). In 2022, after a wasp sting on the forearm, he developed grade IV anaphylactic shock with angioedema, erythema, pruritus, dyspnea, and hypotension. He was treated

with adrenaline and hydrocortisone hemisuccinate, achieving full recovery. A mild episode recurred in 2023.

In early 2024, tests before immunotherapy showed: tryptase 4.75 µg/L, total IgE 417 IU/mL, specific IgE to wasp venom 26.69 kU/L, Ves v1 moderately, Ves v5 significantly elevated, with mildly increased ESR and CRP. Skin testing confirmed sensitization to Dermatophagoides spp. and Blattella germanica.

The patient underwent a rush induction protocol followed by the conventional schedule, reaching a maintenance dose of 100 µg venom every 4–6 weeks, well tolerated. After a subsequent sting, no hypersensitivity reaction occurred, and he remains in the maintenance phase. With the anaphylaxis risk resolved, beta-blocker therapy was safely initiated for hypertension.

Conclusion. This case demonstrates that venom immunotherapy not only prevents severe systemic reactions but also significantly improves quality of life, enabling the safe treatment of comorbidities and confirming its role as a life-saving, disease-modifying therapy.

Thinking outside the box – diagnosing testicular carcinoma with an atypical symptomatology

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Introduction. Testicular cancer has a good prognosis if diagnosed early due to its good response to chemotherapy. In this case report, an atypical case is presented. Due to the aberrant nature of the patient's presentation, a delay in diagnosis and a subsequent delay of treatment initiation occurred. Despite this, the patient responded well to the therapy, favoring a propitious outcome.

Case report. A 44-year-old man was admitted initially to the gastroenterology department for severe lumbar pain that started insidiously 3 weeks prior, fatigue, weight loss, and digestive symptoms. Imaging revealed a large retroperitoneal mass with vascular invasion, multiple pulmonary nodules, and hepatic lesions suggesting metastases. The biopsy revealed a lesion of carcinomatous origin, without pointing toward a specific histological type.

The patient's condition progressively worsened, developing ascites, pleural effusion, respiratory failure and severe anemia requiring transfusions. As no diagnosis could be established he was referred to palliative care. Later on, he was reevaluated in oncology, where testicular ultrasound revealed a small left testicular mass. For this reason, tumor markers were tested (AFP, β-hCG, LDH) and markedly elevated, confirming metastatic testicular carcinoma. Following the diagnosis, chemotherapy with a BEP protocol was initiated, at reduced doses, because of the patient's poor general condition, multiple comorbidities as well as the high risk of spontaneous tumor lysis for which he is treated with allopurinol. The patient showed rapid clinical improvement with decreased pain and recovery of general status.

Conclusion. In this atypical case, the detailed anamnesis and the tumor marker assessment when the biopsy results were inconclusive made the difference in the prognosis of this patient. This highlights the need for thorough evaluation to guide clinical decisions and improve patient outcomes.

Secondary pneumothorax due to pulmonary pneumatoceles in a 4-year-old diagnosed with acute lymphoblastic leukemia: a case report

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Introduction. Pulmonary pneumatoceles are thin-walled air-filled cavities usually following trauma or severe infections. In immunocompromised pediatric patients under chemotherapy (CTx), although generally self-limited, the pneumatoceles may have a poor clinical course with sudden rupture and the appearance of pneumothorax (PTX), requiring close monitoring and prompt intervention.

Case report. A 4-year-old patient diagnosed with acute lymphoblastic leukemia, under induction chemotherapy, with severe medullar aplasia, presented on day 15 vomiting and diarrhea, that rapidly progressed to septic shock. Blood cultures were positive for *Klebsiella pneumoniae*, for which she received antibiotic and supportive therapy, with a favorable outcome. CTx was resumed, but the patient suddenly presented dyspnea, severe chest pain and hypoxemia. A chest X-ray was performed, which showed a massive right PTX with mediastinal shift to the left, collapse of the right lung and left apical PTX. A chest drain tube was inserted with the reduction of the PTX on the control X-ray. On the 2nd day, the patient developed a new episode of dyspnea, this time the imaging revealing massive bilateral PTX with pneumomediastinum. Under supervision and intensive care, the patient's condition stabilized, but because of recurrent PTX, it was decided to omit the last course of CTx. Accordingly, a thoracic CT scan was performed that showed bilateral, multiple, small pneumatoceles. The patient was periodically monitored through imaging and CTx was resumed due to the ameliorating clinical status.

Conclusion. In conclusion, the development of pulmonary pneumatocele in immunocompromised patients with a history of sepsis is a potentially life-threatening complication. Therefore, ongoing monitoring and prompt care are essential to reduce morbidity and mortality.

The little heart that beat the odds – a life-threatening case of neonatal infective endocarditis

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Introduction. Neonatal endocarditis is a rare but life-threatening condition, often challenging to diagnose due to non-specific symptoms that can mimic sepsis or congenital heart disease.

Case report. We report the case of a twelve-day-old female patient who presented with fever, irritability and lack of appetite. Although the physical examination revealed no pathological changes, paraclinical investigations indicated significant leukocytosis, high neutrophil count, and elevated procalcitonin levels (97.83 ng/mL), leading to

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the diagnosis of neonatal sepsis. Empirical antibiotic treatment with Ampicillin, Gentamicin and Cefotaxime was initiated, resulting in clinical improvement. Blood cultures later identified Group B Streptococcus (agalactiae) as the pathogen.

A few days later, the emergence of a new systolic murmur and generalized edema prompted a cardiologic consultation. Echocardiography revealed vegetations on the aortic valve, determining mild aortic insufficiency, which led to the diagnosis of infective endocarditis on native aortic valve with group B Streptococcus. Echocardiographic follow-up showed a significant increase in aortic insufficiency and larger vegetations (from 3/4.77 mm to 5/5.85 mm). NT-proBNP levels rose sharply from 9922 pg/mL to 52396 pg/mL, despite decreasing sepsis parameters. As the patient's condition worsened with significant deterioration of cardiac function, requiring inotropic support, she was urgently transferred to the San Donato Cardiology Centre, Milan, Italy, for the Ross procedure.

Conclusion. Early recognition of neonatal endocarditis is crucial, as it allows prompt treatment and a comprehensive evaluation to determine the need for surgical interventions. A combined medical and surgical approach has been shown to improve outcomes. In this case, despite the severity and several negative prognostic factors, the surgical intervention was life-saving.

From cholestasis to cardiac defects: the multisystemic nature of Alagille syndrome

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Introduction. Alagille syndrome is a multisystemic genetic disorder with various clinical presentations. The condition is usually characterized by cholestasis due to paucity of intrahepatic bile ducts. It also affects the heart, eyes, skeleton, kidneys and has distinctive facial features.

Case report. A premature newborn girl who presented at birth with jaundice caused by cholestatic hepatitis underwent further investigations. The mother's pregnancy was inadequately monitored; prenatal screening tests were not performed, and a SARS-CoV-2 infection occurred during the first trimester.

Laboratory results showed elevated direct bilirubin levels. An echocardiography revealed atrial and ventricular septal defects as well as a patent ductus arteriosus. An abdominal ultrasound and a chest X-ray showed no significant modifications. Metabolic, endocrine, and infectious causes were infirmed. Given the hepatic involvement, heart malformations and dysmorphic facial features, genetic testing was conducted. Mutation in the JAG1 gene led to the diagnosis of Alagille syndrome.

Currently aged 4 years, she presents to the hospital with paroxysmal cerebral events that occurred a week before, consisting of postural tone loss, lateral head drop, and an absence-type seizure with subsequent complete recovery. An EEG was performed and was given antiseizure medication. Growth parameters remained far below the 3rd percentile, a typical manifestation of this syndrome.

Pruritus, the major symptomatic issue, was successfully treated with Maralixibat. Cardiology follow-up indicated progressive heart disease with pulmonary hypertension, with surgical correction being the next step in the patient's management.

Conclusion. This case highlights the importance of early recognition and multidisciplinary management in Alagille syndrome. Targeted therapies can improve quality of life, however close follow-up is essential to prevent complications and optimize surgical timing.

Compound heterozygous WDR73 variants causing Galloway-Mowat syndrome type 1 (GAMOS1): a case report

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Introduction. Galloway-Mowat syndrome (GAMOS) is a rare autosomal recessive neurodegenerative disorder typically characterized by infantile-onset microcephaly, severe psychomotor delay, and frequent nephrotic syndrome. Pathogenic variants in the WDR73 gene are linked to GAMOS type 1 (GAMOS1). Human WDR73 is vital for regulating microtubules in glomerular podocytes and is also involved in organizing neuronal and axonal microtubule networks. We present a case of GAMOS1 diagnosed in a young patient showing developmental delay and microcephaly without renal issues at diagnosis.

Case report. The patient, a 1-year and 9-month-old boy, was evaluated for motor developmental delay and microcephaly. Symptoms began at 8 months, featuring motor delay, tactile aversion, and poor eye contact.

Clinical examination revealed microcephaly, craniofacial dysmorphism (down-slanting palpebral fissures, mild macroglossia), axial hypotonia, moderate intellectual disability, and compound myopic astigmatism. Laboratory investigations were largely unremarkable, with normal hepatic and renal function, a normal thyroid profile, and no signs of inflammation. Latent iron deficiency was identified. A prior brain MRI showed no abnormalities. Due to clinical suspicion of a genetic etiology, whole exome sequencing (WES) was performed.

WES identified heterozygous variants in WDR73: one pathogenic frameshift variant and one likely pathogenic intronic variant. Targeted familial testing confirmed segregation: the father carried the pathogenic variant, and the mother carried the likely pathogenic one. This confirmed the patient's compound heterozygous (in trans) mutation.

Conclusion. This case highlights the diagnostic value of WES in children with microcephaly and psychomotor delay, even when neuroimaging abnormalities or nephrotic syndrome are absent, as these can vary. Identifying the genetic cause was essential for management and enabled accurate genetic counseling.

Ectopic extramammary Paget's disease of the scalp associated with a meningioma – a case report

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Introduction. Extramammary Paget's disease (EMPD) is a rare adenocarcinoma originating from the apocrine glands, which primarily affects the axillary and the anogenital regions. It is exceptionally uncommon for EMPD to affect ectopic sites without apocrine glands, such as the scalp. We report a case of ectopic EMPD of the scalp, which is associated with an intraosseous atypical meningioma, a previously unreported finding.

Case report. A 70-year-old female presents with a persistent erythematous and alopecic scalp lesion (15 cm) that has not been healing properly for approximately ten years. She has a history of multiple meningiomas (diagnosis in 2004) and she has undergone excision of a right frontal one. The scalp lesion has been treated for several years as an eczema or infection without significant improvement. In April 2024, she is referred to a private clinic where differential diagnoses of discoid lupus and intraepithelial neoplasia are considered. Antinuclear antibody (ANA) testing is positive (titer: 1:640). Histopathological analysis confirms ectopic EMPD, while imaging identifies an adjacent intraosseous meningioma. Immunohistochemically, atypical cells were positive for GATA3, CK7, HER2 and AR and negative for p63, CK5/6 and CK20. Surgical resection is performed for the meningioma, and radiotherapy is selected as the treatment modality for EMPD. The patient completes the 25 sessions of photon irradiation at the end of May 2025, with a favorable response to treatment.

Conclusion. Due to its clinical resemblance to inflammatory dermatoses, ectopic EMPD is often under recognized. Given its potential association with malignancies, comprehensive systemic evaluation is paramount. The high recurrence rate following surgical excision demands heeding alternative therapeutic approaches, including radiotherapy, photodynamic therapy or Mohs micrographic surgery. This case highlights the necessity of heightened clinical awareness of atypical scalp lesions.

Cardiac magnetic resonance in the diagnosis of AL amyloidosis secondary to multiple myeloma – a case report

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Introduction. Excessive monoclonal immunoprotein production in multiple myeloma (MM) can cause AL amyloidosis, often affecting vital organs. Cardiac magnetic resonance (CMR) is pivotal for detecting heart involvement, enabling early and accurate diagnosis to guide therapy.

Case report. A 73-year-old man presented with acute cardiac decompensation

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after progressive symptoms over 3–6 months. Labs showed hypoproteinemia, hypoalbuminemia, and reduced IgG. Serum electrophoresis revealed increased α- and β-globulins, with markedly elevated free κ light chains and κ/λ ratio. Urine analysis revealed severe proteinuria with elevated IgG and κ light chains.

CMR findings were consistent with cardiac amyloidosis, showing a normal-sized left ventricle with mildly reduced systolic function (EF 49%), mild basal inferior and mid-anterolateral hypokinesia, and borderline increased mass (153 g) with septal hypertrophy (end-diastolic thickness 15 mm). Both atria and the right ventricle were enlarged, with mitral and tricuspid regurgitation. Tissue characterization demonstrated markedly elevated native myocardial T1 time and increased extracellular volume, indicating diffuse amyloid infiltration. Late gadolinium enhancement was global, diffuse, and predominantly subendocardial, in the basal and mid-septum, with possible atrial and RV involvement.

Cardiac catheterization with endomyocardial biopsy confirmed AL amyloidosis. Severe proteinuria and hypoalbuminemia suggested renal involvement. Bone marrow biopsies showed mildly hypercellular marrow without amyloid deposits. Daratumumab with cyclophosphamide, bortezomib, and dexamethasone was initiated for MM. Heart failure therapy with torasemide, eplerenone, and bisoprolol was started.

Conclusion. This case highlights the importance of CMR in detecting and characterizing cardiac involvement in IgA-κ MM, enabling early diagnosis and guiding management. Multidisciplinary evaluation remains essential to optimize outcomes in patients with amyloidosis.vv

When coagulation turns complex – massive pulmonary embolism with severe thrombocytopenia and COVID-19

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Introduction. Pulmonary embolism and severe thrombocytopenia can occur simultaneously in complex clinical contexts, particularly in elderly patients with recent surgery.Identifying the underlying causes is essential to guide therapeutic management and prevent severe complications.

A 72-year-old female with hypertension and a history of inferior myocardial infarction underwent surgery for gallstone disease complicated by obstructive jaundice. Postoperatively, she developed severe acute renal failure, requiring hemodialysis via a right femoral venous catheter. Subsequently, she presented with progressive dyspnea, and bilateral edema, more pronounced on the right. Chest CT angiography: massive bilateral pulmonary embolism; venous Doppler:occlusive right iliofemoral thrombosis; D-dimers:markedly elevated. While on heparin therapy (accounting for nitrogen retention), progressive thrombocytopenia occurred (56,000→11,000/μL), with extensive cutaneous ecchymoses, no overt bleeding, and no decrease in hemoglobin. Two units of platelet concentrate were transfused. Anti-platelet antibodies were negative, suggesting multifactorial thrombocytopenia (possible HIT or DIC). Subsequently, the patient tested positive for COVID-19, raising the possibility of viral involvement (possibly prediagnostic) in the pathogenesis of PE, DVT, and thrombocytopenia. After adjusting therapy (heparin replaced with fondaparinux, later switched to NOAC, antiviral and supportive treatment), clinical evolution was favorable, with progressive platelet

recovery and improvement in symptoms and clinical and biological markers.

Conclusion. This case highlights the multifactorial etiology of thromboembolism and thrombocytopenia, including recent surgery, insufficient postoperative prophylaxis, femoral venous catheterization, heparin exposure, and COVID-19 infection. Careful monitoring of platelet trends and timely adjustment of anticoagulant therapy were essential for achieving a favorable outcome.

The biophysics behind Alzheimer's Disease – role of biomolecular condensates in pathogenesis

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Introduction. Biomolecular condensates (BCs) are cellular compartments that lack encapsulating lipid bilayers and play a role in regulating key biological processes, such as transcription, RNA splicing and translation. Alzheimer's Disease (AD), the leading cause of dementia, is characterized by the accumulation of amyloid plaques and neurofibrillary tangles in the brain. Emerging research reveals that amyloid β (Aβ) and tau proteins undergo liquid–liquid phase separation (LLPS), forming BCs that promote aggregation and neurotoxicity. Therefore, BCs might be a key component in the mystery of Alzheimer's Disease.

Methods. A total of 8 peer-reviewed scientific articles selected through PubMed and ScienceDirect were included in this review, covering a ten-year period from July 2, 2019 to August 19, 2025.

The primary keywords used for database searches were: biomolecular condensates, Alzheimer's disease, and liquid–liquid phase separation (LLPS).

Results. Mechanistically, BCs accelerate aggregation by local modifications in physical parameters that favour nucleation and β-sheet conversion. BCs can be heterogeneous with different microviscosities and immiscible droplet populations that guide which species progress to pathogenic fibrils.

Experimental studies demonstrate that tau forms BCs *in vitro* and in cells and are mechanistically connected to amyloid formation and altered cellular function. Aβ peptides similarly display LLPS behavior and these lipid-containing BCs accelerate the primary nucleation steps of amyloid formation and can undergo liquid-to-solid transitions that seed fibril growth, providing an early molecular step in the amyloid cascade. Therapeutic strategies - such as epigallocatechin gallate compounds (EGCG)-derived from these observations therefore aim to modulate BCs dynamics with the goal of preventing or reversing liquid-to-solid transitions and blocking condensate-mediated nucleation upstream of irreversible aggregation.

Conclusion. Due to the LLPS property of BCs, these non-membranous organelles play a significant role in Alzheimer's disease and consequently possess a threat to the patient by the aberrant change from liquid-like to solid-like states.

When melanoma returns after a decade – a case of gallbladder and peritoneal metastases

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Introduction. Melanoma is an aggressive malignancy originating from melanocytes, cells derived from the neural crest. While primarily a cutaneous tumour, melanoma tends to spread to any organ of the human body, including the gastrointestinal tract. Metastases can be difficult to diagnose, as they may remain clinically silent and appear years after the initial melanoma. Gallbladder metastases occur in 15–20% of cases but are rarely identified during life; peritoneal dissemination is rarer, at 0.5–4%.

Case report. A 69-year-old female patient, with a history of deltoid region melanoma surgically treated in 2015, and known pulmonary secondary lesions currently under immunotherapy, presents to our department for endoscopic ultrasound evaluation to determine the etiology of a gallbladder fundic wall thickening detected on a contrast-enhanced thoraco-abdomino-pelvic CT performed approximately two months prior. The patient reports episodes of bilious regurgitation, with insidious onset a few years ago.

The abdominal ultrasound revealed an infundibular mass in the gallbladder, retroperitoneal lymphadenopathy, ascites and hepatic steatosis. The CT scan showed multiple pulmonary metastases, alongside significant dimensional progression of a solid posterior-basal nodule (20% growth compared to the previous PET-CT). A voluminous gallbladder mass was identified, confined to the wall without extraparietal extension, associated with distal ileal hypervascular nodular thickenings suspicious for metastases. Endoscopic ultrasound-guided fine-needle aspiration was performed for histopathological evaluation.

Conclusion. This case highlights the exceptionally rare occurrence of gallbladder and peritoneal metastases from cutaneous melanoma. The long latency period of 10 years underscores the potential for delayed recurrence, which can complicate diagnosis. Awareness of such atypical metastatic patterns is essential for timely recognition and appropriate management.

A high-throughput spheroid imaging model to study microglial medulloblastoma interactions

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Introduction. Medulloblastoma is the most common malignant brain tumor in children. Although effective treatment strategies have been developed, the current standard methods remain ineffective for certain patient subgroups. Recent findings seem to indicate that the tumor microenvironment, plays a crucial role in the onset and progression of such tumors. To understand the role that microglia play in this microenvironment, we used a high-throughput imaging platform, which allowed us to assess how the microglia interact with medulloblastoma spheroids.

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Methods. We used two different cell lines for the generation of our spheroids. The first, G1A, was reprogrammed from a patient with Gorlin Syndrome, a known liability factor for medulloblastoma development. We also use G1A 1440, which is a second-generation tumor cell line obtained by G1A implantation in mice and re-harvesting once medulloblastoma develops in the mouse cerebellum. The spheroids were co-cultured with a microglia. To assess the effect of different immune states, the microglia were polarized to either a pro-inflammatory or an anti-inflammatory phenotype, with non-polarized microglia serving as a control. To seed our spheroids, we used a micro-well chip, which allowed us to perform imaging at high resolution. With this experimental design, we assessed microglial invasion and spheroid growth alterations.

Results. Initial testing showed that the chip is an optimal culture vessel for our spheroids. The material allowed for clear imaging without any optical alterations or other artefacts. Subsequent experiments demonstrate adequate visualization of the microglial interactions. The next steps include quantifying the interactions with the pro- and anti-inflammatory microglial phenotypes.

Conclusion. Our model provides a high-throughput method to study microglia interactions within medulloblastomas. Ultimately, we hope that this will lead to the development of more adjuvant or post-resection therapies.

Breaking the pattern – Loeys-Dietz presenting through the heart, not the aorta

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Introduction. Loeys-Dietz syndrome (LDS) is an autosomal dominant connective tissue disorder, primarily known for its aggressive vascular anomalies. While defined by aortic aneurysms, skeletal features, and craniofacial dysmorphism, significant cardiac arrhythmias are considered a rare complication. This case highlights an atypical presentation where such arrhythmias were the primary symptom.

Case report. We present a male patient diagnosed with LDS at age 13. Unusually, the initial presentation was not vascular but arrhythmic, consisting of dizziness and syncope. Clinical workup revealed key diagnostic features: facial dysmorphism (hypertelorism, dolichocephaly), bifid uvula, thoraco-lumbar scoliosis, and a systolic murmur . Echocardiography confirmed aortic root dilatation (Z score = 2.96) and aortic arch dilatation (Z score = 2.13). A 24-hour Holter ECG identified frequent monomorphic ventricular extrasystoles (3%), including bigeminy, trigeminy, and couplets .Genetic testing confirmed the diagnosis by identifying a pathogenic heterozygous mutation in the TGFB2 gene (c.896G>A; p.Arg299Gln) . Oral beta-blocker therapy (Propranolol) was recommended, but patient compliance was reduced. At age 17, a follow-up assessment showed similar aortic root dilatation (Z score 2.4) but a worsening of the ventricular ectopic burden to 9%, now including triplets. Beta-blocker therapy (Bisoprolol) was reinitiated with favorable evolution.

Conclusion. The major particularity of this case is its rare and atypical onset. Syncope caused by ventricular arrhythmia is an uncommon presenting symptom for LDS. This case strongly underscores that while LDS management focuses on aggressive aneurysms, cardiac arrhythmia represents a significant, albeit rare, complication. It highlights the absolute necessity of Holter ECG monitoring for risk stratification in these patients. Genetic analysis remains essential to differentiate LDS from similar connective tissue disorders like Marfan syndrome.

Tirzepatide for post-bariatric obesity relapse – InBody970 case report

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Introduction. Morbid obesity is a chronic, relapsing disease often requiring bariatric surgery and pharmacologic interventions. Weight regain after surgery is common, underscoring the need for effective therapies. Bioelectrical impedance analysis (BIA) with InBody970 offers detailed assessment of fat and muscle compartments, visceral adiposity, and basal metabolic rate (BMR), providing insight beyond body weight alone.

Case report. A 40-year-old male presented with significant weight regain five years after sleeve gastrectomy, despite sustained remission of type 2 diabetes. In September 2024, InBody970 showed weight 112.9 kg, BMI 33.3 kg/m², percent body fat (PBF) 32.7%, body fat mass (BFM) 36.9 kg, skeletal muscle mass (SMM) 42.9 kg, visceral fat area (VFA) 173.2 cm² (normal <100), and BMR 2011 kcal. Tirzepatide was initiated at 2.5 mg weekly for 4 weeks, then titrated to 5 mg for 4 months (highest available dose in Romania at that time), 7.5 mg for 4 weeks, and 10 mg for 5 months. The patient followed a BMR-adjusted nutrition plan emphasizing lean protein, vegetables, whole grains, and unsaturated fats while limiting refined carbohydrates and ultra-processed foods.

In March 2025, weight was 107.1 kg, BMI 31.6 kg/m², PBF 31.6%, BFM 33.9 kg, SMM 41.0 kg, VFA 163.3 cm², BMR 1952 kcal. By September 2025, weight 95.0 kg, BMI 28.1 kg/m², PBF 23.2%, BFM 22.0 kg, SMM 40.8 kg, and VFA 107.3 cm², approaching the normal range, while BMR remained stable at 1946 kcal, confirming preservation of lean mass.

Conclusion. Tirzepatide achieved −17.9 kg (−15.9%) weight loss, with visceral fat reduction and muscle preservation, mirroring SURMOUNT-1 trial outcomes. This case highlights tirzepatide's effectiveness in post-bariatric obesity relapse with ongoing diabetes remission and demonstrates the clinical utility of InBody970 for documenting compositionally favorable weight loss beyond the scale.

Recurrent sacral chordoma – a case report

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Introduction. Chordomas are a family of rare primary malignant bone tumours with notochordal differentiation, predominantly localized within the axial skeleton, in the skull base or the sacrococcygeal bones. Conventional chordoma, dedifferentiated chordoma and poorly differentiated chordoma make up the types of this tumour.

Case report. We report the case of a 68-year old female patient who presented with lumbosacral pain, irradiating to the perineal region, accompanied by paresthesia, without remission after conventional treatment. The MRI scan found a relatively well-confined, heterogeneous sacral tumour. The macroscopic examination of the specimen revealed multiple fragments cumulatively measuring 20/15/5 cm, with a lobulated appearance and gelatinous areas. Histological findings include a proliferation of polygonal tumor cells with vacuolated cytoplasm and mild atypia, forming chords, with an abundant myxoid matrix. Two years prior, the patient was referred for surgery for a sacral tumor with a similar histopathological appearance, showing positivity for AE1/AE3, S100 and EMA. The histopathological results, together with the clinical presentation and imaging findings, are compatible with a recurrence of a conventional chordoma.

Conclusion. This case highlights the importance of an integrated diagnostic approach in chordoma, particularly in the absence of the specific marker (brachyury). The diagnosis is reinforced through the evaluation of the recurrences and long-term clinicopathologic correlation.

Long-term disease control in metastatic pancreatic adenocarcinoma – a case report

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Introduction. Pancreatic cancer is one of the most aggressive malignancies, due to the late onset of the symptoms, leading to mainly diagnosing it in advanced or metastatic stages.

Case report. In 2022, a 51-year-old male presented to the hospital after suffering severe trauma at work. While getting a CT scan, it was discovered the presence of a body-tail pancreatic mass, along with multiple hepatic masses. The pancreatic biopsy result revealed a G2 pancreatic adenocarcinoma, and the liver biopsy confirmed the metastasis. A CT TAP with IV contrast was done, showing a cT4N2M1 tumor, involving the celiac trunk. Surgical resection was not considered due to the stage IV disease, the trauma and the emergency surgery he suffered. Therefore, the patient started first line palliative chemotherapy with FOLFIRINOX, getting 43 rounds of this treatment. After cycle 26, Oxaliplatin was removed, due to the presence of neurotoxicity as a side effect. Considering that the tumor continued to grow, the treatment was changed to the second line with 8 rounds of GEMOX and then only with Gemcitabine for 14 times. Because of the lack of tumoral response, the chemotherapy was switched again to the third line with Capecitabin. In October 2025, the patient came complaining of left hypochondriac pain, associated with anemia, leukocytosis, cholestasis, hepatic cytolysis and an elevated CRP level. According to the clinical, imaging and laboratory findings, the treatment

regimen was modified, and fourth-line therapy with 5-Fluorouracil and Irinotecan was initiated. The patient remained under observation and will continue to attend monthly chemotherapy sessions.

Conclusion. The particularity of this case lies in the unusually long progression of a stage IV pancreatic cancer. Although it is known that the median survival rate for this type of tumor is very low, this patient was diagnosed 3 years ago and still getting palliative chemotherapy, after going through several lines of therapy available.

IgA nephropathy presenting with nephrotic syndrome and severe cutaneous vasculitis – a diagnostic and therapeutic challenge

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Introduction. IgA nephropathy is the most common primary glomerulonephritis worldwide, occasionally associated with systemic IgA vasculitis in adults. The coexistence of ulceronecrotic cutaneous vasculitis and nephrotic-range proteinuria is rare and diagnostically challenging.

Case report. A 68-year-old woman with ulceronecrotic vasculitis, nephrotic syndrome, hypertension, and hypothyroidism presented in the nephrology department with persistent edema and proteinuria after months of dermatologic management for purpuric, bullous, and ulcerative lesions complicated by necrosis and infection. Laboratory results showed creatinine 0.8mg/dL, albumin 3.2g/dL and proteinuria 5.9g/24h, with an active urine sediment. The patient exhibited steroid-resistant nephrotic proteinuria, which improved markedly after Cyclosporine initiation. Proteinuria decreased from 5.9g/24h to 0.9g/24h (from nephrotic to nephritic range), prompting nephritic syndrome differential diagnosis. Autoimmune tests excluded ANCA vasculitis, lupus and cryoglobulinemia. Skin biopsy revealed ulceronecrotic vasculitis with IgA deposits. Renal biopsy confirmed IgA nephropathy with mesangial and endocapillary proliferation and crescents (MEST-C score: M1 E1 S1 T1 C1, moderate chronicity, significant activity).

The patient was diagnosed with IgA nephropathy associated with ulceronecrotic IgA vasculitis, CKD G2A3 (KDIGO). The patient's 5-year risk of kidney function decline was calculated at 11%. In high-risk patients, treatment should combine immunologic control, by reducing immune complex formation (Mycophenolate mofetil and low-dose Prednisone were introduced, TRF-Budesonide was also considered as an alternative), with renoprotective therapy through blood pressure optimization, RAAS and SGLT2 inhibition.

Conclusion. This case emphasizes the diagnostic complexity and therapeutic challenges of IgA nephropathy with systemic IgA vasculitis and highlights the need for individualized, mechanism-based treatment strategies.

Therapeutic strategies in poor-response osteosarcoma with pulmonary oligometastasis – a case report

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Introduction. Primary bone sarcomas (BS) account for <0.2% of malignant neoplasms across all ages. Osteosarcoma (OS) is the most common BS, typically arising in the metaphyseal regions of long bones in adolescents and frequently metastasizing to the lungs. This case emphasizes the therapeutic approach in OS, given its rarity and complexity of management.

Case report. A 17-year-old female presented in August 2022 with progressive pain and swelling of the left distal femur. Imaging revealed a destructive metaphyseal lesion with intra-articular extension and biopsy confirmed conventional osteoblastic OS (T2N0M0). She received six cycles of neoadjuvant MAP chemotherapy (doxorubicin, cisplatin, high-dose methotrexate), followed by distal femoral resection with endoprosthetic reconstruction, achieving negative margins in March 2023. Postoperative pathology demonstrated only 40% necrosis of the tumor, indicating poor histologic response to the preoperative treatment, a known negative prognosis factor. Following guidelines, adjuvant chemotherapy was intensified using the modified MAPIE protocol (MAP plus high-dose ifosfamide), nine cycles, completed in February 2024. The therapeutic plan was complicated with recurrent hepatotoxicity, anemia, leucopenia and catheter-related sepsis. During the follow-up, the patient developed oligometastatic pulmonary recurrence. Management included thoracoscopic wedge resections and radical mediastinal lymphadenectomy in December 2024, followed by stereotactic ablative radiotherapy in June 2025, achieving only partial control. Due to contralateral lung progression, systemic second-line therapy with regorafenib was considered in October 2025, which is still ongoing.

Conclusion. Taking into account the presented case, supporting long-term disease control means optimizing therapeutic approaches. The management of oligometastatic and poor-response OS requires adaptive treatment strategies, multidisciplinary care and the patient's sustained compliance.

High-risk, idiopathic Guillain-Barré Syndrome (GBS) – a case report

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Introduction. GBS describes autoimmune events targeting peripheral nervous structures. 70% of cases follow an infection, from cross-reactive antibodies. Clinically, GBS presents progressive muscle weakness with autonomic implications. Poor-outcome risk factors are ages over 60, a progression of less than seven days until admission, ventilatory support and damage seen in electroneuromyographic (ENMG) findings. Acute inflammatory demyelinizing neuropathy (AIDP) is a GBS variant. This case illustrates the results obtained with a diagnosis with unclear etiology.

Case report. A 71-year-old man comes to the emergency unit with lower limb weakness on 05.07.2025. It began distally during 04.07, and ascends on 05.07 to the upper limbs. Native CT excludes acute changes. On admission to the neurology ward, a lumbar puncture evidencing albuminocytologic dissociation is indicative of GBS. IgG and IgM for eight associated pathogens and an extended autoimmune panel are negative. Nadir is reached on the 6th of July with a GCS of 3, requiring ventilation. Intravenous immune globulins (IVIGs) are administered, thereafter the patient enters cardiac arrest and requires resuscitation. He is transferred to the ICU. ENMG shows AIDP with axonal and glial loss. On 26.07, he is tracheostomized. IVIG is alternated with plasma exchange (PE) upon resistance, both having to be put on hold during hospital-acquired infections. On the 16.09, with resistance to both treatments, his diagnosis is reconsidered as chronic inflammatory demyelinating polyneuropathy (CIDP), wherein corticosteroids are indicated, to no effect. Gradually, he regains a GCS 15. He transfers to rehabilitation in November.

Conclusion. The evolution is complicated via unclear etiology, acute progression, treatment resistance and interruption, in a frail patient. It showcases the limits of indicated treatment methods. Clinicians must maintain a dedication to set realistic goals in accordance with the patient's wishes.

Clinical and functional response to Olipudase alfa in Niemann-Pick disease type A/B – a case report

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Introduction. Niemann-Pick disease is a rare lysosomal storage disorder caused by pathogenic mutations in the SMPD1 gene, resulting in sphingomyelinase deficiency. Sphingomyelin accumulates in a wide range of cells, including macrophages, hepatocytes, and, in the most severe cases, neurons. Olipudase alfa (Xenpozyme) is a new recombinant human enzyme replacement therapy indicated for the non-central nervous system manifestations.

Case report. We present the case of an 8-year-old boy, diagnosed at 10 months of age with Niemann-Pick disease type A/B, homozygous for the p.Trp393Gly mutation in the SMPD1 gene. His medical history includes multiple infectious episodes: recurrent upper respiratory tract infections, acute meningitis (2022), varicella (2024), aspiration pneumonia (2024), streptococcal pharyngitis complicated by post-streptococcal arthritis

Reformulating the etiology of scoliosis – a physiotherapy perspective

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Introduction. This analysis evaluates the intricate connection between birth history, early postural development, and the subsequent risk of scoliosis from an integrated physiotherapy perspective. The initial question historically proposed examining cesarean delivery as a potential risk factor for postural issues. However, the central thesis of this report argues for a fundamental reframing: intrauterine constraint is the main etiological factor that initiates a pathophysiological cascade, rather than the delivery method itself.

Methods. This report is based on a theoretical analysis and review of available clinical data. Specifically, the analysis focuses on studies comparing the clinical severity of Congenital Muscular Torticollis (CMT) in two distinct cohorts: infants born vaginally versus those born by cesarean section. The evaluation criteria included the necessity for stretching exercises or invasive muscle release surgery across both groups.

Results. The review of current data compels us to rethink the initial hypothesis. The analysis reveals that there is no direct causal relationship between the delivery mode and the severity of pathology. Clinical outcomes appear irrespective of the birth method; there is no statistically significant difference in the severity of CMT between the two groups. These findings suggest that both the necessity for a cesarean delivery (often due to fetal malposition) and the development of postural asymmetries (CMT) are common results of a primary prenatal factor: intrauterine constraint.

Conclusion. Intrauterine constraint initiates a specific biomechanical cascade. If untreated, prenatal/perinatal CMT generates a descending kinematic chain, producing a functional cervico-thoracic scoliosis. Under the Hueter-Volkmann principle and exacerbated by the adolescent growth spurt, this functional curve can become a fixed, structural scoliosis. Consequently, early physiotherapy intervention (months 0-12) establishes a vital continuum of care. Treating CMT early is essentially spinal prevention, interrupting the chain before aggressive interventions like orthosis or surgery become necessary.

Defying all odds – direct inoculation of Echinococcus granulosus embryonated eggs in a patient with soft-tissue hydatidosis

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Introduction. Hydatid disease is a zoonotic parasitic infection caused by Echinococcus granulosus, most commonly affecting the liver and lungs. Soft-tissue involvement is extremely rare and represents an atypical manifestation of the disease.

Case report. We report the case of a 72-year-old female who presented to the Department of Surgery, CF Clinical Hospital, Cluj-Napoca, Romania, Romania, with swelling and limited mobility of the left knee. Clinical examination revealed indurated, erythematous skin and a palpable cystic formation in the popliteal fossa. The patient

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had a history of recurrent soft-tissue hydatidosis and multiple surgical excisions over a 24-year period. Notably, she had sustained a dog bite to the same leg in 2001. Imaging investigations (ultrasound and MRI) demonstrated multiple multilocular cystic lesions within the posterior compartment of the left thigh and proximal calf, consistent with hydatid cysts. Laboratory results showed elevated ESR preoperatively and normalization postoperatively. Preoperative antiparasitic therapy with albendazole was administered for two weeks, followed by surgical excision of the main cyst and larger satellite lesions. Ethanol 90% was used intraoperatively for parasitic inactivation. Postoperative recovery was favourable under continued albendazole therapy.

The absence of cysts in other organs and the strict localization of lesions to the site of a previous dog bite strongly suggest direct inoculation of embryonated E. granulosus eggs at the time of injury—a mechanism rarely described in the literature. This hypothesis aligns with the parasite's life cycle and explains the unique presentation and recurrence pattern observed.

Conclusion. This case highlights an exceptional presentation of primary soft-tissue hydatidosis likely resulting from direct percutaneous inoculation. Awareness of this rare transmission route is crucial for accurate diagnosis and management in endemic regions.

The rare coexistence of Primary Sjögren's Disease with positive Anticentromere antibody – focus on scleroderma overlap

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Introduction. Primary Sjögren's Disease (PSD) is a chronic autoimmune disorder that impairs the lacrimal and salivary glands with anti-Ro/SSA and anti-La/SSB antibodies. Anticentromer antibodies (ACA), usually associated with limited cutaneous systemic sclerosis, are rare in PSD. The coexistence of sicca symptoms, ACA positivity and Raynaud's phenomenon highlights a potential predisposition of an overlap syndrome.

Case report. We report a 55 year old woman with managed Hashimoto's thyroiditis, sicca symptoms (3 years) and Raynaud's phenomenon (5 years). Clinical examinations were negative for skin thickening, telangiectasias or digital ulcers. Unstimulated salivary flow and Schirmer's test were positive. Immunological tests showed ANA positivity (1:1280 with centromeric pattern), positive ACA but anti-Ro and anti-La negative. Minor salivary gland biopsy revealed focal lymphocytic sialadenitis with mild atrophy of salivary acini. Parotid, submandibular, lacrimal glands ultrasound showed multiple hypoechogenicity areas (more prominent in lacrimal glands). Nailfold capillaroscopy showed an active scleroderma pattern (megacapillaries, microhemorrhages, low capillary density, some avascular areas). PSD was diagnosed and treatment with Hydroxycloquine and Diltiazem was initiated.

Conclusion. Positive ACA in PSD is rare, showing more scleroderma elements like Raynaud's phenomenon. This case highlights the need for long-term follow-up in these patients due to potential scleroderma-related organ involvement.

Unmasking the etiology of nephrotic syndrome – the value of renal biopsy

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Introduction. Diabetic nephropathy represents the leading cause of chronic kidney disease in diabetic patients, with renal biopsy rarely indicated when clinical presentation is typical. However, atypical features such as rapid onset of nephrotic syndrome, absence of diabetic retinopathy, or discordant proteinuria levels may raise suspicion of a non-diabetic glomerular disease requiring histological confirmation.

Case report. A 48-year-old male with recently diagnosed type 2 diabetes mellitus and history of right leg amputation secondary to sepsis was admitted for newly developed nephrotic syndrome and renal dysfunction. Laboratory evaluation revealed proteinuria of 6.4 g/24h, hypoalbuminemia, and preserved glomerular filtration rate. Immunologic screening (ANA, ANCA, anti-MBG, APLA2R) was negative. Given the recent diagnosis of diabetes and disproportionate proteinuria, renal biopsy was performed under ultrasound guidance. Histopathology demonstrated mesangial matrix expansion with nodular formation, mild interstitial fibrosis (≈15%), and absence of amyloid deposits. Immunofluorescence showed focal IgM and C3 positivity, consistent with diabetic nephropathy class II.

Conclusion. This case highlights the diagnostic importance of renal biopsy in diabetic patients with atypical renal presentations. Even in the presence of diabetes, nephrotic syndrome of recent onset should prompt reconsideration of etiology. Histopathological confirmation remains essential to exclude superimposed glomerular disease and to guide personalized therapeutic management.

A complex phenotype of KMT2D – related disorder with genital ambiguity and severe neurodevelopmental delay: case report

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Introduction. Mutations in the KMT2D gene, encoding a histone methyltransferase essential for embryonic gene activation, cause Kabuki syndrome, a multisystem disorder characterized by distinctive facial features, developmental delay, and various congenital anomalies. Genital ambiguity is rarely described. We present a severe and atypical phenotype expanding the clinical spectrum of KMT2D-related disorders.

Case report. We report the case of a 13-year-10-month-old male patient, followed since infancy, who carries a pathogenic KMT2D variant c.755dupA (p.His252Glnfs*21). This frameshift duplication generates a premature termination codon, resulting in early truncation and loss of the catalytic SET methyltransferase domain, which normally mediates H3K4 methylation and transcriptional activation of key developmental genes.

The pregnancy was uneventful, but fetal sex could not be determined prenatally. At birth, the patient exhibited ambiguous genitalia, bilateral undescended testes, and

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penoscrotal hypospadias. He underwent 13 reconstructive surgeries and 2 hernia repairs, with persistent urinary leakage and a non-palpable left testis.

Facial dysmorphism included low-set ears, microstomia, short philtrum, downslanting palpebral fissures, and a flat nasal bridge. Developmental delay was severe (sat at 2 years, walked at 4.5 years). Speech remains minimal with IQ ≈ 40. Additional findings comprise bicuspid aortic valve, recurrent severe infections, scoliosis, flat feet, obesity with short stature, gluten and lactose intolerance, divergent strabismus, and persistence of primary dentition. He receives only vitamin D and multidisciplinary supportive therapies.

Conclusion. This case exemplifies a loss-of-function frameshift mutation in KMT2D producing an exceptionally severe and multisystemic phenotype. It reinforces the need for early genetic testing, coordinated follow-up, and comprehensive care to optimize outcomes in such complex presentations.

Synchronous rectal and gastric adenocarcinomas

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Objective. To present a rare case of synchronous neoplasms – upper rectal adenocarcinoma and antral gastric adenocarcinoma – managed through a complex, multimodal therapeutic approach, with a favorable postoperative outcome.

Case presentation. A 60-year-old male patient with a history of upper rectal adenocarcinoma previously treated with neoadjuvant chemoradiotherapy, followed by total mesorectal excision (TME) and a protective side-to-side ileostomy.

Concomitantly, the patient was diagnosed with a well-differentiated, focally poorly differentiated antral gastric adenocarcinoma, staged as cT3N1M0 (stage III), for which he received four cycles of neoadjuvant FLOT chemotherapy, followed by subtotal gastrectomy.

Subsequently, the patient was admitted for restoration of intestinal continuity. After thorough preoperative assessment and optimization, restoration of bowel continuity was performed, including closure of the lateral ileostomy with enterorrhaphy, pelvic and subcutaneous drainage, and excision of a suture granuloma.

Conclusion. A multimodal therapeutic approach—integrating neoadjuvant chemotherapy, radical surgery, and restoration of digestive function—is essential for the successful management of synchronous cancers located in different organs. Interdisciplinary collaboration and stepwise treatment planning are key to achieving a favorable prognosis and an optimal postoperative quality of life.

Diagnostic challenges in slowly progressive spastic paraparesis – a case suggestive of de novo hereditary spastic paraplegia

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Introduction. Hereditary spastic paraplegia (HSP) is a group of hereditary neurological disorders consisting of mutations in the SPG genes, which primarily affects the legs due to corticospinal involvement. Primary lateral sclerosis (PLS) is a sporadic motor neuron disease affecting the legs, arms and bulbar muscles. Subacute combined degeneration (SCD) is a neurological disorder caused by vitamin B12 deficiency. It affects the corticospinal tract and dorsal columns, causing both motor and sensory issues. All three cause muscle spasticity and weakness, and hyperreflexia, due to their affliction of the upper motor neurons.

Case report. A 69-year-old female patient, known with Hashimoto's thyroiditis and autoimmune atrophic gastritis, presents for a neurological examination due to decreased muscular force and paresthesia in the lower limbs, as well as mild paresthesia in the right palm and left foot. Her symptoms began 17 years prior, but were attributed to rheumatologic causes, delaying a neurological evaluation. During her neurological examination, she is observed to have hypertonia, hyperreflexia and a positive Babinski sign bilaterally in the lower limbs. She also has a vitamin B12 deficiency, due to the atrophic gastritis impairing its absorption. After nearly five years of being administered a B-complex vitamin therapy along with a peptide-based neurotrophic agent, it is noted that all her initial symptoms, excepting the palmar paresthesia, have not only persisted, but slowly progressed; she began having bilateral plantar clonus as well as mild bilateral spastic gait. It is worth noting that she has no other relatives with these symptoms.

Conclusion. The patient is exhibiting a clinical portrait suggestive for an upper motor neuron affliction, HSP, PLS and SCD are suspected. SCD is ruled out as a root cause due to persistent symptoms despite B12 normalization, as well as the lack of sensory involvement. HSP due to de novo mutations is the most probable diagnosis, given the symptom distribution and lack of familial history. However, genetic testing remains necessary for confirmation.

Diagnostic challenges in atypical teratoid/rhabdoid tumor –a case of mistaken progression

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Introduction. Atypical teratoid/rhabdoid tumor (AT/RT) is a rare, aggressive central nervous system malignancy typically affecting children under 3 years old. Leptomeningeal carcinomatosis (LC) occurs when tumor cells spread to the meninges, carrying a poor prognosis. Diagnosing LC is often challenging, as its clinical, radiological, and cerebrospinal fluid (CSF) features can overlap with infection or treatment-related effects.

Case report. We report a 3-year-old boy previously diagnosed with AT/RT at age one and treated according to the EU-RHAB protocol. He presented to the Emergency Hospital with acute neurological decline and signs of intracranial hypertension. CT imaging revealed hydrocephalus, requiring urgent placement of an external ventricular drain. CSF analysis identified Streptococcus pseudoporcinus, and antibiotic therapy was initiated. Despite resolution of infection markers, the patient's clinical condition remained precarious. Differential diagnoses included AT/RT progression, infectious meningitis, or radiotherapy secondary effects. However, MRI findings and inconclusive CSF cytology suggested leptomeningeal carcinomatosis.

Two months later, follow-up MRI unexpectedly showed a reduction in cerebral lesions despite the absence of antitumor therapy, indicating possible radiation necrosis rather than progression. Contrast MRI confirmed frontotemporal irradiation necrosis and revealed a new lesion in the putamen. Bevacizumab therapy was initiated.

Conclusion. Enhancing meningeal or parenchymal lesions may represent tumor recurrence, infection, or radiotherapy effects. Accurate differentiation is essential for appropriate management, particularly in aggressive tumors such as AT/RT. When diagnostic methods are inconclusive, close clinical and radiological monitoring remains crucial to guide timely therapeutic decisions.

Middle colic vein rupture after blunt abdominal trauma –a multidisciplinary case report

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Introduction. Abdominal trauma following interpersonal aggression remains a major cause of emergency surgical intervention. Rapid diagnosis and prompt hemostasis are crucial to prevent fatal outcomes. We present a case of massive hemoperitoneum secondary to vascular rupture, illustrating the multidisciplinary management required for successful recovery.

Case report. A 24-year-old male, under the influence of alcohol, presented after physical assault, initially complaining of ocular pain due to chemical irritation. During observation, he developed abdominal pain and lipotimia, prompting a CT scan that revealed moderate hemoperitoneum (perihepatic, perisplenic, perigastric, and pelvic). Exploratory laparotomy identified rupture of the right branch of the middle colic vein. Hemostasis, lavage, and drainage were performed. The patient received two units of packed red blood cells, two units of fresh frozen plasma, and 939 mL autotransfusion via Cell Saver. Postoperatively, he was admitted to the intensive care unit, mechanically ventilated, and sedated. Laboratory results showed metabolic acidosis, mild hyperkalemia, dehydration, and rhabdomyolysis. Toxicological screening was positive for fentanyl, ketamine, LSD, and ethanol. The patient was successfully extubated after neurologic evaluation, maintained stable hemodynamics, and progressively recovered under multimodal analgesia, antibiotic prophylaxis, and respiratory physiotherapy.

Conclusion. This case highlights the importance of early imaging and surgical intervention in blunt abdominal trauma with hemoperitoneum. Effective resuscitation, vigilant postoperative monitoring, and multidisciplinary collaboration are essential for favorable outcomes even in complex cases involving substance intoxication and multiple organ involvement.

Integration of robotic technology in challenging retroperitoneal tumor resections

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Introduction. Residual retroperitoneal masses after chemotherapy for testicular germ cell tumors continue to represent one of the most demanding scenarios in urologic oncology, particularly when vital vascular or visceral structures are involved. Although systemic therapy achieves high cure rates, teratomatous components frequently persist because of their chemoresistant nature and therefore require surgical excision. This report describes a complex case of extensive post-chemotherapy retroperitoneal disease managed through a multidisciplinary, robot-assisted approach.

Case report. A 54-year-old man with a history of right inguinal orchiectomy performed in December 2023 for a mixed germ cell tumor (teratoma, yolk sac tumor, and embryonal carcinoma) was referred for persistent retroperitoneal mass following

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BEP chemotherapy. The primary pathology revealed a pT2 Nx LVI1 R0 tumor. Cross-sectional imaging (CT, MRI, and PET-CT) demonstrated a 71×84×120 mm heterogeneous, multilobulated retroperitoneal mass with cystic-necrotic areas and increased FDG uptake, along with a metabolically active peri-iliac lymph node measuring 15 mm (SUV 3.34). On January 20, 2025, the patient underwent robot-assisted retroperitoneal lymph node dissection combined with right nephrectomy due to tumor encasement of the ureter. The 11-hour operation required meticulous dissection from the inferior vena cava, abdominal aorta, and duodenum. Histopathology identified 15 lymph nodes containing mature teratoma, while the resected kidney showed chronic pyelonephritis and hydronephrosis.

Conclusion. This case underscores the surgical challenges of managing post-chemotherapy retroperitoneal disease in testicular cancer. Complete resection remains crucial for teratomatous remnants resistant to chemotherapy. Robotic technology and multidisciplinary collaboration are key to safely performing complex dissections near vital structures and achieving optimal oncologic outcomes.

Crossing paths in rheumatology – an overlap syndrome with articular, pulmonary and neurologic involvement

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Introduction. Features of multiple autoimmune connective tissue disorders (CTD) characterize overlap syndrome. It differs from mixed connective tissue disease by the absence of anti-U1RNP antibodies.

Case report. We report a 63-year-old male patient with neuropathic pain in the lower limbs and significant walking impairment. Additional symptoms consist of xerostomia, xerophthalmia, dyspnea and cough. His medical history includes non-symmetric oligoarthritis of the knees and hips at age 22, followed by symmetric hand arthritis. He refused DMARDs. Physical examination showed livedo reticularis, telangiectasia, frequent blinking, irreversible hand joint deformities, restricted hip mobility, and bilateral lung crackles. Laboratory tests indicated increased inflammatory markers and CK, positive anti-Ro (SS-A), anti-Sm, anti-double-stranded DNA, anticardiolipin and anti-beta2 GP1 antibodies, high-titer ANA (fine speckled pattern) and possible anti-Ku and anti-Mi-2 antibodies, along with low titres of rheumatoid factor and anti-CCP antibodies, while anti-U1RNP and anti-Scl-70 antibodies tested negative. Radiologic findings demonstrated secondary osteoarthritis of the right hip and unilateral sacroiliitis. Thoracic CT revealed usual interstitial pneumonia. The diagnosis comprised CTD, overlapping rheumatoid arthritis, Sjögren's syndrome, features of systemic lupus erythematosus, inflammatory myopathy with interstitial lung disease and secondary peripheral polyneuropathy. Treatment with high-dose corticosteroids and cyclophosphamide led to rapid improvement of symptoms and inflammatory syndrome.

Conclusion. This case highlights the diagnostic challenges of overlap syndromes and the significant disability that can arise from long-term treatment non-compliance. There is an urgent need for orthopaedic evaluation, physical medicine and rehabilitation to maintain function and mobility, as well as careful monitoring for treatment-related side effects and complications.

A crossing between anatomical borders: challenges in invasive colorectal adenocarcinoma

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Introduction. Colorectal cancer represents one of the most common forms of cancer, being the second leading cause of death among oncological patients. It is frequently diagnosed in people aged 50 years old and above and risk factors include: family history, obesity, unhealthy diets, low in fibre and rich in red, processed meats and alcohol. It is often detected at advanced stages, when the options of treatment are limited.

Case report. We report the case of a 54-year-old female patient who presented to the Emergency Department with asthenia, dizziness and faintness. Medical history includes cholelithiasis followed by cholecystectomy, acute enterocolitis, fatty liver disease and supraventricular tachycardia. Laboratory tests revealed severe microcytic hypochromic anemia, inflammatory syndrome, and thrombocytosis. On the physical examination a firm, non-tender mass was found in the left hypochondrium. A colonoscopy and an abdominal CT scan were performed and they showed a large tumoral mass in the transverse colon and splenic flexure, which invaded the inferior stomach wall and a part of the small bowel with 3 coloenteric fistula. A left hemicolectomy was performed with en bloc resection of the affected gastric area by longitudinal resection of about 13 cm using a linear stapler, along with 2 loops of the jejunum invaded by the tumor. Post-op, the patient developed intestinal obstruction, jejunal perforation , colo-colic anastomotic fistula and peritonitis with abscess formation. Therefore, the patient underwent a second surgery with left flank colostomy and lavage of the peritoneal cavity with abscess evacuation. Treatment with broad-spectrum antibiotics and prophylactic anticoagulants was initiated.

Conclusion. This case highlights the importance of early detection in colorectal cancer, emphasizing the need for regular checkups in risk groups in order to prevent complications.

Alport syndrome in an adult without family history – recognizing a sporadic form

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Introduction. Alport syndrome is a rare inherited nephropathy caused by type IV collagen mutations, leading to glomerular basement membrane (GBM) defects, progressive renal failure, and sensorineural hearing loss. While most cases are familial, sporadic adult-onset forms are uncommon and easily missed without a suggestive family history.

Case report. A 39-year-old man with chronic kidney disease (stage G3b) and hypertension presented with persistent microscopic hematuria and nephrotic-range proteinuria (4.3 g/24 h). He had a history of renal impairment of unknown cause, with

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slowly rising creatinine levels over the previous two years. He also had bilateral sensorineural hearing loss attributed to chronic otitis media, but no relatives with renal or auditory disorders. Examination showed normal blood pressure and preserved diuresis.

Laboratory tests revealed creatinine 2.42 mg/dL, normal complement levels, and negative ANA, ANCA, and anti-PLA2R, arguing against immune nephropathies. Renal ultrasound showed mild cortical irregularities with preserved size. Biopsy identified focal mesangial proliferation, tubular atrophy, and interstitial fibrosis. Immunofluorescence detected no immune deposits. Electron microscopy (EM) demonstrated alternating thinning/thickening of the GBM with lamellation of the lamina densa-typical for Alport syndrome. The absence of immune complexes and the EM pattern excluded IgA nephropathy, membranoproliferative glomerulonephritis, and thin basement membrane disease. The patient received ACE inhibitors and diuretics, achieving stable renal function at six months. Family screening was normal, supporting a sporadic form.

Conclusion. Alport syndrome should be considered in adults with unexplained hematuria and hearing loss. When genetic testing is unavailable, renal biopsy-especially electron microscopy-remains decisive. Early ACE inhibition, tight blood pressure control and nephrology follow-up can slow progression and improve outcomes.

Diagnostic challenges in cavitary lung disease – a case of granulomatosis with polyangiitis mimicking tuberculosis

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Introduction. Granulomatosis with polyangiitis (GPA) is a rare ANCA-associated small-vessel vasculitis causing granulomatous and necrotizing inflammation, mainly in the respiratory tract and kidneys. Cavitated pulmonary nodules, typical of GPA, may mimic tuberculosis, complicating diagnosis. Alveolar hemorrhage causing ground-glass opacities can occur without hemoptysis, requiring high clinical suspicion when lungs and kidneys are involved.

Case report. A 74-year-old female presented with fever, night sweats, weight loss, dry cough, dyspnea, arthralgia, and nasal crusting. History included autoimmune thyroiditis and renal cystic disease. Exam showed pallor and lung crackles. Labs revealed elevated CRP (151 mg/L), iron deficiency anemia (Hb 10 to 7.2 g/dL), microscopic hematuria, mild proteinuria, and rising creatinine (0.98 to 1.75 mg/dL). Thoracic CT displayed multiple nodules, some cavitated, plus consolidation and ground-glass opacities. Bronchoscopy found an ulcerative left main bronchus lesion. Biopsy showed necrotizing noncaseating granulomatous inflammation. BAL had >80% lymphocytes, negative for acid-fast bacilli; GeneXpert was weakly positive, causing diagnostic uncertainty.

Progressive anemia and CT findings suggested occult alveolar hemorrhage. Immunology identified c-ANCA (1:320) with anti-PR3 antibodies >200 UR/mL, supporting ANCA vasculitis. Treatment included corticosteroids, cyclophosphamide, and empirical antituberculous therapy. After two months, negative mycobacterial cultures allowed stopping antimicrobials. GPA diagnosis was confirmed multidisciplinary, and

immunosuppression continued with good response.

Conclusion. This case highlights the challenge of distinguishing GPA from tuberculosis in cavitary lung lesions. Integrating clinical, radiologic, histopathologic, and serologic data is crucial. Awareness of silent alveolar hemorrhage and multidisciplinary care prevent organ damage and guide timely immunosuppressive treatment.

Refining aesthetic and functional outcomes in hybrid breast reconstruction through fat grafting

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Introduction. Defined as the integration of implant-based reconstruction with autologous fat transfer, hybrid breast reconstruction (HBR) has gained recognition as an effective technique to enhance both aesthetic appearance and functional outcomes after mastectomy. The current study aims to assess patient-reported outcomes using the modified BREAST-Q questionnaire administered before and after lipofilling, with particular emphasis on satisfaction with aesthetic results, physical comfort, and perceived quality of care.

Methods. Designed as a prospective cohort study, it enrolled patients who received prepectoral implant-based breast reconstruction subsequently complemented by one or more fat grafting sessions between March 2024 and May 2025 at the Institute of Oncology Prof. Dr. Ion Chiricuță, Cluj-Napoca, Romania, Romania. The modified BREAST-Q questionnaire was completed both preoperatively and three months after the final procedure. Statistical analyses were performed to evaluate variations in patient-reported outcomes across aesthetic, functional, and quality-of-care domains.

Results. Totally, 96 patients completed both the preoperative and postoperative BREAST-Q assessments. Statistically significant improvements ($p < 0.01$) were identified in the majority of aesthetic and psychosocial domains, including satisfaction with breast appearance (Q1), psychosocial well-being (Q2), sexual well-being (Q4), and satisfaction with surgical results (Q5). Physical discomfort (Q3) showed a marked postoperative reduction. Overall satisfaction with medical care remained consistently high.

Conclusion. HBR incorporating fat grafting after implant placement provides various advantages in aesthetic refinement, symptomatology, respectively the overall patient satisfaction. The technique demonstrates a favorable safety profile and can be confidently adopted in current clinical practice when appropriate patient selection and meticulous surgical planning are ensured.

Implications of microRNAs in hepatocellular carcinoma

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Introduction. MicroRNAs are small non-coding RNA molecules that play crucial roles in the post-transcriptional regulation of gene expression. Altered expression of microRNAs contributes to the initiation and progression of various malignancies, including hepatocellular carcinoma (HCC), a primary malignant tumor arising from hepatocytes.

Methods. This review analyses 12 articles from the last 10 years, searched through PubMed and ScienceDirect. The oldest study was published in March 2016 and the most recent one in October 2024. The chosen articles focus on the involvement of key microRNAs, particularly miR-122, miR-21, and miR-221 in hepatocarcinogenesis, tumor metastasis, and therapeutic resistance.

Results. In HCC, the expression of the liver-specific tumor suppressor miR-122 is reduced. Downregulation of miR-122 contributes to carcinogenesis and promotes proliferation, migration, and invasion of HCC cells by regulating the Wnt/β-catenin pathway, which subsequently activates the EMT pathway (Wang et al., 2016). MiR-21 and miR-221 are frequently upregulated in HCC, where they act as oncogenic miRNAs. Elevated serum exosomal miR-21 levels are correlated with increased tumor angiogenesis, contributing to a pro-oncogenic microenvironment (Zhou et al., 2018). MiR-221 is a central positive regulator of the NF-κB pathway. Its overactivation is responsible for promoting cancer development and enhancing chemoresistance (Liu et al., 2016). Regarding therapeutic strategies, studies have shown that reintroduction of miR-122 increases sensitivity to sorafenib (Al Ageeli, 2024) and doxorubicin by modulating the expression of multidrug resistance genes (Yahya et al., 2017). Other articles highlight the potential of miRNAs as prognostic biomarkers.

Conclusion. MicroRNAs are crucial in the evolution of hepatocellular carcinoma due to their modulating capacity of Wnt/β-catenin, EMT and NF-κB pathways.

Keywords: Hepatocellular carcinoma, MicroRNA-122, MicroRNA-21, MicroRNA-221

Emerging technologies in the diagnosis and treatment of hepatic hydatid cyst

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Introduction. Hepatic hydatid cyst (HHC), caused by Echinococcus granulosus, remains a major global health issue, especially in endemic regions. Traditional diagnostic tools—ultrasound, CT, MRI, and serology—show limited sensitivity and specificity, while standard pharmacotherapy with albendazole or mebendazole is hampered by poor bioavailability and long treatment duration. These challenges demand innovative,

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multidisciplinary approaches integrating advanced technologies.

Methods. This review synthesizes recent evidence on emerging technologies applied to HHC diagnosis and management, including nanomedicine, theranostics, artificial intelligence (AI), immunohistochemistry, molecular genetics, regenerative medicine, and digital health. Sources were identified through PubMed, Scopus, and Web of Science, focusing on translational and clinical studies published after 2018.

Results. Nanoparticle-based drug delivery systems significantly improve antiparasitic bioavailability and cyst penetration. AI-assisted imaging enhances cyst detection, classification, and surgical planning. Theranostic nanoparticles and microbubbles enable simultaneous diagnosis and targeted therapy. Molecular tools such as CRISPR-based assays offer ultra-sensitive parasite detection, while genomic insights reveal host–parasite interactions relevant to precision medicine. Robotic and image-guided surgery, 3D printing, and smart biomaterials optimize minimally invasive interventions. Mobile health solutions expand access to screening and follow-up in endemic regions.

Conclusion. Integrating nanotechnology, AI, molecular diagnostics, and regenerative approaches can transform HHC management from conventional to precision-based care. Collaborative, interdisciplinary efforts are essential to translate these innovations into affordable, accessible clinical applications.

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Harnessing the body's healing capacity – omental flap treatment for deep sternal complications

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Introduction. Sternotomy remains essential in cardiovascular surgery, yet deep sternal complications occur in 0.5-4% of cases and may carry high mortality. Managing complex presentations is especially challenging when no causative pathogen is identified and inflammation persists despite standard care.

Case report. We present the case of a 26-year-old man with bicuspid aortic valve disease, severe aortic regurgitation, and ascending aortic aneurysm who underwent aortic valve replacement with a mechanical prosthesis and ascending aorta replacement with a tubular Dacron graft. Initial recovery was uneventful. However, six months postoperatively, he developed wound dehiscence at the superior pole of the sternotomy, accompanied by local swelling. Pre-sternal incision produced purulent material. Despite repeated negative pressure wound therapy and multiple culture samples, all secretions remained sterile, indicating a rare aseptic mediastinal reaction of unclear origin.

After temporary improvement followed by recurrence, the persistence of this sterile inflammatory response to graft material prompted surgical re-intervention. Repeat

Ten years later: managing the return of a complicated hydatid cyst

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Introduction. Hydatid disease is a parasitic infection caused by Echinococcus granulosus, usually affecting the liver. It progresses slowly and may stay asymptomatic until cysts enlarge or become complicated. Computed Tomography (CT) and ultrasonography are essential for diagnosis and management. Treatment can be medical, surgical, or minimally invasive. Recurrence may result from intraoperative spillage, incomplete removal, or unnoticed satellite cysts. The main complication is intrabiliary rupture, while rarer ones include transdiaphragmatic, peritoneal, or gastrointestinal rupture and abscess formation.

Case report. We present the case of a 50-year-old man with long-standing hepatic hydatid disease (HHD) who underwent surgery in 2015 for multiple cysts in hepatic segments II–IV, V, and VII, including left hepatectomy, right pericystectomy, and closure of a small biliary fistula. Four years later, recurrence in the right lobe required laparoscopic evacuation and drainage, complicated by postoperative pneumothorax treated with pleural drainage. After years of remission, he was readmitted in May 2025 with epigastric pain, hematemesis, and sepsis. A CT scan showed infected left-lobe cysts with air–fluid levels, suggesting a hepato-gastric fistula, later confirmed endoscopically. After stabilization and antibiotics, he was referred to a tertiary center. MRI and MR cholangiography confirmed a left-lobe abscess and a calcified cyst in segment VII. Ultrasonography showed fistulization into the stomach. In September, he underwent open surgery with laparotomy, adhesiolysis, resection of segments IVa–IVb, subsegmentectomy of segment VII, and cholecystectomy. No active hepato-gastric fistula was found; a small cysto-biliary fistula was repaired. Recovery was uneventful.

Conclusion. This case highlights a late recurrence of HHD with infection and a suspected hepato-gastric fistula, stressing the importance of long-term follow-up and timely management.

Acute abdomen in situs inversus – an important differential diagnosis

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Introduction. Acute appendicitis is a common cause of right lower quadrant pain and emergency surgery. Anatomical variants, including situs inversus viscerum, can mask typical presentations and complicate diagnosis, potentially leading to inappropriate surgical interventions.

Case report. We report the case of a 58-year-old woman presenting with severe right lower quadrant pain for two days, associated with mild nausea. Physical

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examination revealed localized tenderness, rebound tenderness, and positive McBurney's sign. Laboratory results showed mildly elevated inflammatory markers. A history of a malpositioned heart prompted abdominal CT, which revealed complete situs inversus. Surprisingly, the appendix was normal, while acute sigmoid diverticulitis was located in the right lower quadrant. The patient was managed conservatively with antibiotics and supportive therapy and was discharged symptom-free after four days.

Conclusion. Situs inversus can alter classical symptom patterns and complicate surgical diagnosis. This case emphasizes the importance of detailed patient history, careful clinical examination, and imaging before intervention. Awareness of anatomical variants can prevent unnecessary surgery and ensure appropriate management.

Glucocorticoid receptor variant and pain perception in ankylosing spondylitis – a cross-sectional study from Northwestern Romania

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Introduction. Ankylosing spondylitis (AS) is a chronic inflammatory disease of the spine and sacroiliac joints, leading to pain and stiffness, and increased risk of obesity and diabetes. Polymorphisms in BDNF, COMT, SERT, and NR3C1 (glucocorticoid receptor) genes have been linked to pain modulation and metabolic activity. Our study explores the association of selected variants —BDNF (rs6265, rs988748), COMT (Val158Met), SERT (5-HTTLPR), and NR3C1-BclI—with pain perception in AS patients.

Methods. 44 patients with AS from the Clinical Hospital Oradea were included. Venous blood was collected for genotyping (TARMS-PCR, PCR-RFLP). Linear regression analysis (SPSS v26, $p < 0.05$) assessed pain scale differences by SNP, controlling for age, sex, disease duration, inflammatory markers, smoking status and BMI.

Results. In univariate analysis, BDNF rs6265, BDNF rs988748, COMT Val158Met, SERT 5-HTTLPR, or NR3C1 showed non-significant associations with pain perception (all $p>0.05$). After adjusting for potential confounders, BclI in GR gene showed a significant correlation with pain score ($\beta=0.690$, 95% CI:0.141–1.240, $p=0.015$). However, when all polymorphisms were included in the multivariable model, BclI was non-significancant ($\beta=0.468$, 95% CI: -0.159-1.094, $p=0.138$). Tobacco use ($\beta=0.907$, 95% CI:0.236-1.579, $p=0.015$) and elevated C-reactive protein ($\beta=0.167$, 95% CI:0.129-0.206, $p<0.0001$) were associated with higher pain scores. Age, sex, time since diagnosis, ESR and BMI were not significatly associated with pain perception (all $p>>0.05$).

Conclusion. No associations were found for BDNF, COMT, or SERT, while NR3C1-BclI was significant only after controlling for confounders. Further tests are needed to confirm these findings. Population-specific types of alleles in Romania may guide polygenic risk studies and reference genome initiatives such as ROGEN.

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From anemia to dual diagnosis – synchronous gallbladder and colon adenocarcinoma: a case report

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Introduction. Gallbladder carcinoma is a rare and highly aggressive malignancy, typically associated with late clinical presentation. Consequently, many cases are identified incidentally on histopathological examination following cholecystectomy performed for presumed benign gallbladder disease.

Case report. A 76 year-old woman, recently diagnosed with moderate iron-deficiency anemia (IDA), presented with fatigue, nausea, and unintentional weight loss. Given the positive fecal occult blood test, both upper and lower gastrointestinal endoscopies were performed, revealing a 3 cm ulcerated polipoid mass in the ascending colon. Biopsy confirmed colonic adenocarcinoma. Standard staging with thoracic CT and abdominopelvic MRI was initiated to assess metastatic spread. Meanwhile, a routine abdominal ultrasound was performed, unexpectedly revealing an enlarged gallbladder with heterogeneous content: a 21 mm infundibular calculus and a suspicious hyperechoic mass on the inferior wall. The neoplastic nature of the mass was confirmed through a contrast-enhanced ultrasound. Cholangiography-enhanced MRI revealed no definitive evidence of extramural or hepato-duodenal invasion, supporting surgical intervention as the most appropriate treatment option. The patient underwent cholecystectomy with resection of hepatic segments IVb-V, along with a right hemicolectomy. Histopathological analysis confirmed a poorly differentiated gallbladder adenocarcinoma (T2b). Postoperative recovery was favorable, with no immediate complications reported.

Conclusion. Although colorectal cancer represented the expected cause of iron-deficiency anemia, this case illustrates that routine preoperative imaging can uncover clinically silent synchronous malignancies. The incidental identification of gallbladder carcinoma at a surgically resectable stage provided a rare opportunity for curative treatment—underscoring how careful attention to incidental findings can directly influence patient prognosis.

Geriatric frailty – the hidden threat to postoperative outcomes: a case report

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Introduction. Frailty is a complex geriatric syndrome characterized by a reduced physiological reserve and diminished capacity to adapt to stressors. It is a sum of physical and psychosocial factors, which leads to increased vulnerability to postoperative complications.

Case report. A 92-year-old male presented with general weakness and fatigue. His medical history revealed recently diagnosed moderate iron deficiency anemia, moderate dementia, grade I essential hypertension, chronic ischemic heart disease and chronic renal

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disease stage G4 KDIGO. Physical examination showed bradylalia and bradypsychia, decreased calf circumference, reduced handgrip strength and a gait speed of 0.42 m/s. According to the Fried Frailty Index and the Clinical Frailty Scale, the patient was classified at admission as being severely frail. Laboratory findings revealed moderate normochromic normocytic anemia, low ferritin, low transferrin saturation, vitamin B12 deficiency, eGFR = 18.11 mL/min/1.73 m² and a positive fecal occult blood test. Lower gastrointestinal endoscopy revealed a tumoral mass at the hepatic flexure extending into the ascending colon. Subsequently, the patient experienced a decrease in hemoglobin levels and developed hemodynamic instability with hypotension and paroxysmal atrial fibrillation, thus requiring two blood transfusions and palliative surgery. Postoperatively, the patient developed delirium, cardiac decompensation, acute worsening of chronic kidney disease and multiple infectious complications, leading to rapid cognitive deterioration and functional impairment .

Conclusions. This case highlights the major impact of geriatric frailty on surgical outcomes. Frailty reduces the capacity to cope with stress, turning invasive procedures into triggers of multi-organ decompensation. Early identification of frailty and personalized medical care are essential for pre- and postoperative management in geriatric patients.

Distribution of bacterial resistance phenotypes by clinical setting in a county hospital from Northwestern Romania over a five-year period

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Introduction. Antibiotic resistance represents a global challenge for today's healthcare systems. This issue is causing an increase in the rate of antibiotic therapeutic failure in the treatment of infectious diseases, leading to significant economic burden and increased mortality and morbidity rates. A local profile of resistance phenotype distribution by clinical setting can provide valuable insight into emerging trends in antimicrobial resistance and possible issues in medical practice, such as understaffing, poor training, and poor enforcement of hygiene guidelines.

Methods. Data was collected from The Cluj-Napoca, Romania Emergency County Hospital's database and covers a 5-year period from October 2019 to October 2024. Patients' personal information had been anonymised, while relevant data related to the clinical setting and antimicrobial resistance have been retained. We have grouped infections into 4 resistance phenotypes: MRSA, ESBL/AmpC, CRE, and VRE. Hospital wards were categorized as: outpatient department, ICU, medical, or surgical. Statistical analyses were then performed to assess potential correlations between clinical setting and resistance phenotype.

Results. Following the statistical analyses, we found a statistically significant correlation between clinical setting and resistance phenotype for all categories. MRSA and ESBL/AmpC isolates showed higher frequencies in medical wards, whereas CRE and VRE were more prevalent in ICU wards.

Conclusion. The distribution of resistance phenotypes by clinical setting demonstrates a statistically significant correlation, suggesting environmental factors that favor specific resistant strains and may reflect underlying issues in medical practice. Further studies should focus on finding the specific factors causing this distribution with the aim of reducing the burden they cause in high-risk wards.

A stiff elbow, a rare surgery, and a surprising recovery – a case of rheumatoid arthritis

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Introduction. Rheumatoid arthritis (RA) is a chronic autoimmune disease that causes progressive joint destruction and disability. Although elbow involvement is less common than small joint disease, chronic inflammation can result in secondary osteoarthritis requiring surgical management. Total elbow arthroplasty (TEA) remains a rare but effective option for pain relief and mobility restoration in advanced cases.

Case report. We report a 43-year-old female diagnosed with RA in 2016, treated with leflunomide (20 mg/day) and intermittent prednisone. Following a left elbow trauma in 2022, she developed progressive pain, swelling, and functional limitation despite biological therapy (etanercept) and leflunomide (10 mg/day). Imaging revealed erosive changes and joint degeneration consistent with secondary osteoarthritis. The preoperative Mayo Elbow Performance Score (MEPS) was 30 (poor function).

A cemented total elbow arthroplasty (Zimmer Nexel prosthesis) with triceps reinsertion was performed. The postoperative course was uneventful, with moderate pain (maximum 4/10) and rapid functional recovery. At one week, the patient regained 70–80% of daily activity. Six months postoperatively, MEPS improved to 95 (excellent function), with almost full range of motion, no pain, and complete return to normal activity. Rheumatoid disease remained in remission under biological therapy.

Conclusions. This rare case of total elbow arthroplasty for rheumatoid arthritis with secondary osteoarthritis demonstrates excellent recovery and functional outcome. Early diagnosis, multidisciplinary management, and strict therapy adherence contributed to sustained remission and near-complete restoration of elbow function.

Atypical inferior vena cava obstruction mimicking leg deep vein thrombosis – a case report

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Introduction. Renal cell carcinoma (RCC) can rarely extend as a tumor thrombus (TT) into the inferior vena cava (IVC), most commonly in an anterograde direction toward the heart. Like other neoplasms, RCC is associated with a hypercoagulable state, therefore, the differential diagnosis of a venous obstruction in this context should include both *in situ* (bland) paraneoplastic thrombosis and obstruction caused by a TT.

Case report. We present the case of a 75-year-old female patient with a history of right RCC with IVC extension, undergoing chemotherapy, who was urgently admitted to our clinic with bilateral leg swelling, pain and erythema, raising suspicion of local deep vein thrombosis (DVT).

Abdominal ultrasound (US) showed the complete invasion of the retrohepatic

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segment of the IVC by the TT, extending into the left renal vein and upwards to within 2 cm of the right atrium. Posteriorly cavo-caval collaterals were noted, some of which appeared thrombosed. At the confluence MYOSITISPOLof the iliac veins, the IVC was also partially thrombosed, with a small eccentric flow jet, the thrombus extending into the left common iliac vein. The external iliac and femoral veins were patent. Meanwhile the leg US showed no signs of DVT, suggesting that the clinical manifestations were due to impaired venous return caused by the combined IVC obstruction and collateral vein thrombosis.

The patient's clinical course was favorable under pharmacological therapy, with complete remission of symptoms. Given the origin of the IVC obstruction, anticoagulant therapy was not deemed necessary upon discharge.

Conclusion. Neoplastic invasion of the IVC represents an uncommon but major clinical challenge with a generally poor prognosis. Early recognition of venous obstruction, accurate imaging, and careful differential diagnosis are essential to establish the underlying cause, guide management, and aid in prognostic evaluation.

Diagnostic challenges in inclusion body myositis associated with autoimmune disease

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Introduction. Inclusion body myositis (IBM) is the most common acquired myopathy in adults over 50, characterized by slow progression, asymmetric weakness, and poor response to immunosuppressive therapy. Despite these features, IBM is often misdiagnosed as polymyositis or neuromuscular junction disorders. Diagnosis becomes even more challenging when associated with autoimmune diseases that can cause similar symptoms and misleading laboratory results.

Case report. A 64-year-old woman with an 11-year history of progressive proximal lower limb weakness, muscle pain, and gait disturbance showed great creatine kinase elevation and high-titer ANA (1:320), suggesting an autoimmune process, although myositis-specific antibodies were negative. She was diagnosed with polymyositis and treated with corticosteroids and methotrexate. Despite therapy, symptoms worsened, with dysphagia for solids, proximal upper limb weakness, and palpebral ptosis. Electroneuromyography revealed a chronic myogenic pattern with active denervation. The first deltoid biopsy was nonspecific, while secondary myopathy causes and myasthenia gravis were excluded.

Given the progressive course, IBM was suspected and confirmed by a second biopsy from the right vastus lateralis, guided by MRI findings. Histology revealed fiber size variability, rimmed vacuoles, mitochondrial aggregates, necrosis, regeneration, focal inflammation, and MHC class I overexpression. ANA positivity was later attributed to coexisting primary biliary cholangitis, confirmed by cholestatic liver tests and anti-mitochondrial antibodies. Supportive management with physiotherapy, L-carnitine, and coenzyme Q10 was continued, as immunosuppressive therapy proved ineffective.

Conclusion. This case illustrates the diagnostic challenge of distinguishing IBM from other inflammatory myopathies and underlines the key role of MRI-guided muscle biopsy in confirming diagnosis, avoiding unnecessary immunosuppression, and optimizing supportive care.

Out-of-the-box diagnostic approach in ampullary cancer – a case report

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Introduction. Ampullary carcinomas are defined as malignant epithelial neoplasms originating in the ampullary complex, distal to the confluence of the common bile duct and the pancreatic duct. This case report aims to shed light on an out-of-the-box diagnostic approach.

Case report. A 54-year-old woman was admitted to the gastroenterology ward for asthenia, nocturnal diaphoresis, fatigue, weight loss, and jaundice. Medical history was not significant. Physical examination revealed epigastrium and right hypochondrium tenderness, and jaundice of the sclera and skin. Bloodwork showed inflammation, liver cytolysis, cholestasis, conjugated hyperbilirubinemia, and mild anemia.

Abdominal ultrasound found a nodule in the pancreatic head with intra-choledochal protrusion, whose malignant nature was proven by contrast-enhanced ultrasonography (CEUS) less than 1 hour after presentation. We suspected a vaterian ampulloma, which needed to be distinguished from distal cholangiocarcinoma. CEUS reinforced the suspicion of intracholedochal protrusion, confirmed later by contrast-enhanced magnetic resonance cholangiopancreatography (MRCP), ruling out a periampullary cephalic pancreatic tumor.

Duodenoscopy was not available, but we considered that axial-view endoscopy could visualize the papilla enough to confirm or rule out the ampulloma. A protruding, ulcerated, spontaneously bleeding papilla, with franc tumoral aspect was viewed. The forceps biopsies set the definitive diagnosis of ampulloma.

Conclusion. Ampullary cancers are rare malignant entities which develop due to unstable transitions from pancreatobiliary to intestinal epithelium, constantly irritated chemically and mechanically. They are differentiated from other periampullary cancers by their early symptomatology. Our original approach was to use CEUS for the confirmation of a malignant tumor and axial-view endoscopy for its direct visualization, accelerating thus the diagnostic approach.

From nickel allergy to earlobe reconstruction – a case presentation

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Introduction. Allergic contact dermatitis is a frequent condition, with nickel as a common trigger. Prolonged exposure may cause chronic inflammation, ulceration, impaired healing, and pruritus. These changes can lead to locally severe complications and pose diagnostic challenges in distinguishing reactive hypertrophic scars from true keloids.

Case report. We report the case of a 35-year-old woman with previously suspected chronic prurigo who presented with multiple pruritic, antihistamine-resistant leg ulcerations. At age 14, she underwent improper ear piercing, which caused acute

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contact dermatitis due to an unrecognized nickel allergy. The subsequent eczema, infection, and chronic inflammation led to bilateral earlobe lesions that became nodular, fibrotic, and indurated, with yellow-crusted erosions but no dissemination. Patch testing later confirmed a strong positive reaction to nickel. Dermatitis artefacta was identified as the underlying cause of leg ulcerations and a contributing factor to the chronic earlobe scarring.

Considering the chronicity, fibrosis, and psychological background, surgical intervention was deemed appropriate. Under local anesthesia, the lesions were completely excised and reconstructed using a preauricular rotational flap oriented perpendicular to the mandibular line. Deep sutures restored the natural earlobe contour, and a retroauricular flap was used to close the posterior defect. Histopathology confirmed hypertrophic scarring with a collagen-rich dermis and a mixed inflammatory infiltrate. Healing was uneventful, with complete recovery and no recurrence.

Conclusion. This case highlights a rare coexistence of nickel-induced dermatitis, chronic inflammation, and dermatitis artefacta leading to hypertrophic earlobe scarring, a combination rarely reported in the literature. The management was also distinctive, as surgical reconstruction provided a unique and effective therapeutic approach, achieving functional and aesthetic improvement.

Oral tongue squamous cell carcinoma: surgery as the cornerstone of treatment

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Introduction. Oral tongue squamous cell carcinoma (OTSCC) is the most common malignancy of the oral cavity. Surgery is considered a cornerstone of treatment for achieving local and regional control and improving survival outcomes.

Case report. A 49-year-old man diagnosed with OTSCC following a CT scan and biopsy was selected for surgery. The CT revealed a mass of 2.8/1.7/1.5 cm (AP/LL/CC) in the right anterior hemilingual region with minimal contralateral extension (0.8/0.5 cm), and cN0. Surgical excision of the tumor was performed, achieving standard oncological margins of 1 cm. Laterocervical lymphadenectomy was undertaken, including levels I-IV on the right and levels I-III on the left. The thyro-linguo-facial trunk, facial artery, and superior thyroid artery were dissected to facilitate vascular anastomosis. A free fasciocutaneous thigh flap was harvested by the plastic surgery team under US-Doppler guidance, shaped, and transferred to reconstruct the tongue defect. Microvascular anastomosis was performed with the previously dissected arteries. Histopathological examination revealed contralateral lymph node metastasis measuring less than 0.3 cm, without extranodal extension. The tumor was staged as pT2N2cL0V0Pn1G1R0.

Discussion. Accurate preoperative staging of OTSCC remains challenging, as pathology findings contradict the initial cN0. Although the contralateral extension was minimal, the neck dissection was justified by the pN2c/pPn1 status, which represents intermediate-risk factors, influencing the therapeutic plan and warranting postoperative radiation therapy. This approach aligns with published evidence demonstrating reduced recurrence in similar intermediate-risk patients. A multidisciplinary team is crucial for the successful management of OTSCC.

Conclusions. This case highlights the central role of surgery in the management of OTSCC, which remains the primary curative treatment.

When endometriosis mimics malignancy – a rare case of intestinal obstruction

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Introduction. Endometriosis is a disorder characterized by the presence of tissue similar to the endometrium outside the uterine cavity. It affects approximately 1 in 10 women of reproductive age. While the most common sites of endometriotic lesions include the retroperitoneum, ovaries, and myometrium, involvement of the gastrointestinal tract is uncommon, accounting for less than 15% of all cases.

Case report. We report the case of a 35-year-old woman presenting with diffuse abdominal pain, fatigue, vomiting, and absence of intestinal transit for 48 hours. Examination showed abdominal tenderness, hyperresonance to percussion, and no hernias. Laboratory results were normal. Imaging revealed distended loops and multiple hydro-aeric levels. Exploratory laparotomy identified a stenotic tumor-like mass near the ileocecal valve. Right hemicolectomy was performed due to initial suspicion of malignancy. Histology revealed extensive endometriosis. The patient recovered well and was discharged after seven days.

Conclusions. Bowel endometriosis is rare and often misdiagnosed. Clinicians should consider it as a differential, especially in young, nulliparous women. Early recognition allows appropriate management and avoids surgical procedures.

Atypical intussusception induced by a jejunal tubulovillous adenoma

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Introduction. Intussusceptions are medical emergencies in which one segment of the intestine telescopes inside of another. It is most common in children between three months and three years, while only 1% of adult bowel obstructions are caused by this condition. In adults, intussusception is typically due to a pathologic lead point in the bowel, which is malignant in over 50% of cases.

Case report. My case is about a 29-year-old female patient who presented to our emergency department complaining of abdominal pain. Her laboratory investigations were within normal limits. The CT revealed a voluminous formation in the left hemi-abdomen. Two days later, she developed signs of acute occlusive abdomen, for which surgery was needed. During the intervention, an entero-enteric intussusception caused by a large polyp of the first jejunal segment is identified. Intussusception reduction and segmental enterectomy with double-layer T-T entero-enteric anastomosis and Douglas drainage are performed. Histopathological examination reveals that the jejunal formation is a tubulovillous adenomatous polyp.

Conclusion. The classic triad of intussusception is: abdominal pain, a palpable sausage-shaped mass and heme-positive stools, but they are rarely present together. Pediatric intussusception is often acute, while adults may present with acute, subacute or chronic nonspecific symptoms. There are also controversies around whether to reduce

the intussusception before resection. If malignancy cannot be ruled out, it can lead to the dissemination of malignant cells, so it is better to avoid a reduction. CT is the most accurate diagnostic tool for preoperative diagnosis.

In conclusion, intussusceptions are rare in adults, especially secondary to a polyp. Tubulovillous adenomas are a type of precancerous polyp more commonly found in the colon and rectum, a jejunal involvement is therefore much less common.

Megadolichosigmoid – when anatomy sets the stage for obstruction

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Introduction. Sigmoid volvulus represents a gastrointestinal emergency resulting from the rotation of the sigmoid colon around its mesenteric attachment, producing luminal obstruction. Although it predominantly affects elderly individuals, it may also appear in younger patients with predisposing factors such as long-standing constipation or congenital anatomical variations. In these cases, chronic distension and elongation of the sigmoid segment make it prone to torsion.

Case report. A 25-year-old man with a known history of chronic constipation presented with sudden diffuse abdominal pain accompanied by progressive distension. On physical examination, the abdomen was markedly tympanic and tender on both superficial and deep palpation, with absent bowel sounds. Abdominal CT identified a massively dilated sigmoid colon showing the whirl (spiral) sign of the mesentery, suggestive of volvulus, along with compression of the stomach and transverse colon. Endoscopic decompression was successfully achieved, restoring normal intestinal transit. However, eight months later, the patient returned with a new episode of acute intestinal obstruction, confirmed radiographically by the coffee-bean sign and ultrasonographically by severe meteorism. Other potential causes of acute large bowel obstruction considered included colonic carcinoma, diverticulitis with secondary stenosis, and paralytic ileus. Specific imaging findings, particularly the coffee-bean sign on X-ray and whirl sign on CT, helped establish the diagnosis of sigmoid volvulus. Further evaluation demonstrated a megadolichosigmoid (70 cm in length, 6 cm in diameter) — an excessively long and distended sigmoid loop with a narrow mesenteric base, predisposing to torsion. This configuration leads to venous congestion, subsequent ischemia, and progressive obstruction. As endoscopic decompression during the recurrence failed to provide lasting relief, the patient underwent a laparoscopic sigmoidectomy with end-to-end colorectal anastomosis, which successfully prevented further episodes.

Conclusion. In patients with megadolichosigmoid, recurrent sigmoid volvulus is frequent, making endoscopic decompression a temporary measure. Elective laparoscopic resection of the sigmoid colon remains the definitive therapeutic approach, effectively preventing severe complications such as ischemia and perforation.

Beyond the genes – genotype–phenotype correlation in a patient with osteogenesis imperfecta

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Introduction. Osteogenesis imperfecta (OI) comprises a heterogeneous group of rare inherited disorders of connective tissue, characterized by decreased bone mass, diminished bone mineral strength, and consequent skeletal fragility that can result in deformity and functional impairment. The disorder primarily arises from pathogenic variants in genes encoding type I collagen, the most abundant structural protein in the human body, which forms a triple helix composed of two α1 and one α2 chains and provides tensile strength to bone, skin, tendons, and other connective tissues. Among these, mutations in the COL1A1 gene located on chromosome 17q21.33, which encodes the pro-α1 chain of type I collagen, disrupt the integrity of collagen synthesis and assembly, leading to the phenotypic spectrum observed in OI.

Case report. A 4-year-old boy presented with a history of seven distinct fractures, which, along with the presence of striking blue sclerae identified upon physical examination, raised a clinical suspicion for osteogenesis imperfecta. The family history was notable for the father's history of multiple fractures, further supporting a hereditary connective tissue disorder. Comprehensive molecular analysis using the Blueprint Genetics Osteogenesis Imperfecta Panel revealed a heterozygous COL1A1 c.1299+1G>A (NM_000088.3) splice donor variant. This pathogenic alteration disrupts the canonical donor splice site, leading to exon 19 skipping and aberrant collagen type I formation, as previously documented in several cases of osteogenesis imperfecta. Taken together, the clinical phenotype, familial pattern, and molecular findings establish a definitive diagnosis of autosomal dominant osteogenesis imperfecta type I.

Conclusion. This case highlights the crucial value of integrating clinical and molecular findings for precise diagnosis and classification of osteogenesis imperfecta. Recurrent fractures and blue sclerae suggested the phenotype, while identification of a pathogenic COL1A1 splice-site variant confirmed the molecular cause. Defining this genotype–phenotype correlation is vital for accurate diagnosis, prognosis, personalized management, and informed genetic counseling.

Beyond the symptoms – discovering a silent gastric neuroendocrine tumor

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Introduction. Gastrointestinal neuroendocrine tumors (NETs) represent a rare and heterogeneous group of neoplasms, accounting for less than 1% of all gastric malignancies. They often present incidentally, due to their indolent course and nonspecific symptoms. Proper diagnosis requires a combination of endoscopic, imaging, and immunohistochemical evaluation.

Case report. We present the case of a 53-year-old male patient, admitted for urinary symptoms (pollakiuria, nocturia, episodes of urinary incontinence), appetite loss, and weight loss (5 kg in two months). Routine investigations, including abdominal ultrasound and laboratory tests, were within normal limits. Upper digestive endoscopy revealed a 2.5–3 cm submucosal, centrally umbilicated lesion on the posterior wall of the stomach, with normal overlying mucosa. Endoscopic ultrasound suggested a third-layer subepithelial gastric lesion, most consistent with a neuroendocrine tumor. Fine-needle aspiration cytology and immunohistochemistry (chromogranin A and synaptophysin positive) confirmed a well-differentiated neuroendocrine tumor (G1). Ki-67 index was <3%, and mitotic index <2/2 mm². Abdominal CT identified no metastases. The patient underwent atypical gastrectomy with R0 resection. Final pathology confirmed a well-differentiated gastric neuroendocrine tumor (WDNET G1), pT2NxL0V0Pn0R0. The postoperative course was uneventful. Associated findings included a bulbar urethral stricture and detrusor muscle hypertrophy.

Conclusion. This case illustrates an incidentally discovered, sporadic, well-differentiated gastric neuroendocrine tumor in a patient investigated for unrelated urinary symptoms. Despite their rarity, early recognition and complete surgical resection are crucial for favorable prognosis. Long-term follow-up with imaging and biochemical markers is essential to monitor recurrence.

Massive upper gastrointestinal bleeding caused by duodenal tumor invasion – multidisciplinary surgical management

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Introduction. Massive upper gastrointestinal bleeding caused by a duodenal tumor invading adjacent organs is a rare but severe surgical emergency requiring a multidisciplinary approach. Duodenal cancer accounts for less than 1% of all digestive malignancies reported in the European Union. Rapid diagnosis and coordinated surgical intervention are essential to achieve hemostasis, ensure oncologic radicality, and restore digestive continuity. Among life-saving options, cephalic duodenopancreatectomy remains technically demanding yet curative when performed timely, with reported severe morbidity rates up to 46.1% in emergent settings.

Case report. A 62-year-old male presented with massive upper gastrointestinal

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bleeding, severe anemia (Hb 5.2 g/dL), leukocytosis, and prolonged activated partial thromboplastin time (166.2 s). The patient was hemodynamically unstable, requiring urgent transfusion. Contrast-enhanced CT showed a duodenal tumor in the third portion, invading the pancreatic uncinate process, with active bleeding due to vascular effraction of the inferior duodenopancreatic trunk. Possible invasion of the proximal transverse colon was noted. Two endoscopic hemostasis attempts failed, making surgery the only remaining option. The patient underwent cephalic duodenopancreatectomy with right hemicolectomy for complete resection and hemorrhage control. Digestive continuity was restored through pancreaticojejunal, gastrojejunal, biliojejunal, and ileocolic anastomoses. Postoperative recovery was favorable, with discharge after 10 days and no complications or recurrence at 3, 6, and 18 months.

Conclusions. This case emphasizes the rarity and complexity of duodenal tumors presenting with acute hemorrhage and vascular effraction. Despite high operative risks, timely multidisciplinary management and radical surgery ensured hemostasis, tumor clearance, and long-term favorable outcome.

The hidden threat – hepatocellular carcinoma in a non-cirrhotic liver: a case report

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Introduction. Hepatocellular carcinoma (HCC) is one of the most common causes of cancer related death worldwide, accounting for approximately 90% of primary hepatic malignancies. Risk factors for HCC include chronic liver diseases, cirrhosis, chronic alcoholism, and nonalcoholic fatty liver disease.

Case report. We report the case of a 51-year-old male patient, with a history of type B chronic hepatitis for which the patient was receiving antiviral medication with Tenofovir. At his 3 months check-up, the abdominal ultrasound revealed a hypoechoic lesion in the 8th segment of the liver, measuring 25/22 mm. The abdominal MRI confirmed the presence of the lesion, classified as LI-RADS 5, most likely being an HCC. The alpha-fetoprotein levels were extremely elevated (3744 ng/ml, while the normal range being under 40 ng/ml). The surgical procedure included exploratory laparotomy, atypical liver resection of 5th segment and interhepatophrenic, subhepatic and subcutaneous surgical drainage. The surgical mass was sent to histopathology, where the diagnosis of hepatocellular carcinoma was confirmed. Postoperative ultrasound was within the normal limits, without the presence of any intraperitoneal collections. HCC remains one of the deadliest malignancies globally, typically developing within a liver affected by cirrhosis. However, this case highlights the critical subset of patients who develop HCC in a non-cirrhosis liver, which stands for 10 to 20% of all primary liver cancers, this being most likely attributed to the direct oncogenic potential of the Hepatitis B Virus. Unlike Hepatitis C, HBV is a DNA virus capable of integrating its genetic material into the host hepatocyte genome. This can lead to insertional mutations, disrupting tumor suppressor genes and activating proto-oncogenes independent of the inflammatory progression to cirrhosis.

Conclusion. In conclusion, timely and effective treatment of hepatocellular carcinomas is crucial in preventing the disease from worsening. The management of such cases include a multidisciplinary team, adequate imaging, pristine surgical technique and histopathological examination for final diagnosis.

Successful multimodal therapy in a pediatric group 3 medulloblastoma – correlation between molecular profile and outcome

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Introduction. Medulloblastoma is the second most common malignant paediatric brain tumour, representing around 20% of central nervous system neoplasms. According to the WHO CNS5 classification, all medulloblastomas are Grade 4 and are divided into WNT-activated, SHH-activated (TP53-wildtype or mutant), and non-WNT/non-SHH (Groups 3 and 4). Group 3 tumours occur mainly in young boys, are linked to MYC amplification, TP53 status, and chromosomal alterations, and carry a poor prognosis.

Case report. A 3-year-old boy presented with broad-based gait and unsteady walking. MRI revealed a giant 5-cm posterior fossa mass in the fourth ventricle, causing brainstem compression, herniation of the cerebellar tonsils through the foramen magnum, and secondary obstructive hydrocephalus. He underwent a bilateral telovelar suboccipital craniotomy with near-total resection, limited by adherence to the caudal ventricular floor. Postoperatively, chemotherapy (VEC: vincristine, etoposide, cisplatin) was initiated. Follow-up MRI showed nodular enhancement with astrocytic differentiation at the margins, prompting a second resection of residual tumor tissue. Additional chemotherapy was given, followed by craniospinal irradiation: 23.4 Gy in 13 fractions and a posterior fossa boost of 30.6 Gy in 17 fractions, totalling 54 Gy in 30 fractions under sedation.

Molecular profiling confirmed Group 3, subgroup II medulloblastoma, TP53 wild-type, non-WNT/non-SHH, without MYC amplification, unmethylated MGMT promoter, with monosomy 6 and 9 plus heterozygous loss of CDKN2A/B. Cerebrospinal fluid cytology was negative. The patient currently shows no signs of recurrence.

Conclusion. Early multimodal therapy in Group 3 medulloblastoma without MYC amplification or TP53 mutation can provide durable tumour control. Given the patient's age, lifelong follow-up and management of treatment-related effects are essential. Molecular profiling remains key for prognosis and personalised management.

Impact of antiretroviral therapy on telomere biology: a systematic review with a laboratory workflow for PBMC isolation

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Introduction. Telomere shortening is accelerated in HIV infection, reflecting premature cellular aging, but the long-term effects of sustained antiretroviral therapy (ART) on telomere length (TL) remain unclear. Some nucleoside reverse transcriptase inhibitors (NRTIs) inhibit telomerase *in vitro*. This review examines how different ART regimens affect TL in adults and children exposed to HIV.

Methods. A systematic PubMed, Scopus, and Google Scholar search following PRISMA guidelines identified 19 of 125 studies. Included studies assessed ART effects

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on TL or telomerase activity in HIV-infected adults, children, or HIV-exposed uninfected (HEU) children. Two reviewers excluded studies lacking regimen details or using animal models. In parallel, we performed peripheral blood mononuclear cells (PBMCs) isolation and DNA extraction to support TL measurement and to optimize sample handling.

Results. In adults, most studies found no major TL differences across ART classes: integrase inhibitors (INSTIs), protease inhibitors, or NNRTIs, though some drug-specific effects appeared. Efavirenz was linked to shorter TL, and tenofovir reduced telomerase activity and TL in CD8+ T cells. Integrase-based or dual therapies often stabilized or slightly increased TL, and long-term ART slowed telomere loss. In pediatric studies, ART exposure was not associated with TL shortening; some cohorts showed longer TL at birth with zidovudine. Over follow-up to 19 years, TL decline tracked with age rather than HIV or ART.

Conclusion. Telomere loss in HIV is driven primarily by immune activation and co-factors, not ART. Certain drugs may transiently affect TL, but suppressive ART, particularly INSTI-based or dual regimens, can limit or partially reverse telomere loss. Pediatric data are reassuring, with minimal risk of telomere compromise. An optimized PBMCs isolation protocol enables future translational studies on molecular aging markers.

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Unusually large lumbosacral lipoma with two-decade progression – a case report

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Introduction. Lipomas represent nearly 50% of benign mesenchymal tumors and are most commonly located on the trunk and proximal extremities. Although typically small and asymptomatic, giant lipomas (>10 cm) are uncommon and may pose diagnostic challenges due to their size, deeper extension, or resemblance to malignant lesions. Their low incidence, especially in anatomically complex regions, makes atypical presentations clinically noteworthy.

Case report. We report a case of a 54-year-old patient with a progressively enlarging lumbosacral mass evolving over approximately 20 years. Clinical examination revealed a multinodular subcutaneous tumor measuring 45/18 cm, relatively fixed to deeper tissues, with intact overlying skin and no regional adenopathy. MRI described a well-delimited lipomatous formation located in the lower lumbar subcutaneous tissue, with a cranio-caudal extension of 182 mm—from L3 to S5—an anteroposterior thickness of 67 mm, and an impressive lateral extension of approximately 400 mm, without muscular or osseous involvement and without pathologically enlarged pelvic lymph nodes. Surgical excision was performed under general anesthesia with placement of double aspirative drainage. On postoperative day two, the patient developed significant hemorrhage with acute anemia, requiring transfusion and urgent reintervention for hematoma evacuation and hemostasis. The subsequent evolution was favorable. Histopathology confirmed a benign lipoma composed of mature adipocytes with a thin capsule and no cell atypia.

Conclusion. This case stands out due to the unusually large size of the lipoma, its rare location in the lumbosacral region, and its exceptionally slow, 20-year progression. Despite its impressive size, the lesion remained benign, well-encapsulated, and non-invasive. The postoperative hemorrhage further complicates the case, showing the importance of close postoperative monitoring.

When infection masks malignancy – a fatal case of delayed diffuse large B-cell lymphoma diagnosis

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Introduction. Late presentation of HIV infection remains a major clinical and public health challenge, as it is frequently associated with profound immunosuppression and an elevated risk of severe opportunistic complications, including lymphoproliferative malignancies.

Case report. We report the case of a 31-year-old woman with HIV infection and a history of miliary tuberculosis (diagnosed in 2020), who presented in June 2023 with severe abdominal pain. Abdominal CT revealed extensive mesogastric and hypogastric lymphadenopathy, suggesting a lymphoproliferative disorder. Exploratory laparoscopy found multiple confluent adenopathic masses involving the transverse mesocolon and mesenteric root, with purulent fluid in the Douglas pouch. Histopathology suggested a high-grade lymphoproliferative lesion, but immunohistochemistry was inconclusive, failing to distinguish between a reactive process and B-cell lymphoma.

Given her infectious history and nondiagnostic pathology, empirical antituberculous therapy was started in October 2023. Ultrasound-guided biopsies performed in Italy (December 2023) remained nondiagnostic. A repeat laparoscopy in February 2024 finally confirmed diffuse large B-cell lymphoma (DLBCL), and chemotherapy was initiated. Despite treatment, PET-CT scans in May and August 2024 demonstrated metabolic, dimensional, and numeric progression of lymphomatous lesions, with new hepatic, pleural, and peritoneal involvement (stage IVB DLBCL). Clinical deterioration ensued, and the patient unfortunately died in December 2024.

Conclusion. This case highlights the considerable diagnostic challenges encountered in HIV-positive late presenters, where overlapping features of infectious and neoplastic disease, atypical imaging, and inconclusive histopathology may substantially delay diagnosis. Early and accurate differentiation between infection-related and malignant pathology is crucial to improve outcomes, particularly in young patients at risk for aggressive lymphomas.

Early detection of distal pancreatic tumors – evaluation of diagnostic accuracy and challenges

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Introduction. Pancreatic neoplasms are highly aggressive malignancies, often diagnosed late with limited treatment options. Tumor location influences detection: proximal tumors (head and neck) are often identified earlier, while distal tumors (body and tail) remain largely asymptomatic, delaying diagnosis and worsening Medical Clinic prognosis. Early detection is crucial, yet conventional imaging and biomarkers have limited sensitivity for distal tumors. This paper explores current diagnostic methods for distal pancreatic tumors and evaluates their effectiveness and challenges in early detection.

Methods. A systematic search of PubMed and Scopus was performed for studies published between 2015 and 2025 evaluating diagnostic methods for tumors of the pancreatic body and tail, with study selection and data extraction conducted in accordance with PRISMA guidelines.

Results. Conventional imaging, including CT, MRI, and endoscopic ultrasound, shows limited sensitivity for early-stage tumors in the body and tail due to their retroperitoneal location and small size at presentation. Blood biomarkers such as CA 19-9 are commonly used but have limited specificity and sensitivity in asymptomatic patients. Emerging approaches, including AI-assisted imaging, radiomics, and novel biomarker panels, demonstrate promise in improving early detection, though studies are preliminary and heterogeneous. Despite these advances, early-stage distal tumors remain frequently underdiagnosed, and no single method reliably identifies all cases.

Conclusion. Early detection of distal pancreatic tumors remains challenging. Integration of advanced imaging, biomarkers, and AI-assisted diagnostics may enhance diagnostic accuracy and patient outcomes, but further research is required.

Extreme asystole documented during tilt test: an indication for emergency pacing

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Introduction. Syncope, a transient loss of consciousness and postural tone due to cerebral hypoperfusion, is a common clinical symptom. While neuro-mediated syncope (vasovagal) is most frequent, severe cardioinhibitory forms can mimic intrinsic sinus node disease (Sinus Node Dysfunction - SND). The Tilt Table Test is crucial for risk stratification, reproducing symptoms and revealing the mechanism. We report a case of recurrent syncope with an exceptional sinus pause during Tilt Table testing, requiring urgent intervention.

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Case report. A 74-year-old woman was admitted for recurrent syncope. Initial work-up excluded significant structural heart disease. During the pharmacological phase of Tilt Table testing, after nitroglycerin spray, she developed severe bradycardia (100→50 bpm) with marked hypotension (122/77→68/48 mmHg), rapidly progressing to asystole. ECG analysis captured a total electrical pause of ~42 seconds, confirming advanced SND with a life-threatening cardioinhibitory component. Given a class I pacing indication, a single-chamber VVI pacemaker (VITATRON G20A2) was implanted with active right ventricular fixation and basic VVI programming at 70/min. The pacemaker was left programmed with hysteresis. The post-procedural course was favorable, and the patient was discharged improved.

Conclusion. ECG monitoring during Tilt Table testing can objectively document the severity of cardioinhibitory responses. In this case, a prolonged asystolic pause of about 42 seconds—farexceeding the 6-second pathological threshold defined by ESC guidelines—confirmed advanced sinus node dysfunction with a life-threatening cardioinhibitory component. Immediate VVI pacemaker implantation effectively prevented recurrence and potential fatal complications. This case underscores the diagnostic and therapeutic value of the Tilt Test in identifying patients requiring urgent pacing.

A silent lymphoma unleashing hemophagocytic lymphohistiocytosis

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Introduction. Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare cytotoxic T-cell lymphoma resembling panniculitis. It is presented with subcutaneous nodules and is often mistaken for a benign skin disorder. Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening immune hyperactivation syndrome induced by underlying conditions. SPTCL with HLH may suggest a fulminant course.

Case report. We report the case of a 45-year-old female admitted for malaise, low-grade fever, epigastric and left flank pain, abdominal skin induration, and painful erythematous nodules on both legs. Her medical history included bilateral erythema nodosum three months prior and mesenteric panniculitis with persistent lymphopenia. Laboratory tests showed hypochromic microcytic anemia, lymphopenia, inflammatory syndrome, raised CA 125 and CA 15-3. CT-TAP revealed ascites and diffused abdominal wall thickening. Ascitic fluid was exudative with erythrocytes, lymphocytes, and atypical cells with irregular nuclei. Bone marrow aspirate and biopsy demonstrated hemophagocytosis. Together with fever > 38.5°C, splenomegaly, hypofibrinogenemia, elevated soluble IL-2 receptor, and ferritin, these findings supported HLH. As infectious, autoimmune, and drug-induced causes were excluded, a neoplastic origin was suspected. Histopathological and IHC analysis of epiploic fat biopsy revealed diffuse CD8+ T-cell infiltrate with atypical nuclei and adipocyte necrosis, confirming HLH secondary to SPCL. PET-CT revealed diffuse subcutaneous and mesenteric fat infiltration. First-line CHOP + Etoposide was initiated. Severe neutropenia after cycle 1 was managed with pegfilgrastim and antibiotics. Subsequent cycles were well tolerated. Follow-up showed mild lymphopenia and complete metabolic remission on 3-month PET-CT.

Conclusion. Most SPTCL cases show a favorable outcome with slow progression and low systemic spread, but HLH sharply worsens prognosis through intense inflammation and multiorgan failure.

Bilateral prophylactic mastectomy and immediate breast reconstruction in a BRCA1 positive patient

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Introduction. With more than 2 million women being diagnosed every year, breast cancer (BC) is the most common oncological pathology affecting females. In recent years, Romania has seen an increase in genetically-predisposed patients' requests for bilateral prophylactic mastectomy followed by immediate breast reconstruction (IBR). This procedure represents a suitable option for such patients, lowering the chances of BC onset by more than 90%, while minimizing the psychological impact of the mastectomy.

Case report. A 41-year-old patient presented to the oncology department after her 43-year-old sister had been diagnosed with BC. The significant familial occurrence supported further investigations, with expanded gene panel testing, mammography and breast echography being performed. As results were positive for BRCA1, the patient was considered at high risk for developing BC. After consulting with a multidisciplinary team, she decided to undergo bilateral prophylactic nipple-sparing mastectomy, followed by IBR. The tumescent technique, infiltrating a mixture of lidocaine and epinephrine subcutaneously, ensured easier dissection and minimal bleeding. An inframammary incision was performed laterally, followed by the complete dissection of the mammary gland, with the vascularization of the nipple and areola being preserved. After the gland was excised, IBR was completed using polyurethane-coated breast implants. The procedure was performed bilaterally, with final adjustments ensuring a symmetrical postoperative outcome. One-month follow-up showed no complications. Given the residual risk of developing BC, yearly imaging was recommended.

Conclusion. Considering the high prevalence of BC, bilateral prophylactic mastectomy can prove to be a simple yet effective approach to this pathology, lowering the risk of malignancy in genetically predisposed patients and ensuring a high quality of life, therefore the patients' increasing interest in this procedure.

When cure becomes curse – arsenic therapy and adult cirrhosis: a case report

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Introduction. Cirrhosis is a progressive liver disease marked by fibrosis and regenerative nodule formation following chronic injury, leading to structural distortion and loss of function. It may result from viral infections, toxic exposures, metabolic disorders, or autoimmune mechanisms. Although fibrosis initially preserves hepatic integrity, persistent injury gradually replaces healthy parenchyma, culminating in cirrhosis. Cases with uncommon causes, such as arsenic exposure, offer valuable insight

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into the multifactorial nature of liver disease.

Case report. We report the case of a 52-year-old man diagnosed with Child-Pugh C ethanolic cirrhosis with parenchymal and vascular decompensation and associated chronic pancreatic damage. The patient presented with disorientation, daytime somnolence, and progressive abdominal distension over two weeks. On admission, he exhibited grade III portosystemic encephalopathy, significant hepatic dysfunction, and systemic inflammation.

Abdominopelvic ultrasound revealed a nodular, microgranular liver and a microcalcified pancreas with an ill-defined hypoechoic lesion in the cephalic region. CT imaging confirmed heterogeneous hepatic parenchyma, compression of the inferior vena cava, and moderate ascitic fluid accumulation. Histopathology later confirmed chronic pancreatitis.

The one-year follow-up revealed a history of psoriasis in childhood, treated with arsenic. The arsenic exposure and chronic alcohol consumption have significantly contributed to the development of hepatic impairment.

Conclusion. To conclude, this case illustrates the multifactorial etiology of hepatic cirrhosis, where arsenic exposure and alcohol intake likely acted synergistically to produce severe hepatic damage. The coexistence of hepatic decompensation, portosystemic encephalopathy, and chronic pancreatitis underscores the importance of comprehensive evaluation, ongoing surveillance, and individualized management to prevent further deterioration.

The microsurgical approach of lymphedema following breast cancer treatment. A case report

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Introduction. Upper extremity lymphedema (UEL) is characterised by an excessive buildup of interstitial fluid in soft tissues caused by impaired lymphatic transport. Although the conservative approach, CDT (Complete Decongestive Therapy), remains the gold standard for lymphedema management, promising outcomes have been reported in patients treated with reconstructive microsurgical techniques, such as lymphaticovenular anastomosis (LVA) and vascularised lymph node transfer (VLNT).

Case report. We present the case of a 48-year-old woman diagnosed with triple-negative breast cancer. The patient underwent lumpectomy, axillary lymphadenectomy, and adjuvant radiotherapy. Two years later, she developed swelling, erythema, and pitting oedema of the left UE. The patient was diagnosed with secondary stage II lymphedema, initially inadequately managed with CDT. Consequently, LVA and VLNT were performed to achieve better outcomes.

Surgery began with the dissection of the left axilla. For VLNT, an omental flap was laparoscopically harvested from the stomach, containing associated lymph nodes and the right gastroepiploic artery and vein. These were microanastomosed end-to-end to the circumflex scapular artery and vein following transposition into the axilla. For LVA, Verdye was injected to visualise and mark the lymphatic vessels, while the superficial veins were identified using AccuVein. A successful end-to-end LVA was performed.

Postoperatively, anticoagulant prophylaxis was administered, and at the two-week follow-up, improved lymphatic drainage was observed without complications.

Conclusion. This case illustrates a clinical scenario in which the microsurgical procedure under study achieved satisfactory outcomes when conservative treatment proved ineffective. The results of the surgery align with recent literature, supporting the technique's effectiveness and its short- and long-term benefits, and advocating for its broader application.

Rives-Stoppa repair of a giant umbilical hernia and diastasis recti abdominis

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Introduction. An umbilical hernia is a lesion involving the abdominal wall near the umbilicus that results in a protrusion typically containing peritoneal fat, omentum, or a portion of the intestine. Hernias exceeding 4 cm in diameter are classified as large and can pose numerous complications, such as incarceration and strangulation. Diastasis recti is an abdominal wall defect causing an increased distance between the rectus abdominis muscles.

Case report. A 61-year-old male presented with localized pain near the umbilicus, fatigue, and general weakness. The patient's history reveals stage 2 essential hypertension, type 2 diabetes mellitus, and asthma. Clinical examination indicates abdominal obesity accompanied by a large protruding mass in the umbilical region. Another clinical finding was an anterior abdominal wall defect causing the separation of the rectus abdominis along the linea alba, interpreted as diastasis recti abdominis. Abdominal computed tomography confirmed the presence of a giant subumbilical hernia measuring 18/9 cm with involvement of intestinal loops that presented no signs of obstruction.

The selected procedure was the Rives-Stoppa technique, which consisted of a supraumbilical incision followed by the isolation of a large hernia sac. Upon entering the peritoneal cavity, an umbilical wall defect was identified, as well as significant diastasis recti abdominis. After the dissection of the recti abdominis borders and the excision of the hernia sac, the anterior layer of the rectus abdominis sheath was dissected and the posterior layer was sutured. A polypropylene mesh was placed, and the anterior layer of the rectus abdominis sheath was attached to it. The postoperative course was uneventful.

Conclusion. This case illustrates the complexity of repairing both a giant umbilical hernia and diastasis recti abdominis. While this overlap is not uncommon, the considerable size of the hernia presents surgical challenges.

Case report: Kestenbaum-Anderson procedure in a case of infantile nystagmus

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Introduction. Nystagmus is an involuntary, rhythmic movement of the eyes occurring in various patterns, including horizontal, vertical, and circular. Individuals with nystagmus may also experience abnormal head positions and reduced visual acuity. The Kestenbaum-Anderson procedure is a surgical technique that corrects the abnormal head posture associated with nystagmus. It involves recession and resection of the lateral and medial rectus muscles, adjusted according to the direction and degree of head turn.

Case reports. A 6-year-old patient presents with an abnormal leftward head rotation, rhythmic horizontal eye movements, and reduced visual acuity. Upon examination, the patient exhibited horizontal, pendular nystagmus characterized by large amplitude and high-latency oscillations. Goniometry measurements revealed a prominent compensatory head position featuring a 90-degree leftward turn. This orientation was considered the null point for the nystagmus when the patient gazed to the right, indicating that this head position provided the most stable visual experience in that direction.

The patient underwent surgical correction using the Kestenbaum-Anderson procedure, aiming to shift the null point into primary gaze. This involved surgically adjusting the tension of the medial and lateral rectus muscles via recession and resection. In this case, the right eye functioned as the abducting eye and the left as the adducting eye. Accordingly, a recession of the right lateral rectus and left medial rectus was performed, along with a resection of the right medial rectus and left lateral rectus. Postoperative outcomes showed significant improvement in head posture and improvement of nystagmus.

Conclusion. This case highlights the clinical value of the Kestenbaum-Anderson procedure in managing infantile nystagmus associated with abnormal head posture. Postoperative results showed improved alignment, visual stability, and reduced nystagmus amplitude in primary gaze.

When circulation fails the drug – topical antibiotic success in infected varicose ulcers

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Introduction. Systemic antibiotics are standard in infection management, but their efficacy may be limited in patients with chronic venous insufficiency due to poor tissue perfusion. Topical antibiotics achieve higher local concentrations and faster healing with fewer systemic effects; however, their limited penetration in deep tissues and risk of local resistance restrict their use to well-defined, superficial infections.

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Case report. A 63-year-old woman with obesity, hypertension, and chronic venous insufficiency was admitted with sepsis of dual origin—pulmonary (right parahilar pneumonia) and cutaneous (right leg cellulitis with multiple bilateral varicose ulcers). Despite sequential intravenous antibiotic therapy (Ceftriaxone + Doxycycline, then Clindamycin + Vancomycin), cutaneous lesions showed minimal improvement. The patient's severe chronic venous insufficiency and peripheral circulatory impairment likely limited systemic antibiotic bioavailability at the infection site, hindering tissue penetration and delaying healing. Given this challenge, an alternative approach was adopted—rigorous local management with daily cleansing using water and soap, gentamicyne and topical administration of Baneocin (Bacitracin + Neomycin), ensuring high local antibiotic concentration and direct antibacterial activity at the ulcer surface. Under this combined approach, the patient showed progressive reduction of inflammation, clean ulcer bases, and partial scarring. The patient was fully compliant and discharged in improved condition with recommendations for continued local care and follow-up.

Conclusion. This case highlights the therapeutic value of topical antibiotics in patients with poor peripheral circulation. When systemic therapy alone fails due to low tissue bioavailability, localized antibiotic application can enhance infection control, promote wound healing, and improve clinical outcomes in similar cases.

Pancreatic neuroendocrine tumor mimicking groove pancreatitis – a diagnostic challenge

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Introduction. Pancreatic neuroendocrine tumors (PNETs) represent less than 3% of pancreatic neoplasms and may be functional or non-functional. Their variable presentation and overlap with inflammatory lesions, especially groove pancreatitis, make diagnosis challenging. This case illustrates a well-differentiated PNET masked by inflammatory changes.

Case report. A 55-year-old male presented with jaundice, dark urine, pale stools, right upper quadrant pain, and fever. Labs showed cholestatic liver injury and elevated inflammatory markers. Ultrasound revealed bile duct dilatation and pancreatic head enlargement. ERCP identified biliary microcalculus; a plastic stent was placed, improving symptoms. CEUS and CT showed a hypovascular mass in the pancreatic head extending to the duodenal groove and a hypervascular nodule in the isthmus. The lesions exhibited close contact with the gastroduodenal artery and narrowing of the spleno-mesenteric confluence, raising concern for neoplastic involvement. EUS-FNB confirmed a well-differentiated neuroendocrine tumor, grade 2 (Ki-67~4%), chromogranin A and synaptophysin positive, gastrin negative. Biochemistry confirmed elevated chromogranin A, serotonin, and urinary 5-HIAA. Considering vessel invasion, surgery was not feasible and medical treatment with octreotide was proposed.

Conclusion. This rare PNET masked by inflammatory pseudotumoral changes highlights diagnostic challenges. Correlating imaging, biochemical, and histopathological data was essential for accurate diagnosis.

Preoperative IV iron reduces transfusions and length of stay in major surgery – a retrospective patient blood management study

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Introduction. Preoperative iron deficiency anemia (IDA) is frequent and linked to increased morbidity and transfusion use. Given the inherent risks of allogeneic blood transfusions, Patient Blood Management (PBM) programs demand proactive optimization. Intravenous (IV) iron, unlike oral therapy, allows for rapid repletion. This retrospective study compared outcomes between anemic patients optimized with IV iron administered before the surgery versus non-optimized patients.

Methods. The hospital records were searched for anemic patients who underwent optimization, from the initiation of the program in June 2024 to present. Optimization consisted of IV ferric carboxymaltose, administered 7 to 14 days prior undergoing major surgery. Major surgery was defined as operations expected to last more than 120min or with an expected blood loss of at least 500 mL. Eligible patients were matched with anemic patients who did not receive iron preoperatively. The non-optimized group was matched based on primary diagnosis, surgical procedure, American Society of Anesthesiologists Physical status score, Charlson Comorbidity Index, gender and age. The primary outcome was the number of allogeneic red blood cell (RBC) units transfused while the secondary outcome was length of hospital stay (LOS). t-Test was performed for statistical analysis.

Results. 8 patients out of a total of 29 optimized patients were matched and eligible for inclusion. Optimized patients required significantly fewer RBC transfusions (0.00 ± 0.00 vs. 1.33 ± 1.03 units, $p = 0.003$) and had a shorter LOS (7.6 ± 1.9 vs. 11.2 ± 3.8 days, $p = 0.038$). Other outcomes such as hemoglobin levels and ICU stay were not statistically significant.

Conclusion. Preoperative IV iron optimization provides substantial clinical benefit, achieving significant reductions in both transfusions and hospital stay. These findings affirm that IV iron repletion is an essential, high-impact element of contemporary PBM.

Recurrent insulinomas in the remnant pancreas – a surgical case report

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Introduction. Insulinoma is a rare neuroendocrine tumor that develops in the pancreas, originating from the β (beta) cells. In most cases, these tumors are benign. The most common clinical manifestations include episodes of confusion, weakness, and, in some cases, more severe neurological symptoms caused by markedly low blood glucose levels.

This case report presents a 51-year-old man with a history of previous surgical interventions, who was admitted to the general surgery department after being diagnosed

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with two neuroendocrine masses located in the remaining portion of a partially resected pancreas.

Case report. The patient presented to the general surgery department following a CT examination, which revealed the presence of neuroendocrine tumors attached to the remaining pancreatic head, gallbladder lithiasis, biliary cysts, and hepatomegaly. His medical history included a distal segmental pancreatectomy and splenectomy performed for the same type of tumor. So, the exploratory laparotomy, adhesiolysis, and corporeo–isthmic pancreatectomy procedure was chosen, the operation went well and the patient was discharged eight days later.

Conclusion. Although insulinomas are relatively rare tumors, they can easily lead to complications in patients' lives, especially in those with associated risk factors. This case highlights the high possibility of tumor recurrence, emphasizing the importance of regular follow-up and monitoring of these patients. Moreover, the multidisciplinary teams are a real help in the treatment process.

Chronic graft rejection and liver retransplantation in Wilson's disease

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Introduction. Wilson's disease is an autosomal recessive disorder and a rare cause of liver cirrhosis that, when it progresses to decompensation, may require liver transplantation.

Case report. We present the case of a 36-year-old female patient who was diagnosed with the hepatic form of Wilson's disease at the age of 15 in 2004. In 2006, despite treatment, her disease progressed to a state of decompensated cirrhosis with refractory ascites. In 2010, she underwent her liver transplantation with whole liver from a brain-dead donor in Bologna, Italy.

Following her liver transplantation her course was complicated by adverse effects of prednisone-based immunotherapy such as depression. Prednisone was therefore replaced with Tacrolimus and MMF, however the MMF treatment was discontinued as well during her pregnancy to avoid teratogenic effects on the fetus and later replaced with Everolimus, which was subsequently discontinued due to unavailability in Romania. Noncompliance and interruptions in immunosuppressive therapy ultimately resulted in chronic graft rejection in 2025.

The chronic transplant rejection was confirmed by biopsy and manifested through the recurrence of the complications of portal hypertension such as refractory ascites and recurrent variceal bleeding. She was then relisted for liver transplant. While on the waiting list, a transjugular intrahepatic portosystemic shunt (TIPS) procedure was performed to alleviate portal hypertension.

On April 12, 2025, an orthotopic liver retransplantation with a whole liver from a brain-dead donor was successfully performed, with favorable postoperative outcomes.

Conclusion. This case emphasizes the importance of a personalized immunosuppressive regimen tailored to each patient's individual needs, as failure to comply with the treatment often results in the need of liver transplantation.

Innovative therapeutic strategies for tumoral biliary obstruction in a young patient – a case report

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Introduction. Cholangiocarcinomas arise from the epithelial cells of the bile ducts and can be classified as intrahepatic, perihilar or extrahepatic. Identified risk factors are: primary sclerosing cholangitis, chronic intrahepatic stone disease, chronic liver disease and genetic conditions.

Case report. A 44-year-old female is admitted for: nausea and vomiting for 3 weeks, significant weight loss and fatigue. Physical examination reveals jaundice, hepatomegaly and abdominal tenderness in the right upper quadrant. The patient has a history of chronic hepatitis B virus infection, without ongoing antiviral therapy. Blood tests indicate: hepatocellular injury, cholestatic syndrome, elevated serum bilirubin levels, inflammatory syndrome and mild anemia. p-ANCA were negative. Tumor marker analysis reveals elevated CA19-9 levels with normal AFP and CEA. Transabdominal ultrasonography shows a hilar mass and multiple intrahepatic secondary lesions. CT identifies the fibrous component of the mass, intrahepatic ducts dilatation in both hepatic lobes and normal extrahepatic ducts. Perihilar hepatic and retroperitoneal lymph nodes are noted. MRCP confirms a Bismuth type IV biliary tract tumor. An ultrasound-guided percutaneous transhepatic biliary drainage and a liver biopsy were performed. Only the left hepatic lobe was successfully drained. Due to anatomical relations, only a secondary lesion was biopsied. Histopathological and immunohistochemical findings suggest a poorly differentiated carcinoma, most likely a hepatocholangiocarcinoma. The patient starts chemotherapy based on TOPAZ-1 trial: Durvalumab plus Gemcitabine and Cisplatin. Four months later, a percutaneous transhepatic cholangiogram is performed and an uncovered biliary stent is successfully placed.

Conclusion. This case illustrates the complex management of biliary obstruction in a young patient, in which the TOPAZ-1 treatment and percutaneous stent placement were chosen to improve quality of life.

Reccurence of a right frontal oligodendroglioma in a young patient - clinical, molecular and imaging correlations in an atypical

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Introduction. Oligodendroglioma is a diffusely infiltrating glial tumor characterized by the presence of an IDH1 or IDH2 gene mutation and 1p/19q chromosomal codeletion, molecular alterations that define its distinct prognosis: slow-growing, but with a significant potential for recurrence and transformation into more aggressive forms.

Case report. A 21-year old male presented to the hospital with headache, nausea, vomiting and diplopia. A cranial tomography was performed and it revealed the presence of a fronto-medial and right paramedian tumor with mixed cystic and calcified areas and orbital and frontal sinus invasion. Histopathological examination confirmed a grade II oligodendroglioma, positive for IDH1, Olig2, p53 and S100, with confirmation of 1p/19q codeletion.

Even though the patient initially presented a good recovery after the complete surgical resection, a recurrence extending to the contralateral frontal region was detected one year later, and required another surgery. The new histopathological examination revealed an IDH2-R172K mutation and CDKN2A/2B deletions, indicating the progression to a more aggressive form. One year later, the patient developed secondary epileptic seizures due to irregular intake of Levetiracetam and also experienced another recurrence, which was managed conservatively. He is currently under palliative care.

This case is remarkable for several clinical and genetic particularities, including its unusually early appearance, the rare extracerebral extension into the right orbit and frontal sinus, which is atypical because oligodendroglioma usually remains in the cortical area and the early recurrence, reflecting a more aggressive biological behavior than expected.

Conclusions. In conclusion, the complexity of this case lies not only in the molecular, genetic and anatomical features that shaped the unexpected evolution, but also in highlighting the importance of applying a multidisciplinary approach at every stage of evolution, ensuring that the patient, whose quality of life progressively declined, receives the best support.

Interlayer dural split decompression – a minimally invasive approach for Chiari malformation type I with syringomyelia

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Introduction. Chiari malformations (CMs) are herniations of brain tissue via the foramen magnum and are classified into four categories. Chiari malformation type I (CMI) is distinguished by the cerebellar tonsils passing through the foramen magnum for at least 3-5 mm, along with abnormalities in cerebrospinal fluid (CSF) flow. The CMI treatment comprises of decompressing the foramen magnum using craniectomy, duraplasty, and cerebellar tonsil removal. These operations have varying success rates, and there is much controversy over whether additional or less intrusive approaches are necessary.

Case report. We present the case of a 46-year-old female who complained of severe headaches, nausea, vertigo, and ataxia. She was unresponsive to conservative therapy. An MRI indicated a unilateral fall of the right cerebellar tonsil and significant syringomyelia. We chose the Interlayer Dural Split procedure, which has a minimal risk of CSF fistula and recurrence rate, as it combines invasive and minimally invasive approaches by incising the dura mater's external layer, while avoiding the subdural regions and performing autologous duraplasty. There was no CSF leakage or pneumocephalus detected during postoperative imaging exams. She remains symptom-free 8 months after surgery.

Conclusion. This example demonstrates that CMI in adults can be successfully treated using the new technique of incising the outer dural layer and carefully separating it from the inner one. This technique offers the advantage of lowering the likelihood of postoperative complications such as CSF leakage, pseudomeningocele, or aseptic meningitis, while also being appropriate for individuals with syringomyelia. However, closing the outer dura layer requires a longer operative time.

Postpartum varicophlebitis and venous leg ulcer

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Introduction. Chronic venous insufficiency (CVI) of the lower extremities is a common vascular condition that can present with a wide spectrum of clinical manifestations, ranging from cosmetically unpleasant varicose veins to more severe problems such as thrombophlebitis or venous ulceration.

Case Report. We report the case of a 32-year old woman, from a rural area who was diagnosed with advanced CVI. She presented with painful varicose ulcer near the left medial malleolus associated with localized swelling and inflammation on the left calf. Her medical history revealed a 12-year period of varicose disease, noted in the postpartum period, for which she had not received prior medical treatment.

On examination, a single superinfected ulcerus was observed with a surface of 2-3 cm with well defined margins, present discharge and foul odor. The surrounding skin was hyperpigmented, indurated presenting palpable superficial varicosities and tenderness suggesting varicophlebitis. Varicose veins were present on the right lower limb as well.

Doppler ultrasound confirmed bilateral ostial insufficiency with reflux in the great saphenous vein and lower leg perforators, with thrombi at the level of the left calf. The final diagnosis was bilateral superficial CVI (CEAP class VI on the left, CEAP class IV on the right).

The treatment prescribed was an antibiotic (cephalosporin), based on a secretion probe from the ulcer, anticoagulant, NSAIDs and phlebotropics. A follow-up at three weeks was recommended, with surgical debridement of the ulcer planned. Varicose vein surgery was indicated as well.

Conclusion. This case emphasizes the importance of early recognition and management of venous disease, especially for postpartum women and for patients with limited access to healthcare. Timely intervention and patient education are crucial to prevent severe, life-threatening complications.

Completing the cure – laparoscopic 3D management of a post-chemotherapy retroperitoneal mass

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Introduction. Testicular germ cell tumors are rare malignancies, representing less than 1% of male cancers. Among them, non-seminomatous types are characterized by aggressive biological behavior but high chemosensitivity. Even after systemic therapy, residual retroperitoneal masses may persist, requiring surgical management to exclude viable tumor and achieve accurate oncologic assessment.

Case Report. A 22-year-old male was diagnosed with a left non-seminomatous germ cell tumor (pT2L0V1Pn0R0, stage IIIB, intermediate risk) and treated with four cycles of BEP chemotherapy (Bleomycin, Etoposide, Cisplatin). Imaging follow-up revealed a retroperitoneal residual mass of approximately 6-7 cm, in close contact with

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the bowel and left ureter. The persistence of this mass post-chemotherapy required surgical removal. We opted for a laparoscopic 3D retroperitoneal lymph node dissection, using the standard unilateral template. The procedure was technically demanding due to dense post-chemotherapy adhesions, with partial bowel injury caused by the tumor's adherence to intestinal loops. Postoperative recovery was favorable, with early restoration of digestive function.

Histopathological examination demonstrated complete necrosis of metastatic tissue within one lymph node and seven tumor-free nodes, confirming a complete pathological response after chemotherapy.

Conclusion. This case demonstrates that even complex post-chemotherapy retroperitoneal surgery can be safely performed using a laparoscopic approach. The complete and safe resection achieved proves that minimally invasive surgery can combine oncologic radicality with gentle tissue handling. Attention to detail, patience, and precise technique were key to overcoming severe adhesions and achieving a curative result.

When an acute fall eclipses a chronic bleed – a case of diagnostic overshadowing

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Introduction. Diagnostic Overshadowing is a cognitive bias where an acute, compelling condition dominates clinical focus, preventing the timely investigation of concurrent, severe symptoms. We present a patient whose workup for severe anemia (Hb 3.7g/dL) was delayed after an in-hospital fall caused a Traumatic Brain Injury (TBI). The acute TBI overshadowed the anemia, postponing the diagnosis of an underlying malignancy.

Case Report. A 90-year-old male presented with severe anemia (Hb 3.7 g/dL), requiring transfusion. An initial abdominal ultrasound revealed ascending colon wall thickening, recommending colonoscopy. During admission, the patient fell, sustaining a TBI with a temporo-parietal hematoma and subarachnoid hemorrhage. This neurological event halted all investigations for the anemia. The clinical focus shifted entirely to the TBI, necessitating seven cranial CT scans during a month-long admission. New gastrointestinal symptoms, including vomiting, were attributed to the TBI rather than an abdominal pathology. Despite persistent moderate anemia and the suspicious initial ultrasound, no further abdominal imaging occurred. The patient was discharged and readmitted a month later with intestinal obstructive symptoms. An abdomino-pelvic CT finally revealed a 72 mm, stenosing, locally invasive tumor at the right colic angle. Given his advanced disease and comorbidities, he underwent a palliative hemicolectomy.

Conclusion. This case clearly illustrates Diagnostic Overshadowing in a complex geriatric patient with multimorbidity. The TBI functioned as the overshadowing diagnosis, consuming clinical focus and investigative resources while the work for the life-threatening anemia was postponed. Attributing his vomiting to the TBI, rather than the underlying colonic obstruction, highlights the anchoring bias. This case serves as a powerful reminder for clinicians to re-focus and maintain a broad differential, despite an acute, diverting event, to avoid diagnostic delays.

Tight space, a critical case – fourth ventricle tumor in a pediatric patient

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Introduction. Tumors of the Fourth Ventricle, located within the posterior fossa, represent a major neurosurgical challenge in pediatric patients due to their proximity to vital brainstem and cerebellar structures. These lesions commonly obstruct cerebrospinal fluid pathways, resulting in acute obstructive hydrocephalus. Prompt recognition and radical surgical management are essential to relieve intracranial pressure and optimize both neurological and oncological outcomes.

Case report. A previously healthy 9-year-old boy presented to our emergency department with projectile vomiting severe headache, immune to medication and marked somnolence. Neurological examination revealed signs of raised intracranial pressure and a new-onset divergent strabismus, a focal sign indicative of brainstem compression or cranial nerve dysfunction. Brain MRI demonstrated a compressing mass centered in the Fourth Ventricle, obstructing the cerebrospinal outflow, leading to secondary triventricular hydrocephalus. Initial management involved placement of an External Ventricular Drain for immediate intracranial pressure relief. Subsequently, the operation was performed via a posterior fossa craniotomy and a suboccipital median transvermian approach, which enabled gross total tumor resection. The postoperative course was uneventful, with complete resolution of hydrocephalus and neurological symptoms. Follow-up MRI confirmed total tumor removal. The patient was discharged and referred to Pediatric Oncology for histopathological confirmation and adjuvant therapy.

Conclusion. To conclude, gross total resection remains the treatment of choice for symptomatic Fourth Ventricle tumors, ensuring rapid decompression and favorable neurological recovery. This case highlights the importance of a multidisciplinary, stepwise approach—combining emergent CSF diversion, meticulous microsurgical resection and coordinated oncological management. Not only that but, pediatric neurosurgical emergencies demand more than just technical skill. They require a good communication with the parents, trust and accountability, mandatory for good patient outcomes.

Male breast pathology – etiology and diagnostic methods

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Introduction. Male breast pathology is uncommon compared to that in females. Diagnosis is mainly clinical, with imaging support. Although benign lesions predominate, malignant forms may occur, with male breast cancer accounting for 1% of all breast cancers. This paper aims to review the etiology and diagnostic methods of the most frequent male breast diseases.

Methods. A PubMed literature analysis was performed, including systematic reviews published within the last year. The phrases used were breast imaging male, male

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breast disease, male breast cancer, and gynecomastia. 49 studies were identified, and after applying inclusion and exclusion criteria and removing duplicates, 12 relevant studies were analyzed.

Results. Gynecomastia is the most common benign male breast disease, caused by ductal and epithelial proliferation due to increased estrogen levels relative to testosterone. It may occur physiologically (in newborns, teenagers, older people), pathologically (hypogonadism, obesity, Klinefelter syndrome, HIV, cirrhosis, renal failure), or drug-induced (antiandrogens, antipsychotics, antiretrovirals). Ultrasound is the first-line investigation, with mammography useful for differentiating forms. Other benign lesions include lipomas, desmoid tumors, hemangiomas, and neurofibromas. Male breast carcinoma, though rare, is aggressive and usually occurs after age 60. It is associated with BRCA1/2, CHEK2, and PALB2 mutations, family history, radiation exposure, and hormonal imbalance. Ductal carcinoma predominates, while lobular carcinoma occurs only in the presence of gynecomastia. Ultrasound and mammography establish diagnosis and local extension, while MRI rarely adds useful data.

Conclusion. Male breast pathology is dominated by gynecomastia and other benign lesions. Although rare, male breast cancer requires careful evaluation and differential diagnosis. Ultrasound and mammography are generally sufficient, with MRI adding limited benefit.

Carcinomatous meningitis masquerading as inflammatory neuropathy – a diagnostic challenge

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Introduction. Carcinomatous meningitis represents a rare but severe manifestation of systemic malignancy, often mimicking infectious or inflammatory neurological disorders. Early recognition is challenging, as initial symptoms may be nonspecific or misleading. We report a case of rapidly progressive neurological deterioration in an undiagnosed patient, ultimately attributed to carcinomatous meningitis.

Case Report. A 50-year-old obese male, heavy smoker (60 cigarettes/day) with no prior treatment history, was admitted for acute-onset bilateral fronto-orbital headache, mild vertigo, and left eyelid ptosis. Neurological examination revealed gait instability, bilateral oculomotor involvement, and decreased tendon reflexes without sensory loss. Laboratory tests showed hyperglycemia and elevated HbA1c, confirming newly diagnosed diabetes mellitus. Brain MRI displayed T2 pontine hyperintensities suggestive of inflammatory changes, as well as left ethmoido-frontal sinusitis and mastoiditis. Under corticosteroid, neurotrophic, and antidiabetic therapy, transient improvement occurred, followed by new paresthesias and muscle cramps. The patient was readmitted for worsening gait and lower limb weakness. Differential diagnoses of neuroborreliosis and inflammatory neuropathy were initially considered. During a subsequent hospitalization at a tertiary center, cerebrospinal fluid analysis and imaging confirmed the diagnosis of carcinomatous meningitis. Despite supportive treatment, the patient's condition rapidly declined, and he died shortly thereafter.

Conclusion. This case underscores the diagnostic difficulty of carcinomatous meningitis, which may present with misleading symptoms resembling metabolic, infectious, or inflammatory neuropathies. A high index of suspicion and early comprehensive investigation are essential for timely diagnosis and management of this rare but fatal condition.

Association between VKORC1 gene polymorphisms and osteopenia and osteoporosis – a systematic review and meta-analysis

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Background. The vitamin K epoxide reductase complex subunit 1 (VKORC1) plays a central role in the vitamin K cycle, which is essential for γ-carboxylation multiple bone-related proteins. Genetic variants in VKORC1 may influence bone mineral density (BMD) and osteoporosis risk.

Methods. A systematic review and meta-analysis were conducted to evaluate the association between VKORC1 polymorphisms and osteopenia and osteoporosis. Relevant studies were identified through PubMed, Scopus, and Web of Science databases. Data on study characteristics, genotypes, BMD measurement, ethnicity, sex, and menopausal status were extracted.

Results. Six studies comprising 7335 participants were included. All studies assessed BMD using dual-energy X-ray absorptiometry (DXA). The mean participant age ranged from 41.9 to 63.7 years. The VKORC1 variants most frequently studied which were included in the meta-analysis were rs9923231 and rs9934438. The overall effect of VKORC1 risk alleles on osteopenia/osteoporosis were significant with a $p = 0.041$ (fixed effects OR = 1.16, 95% CI = 1.01–1.35). Heterogeneity among studies was insignificant ($I^2 = 0\%$, $p = 0.893$).

Conclusion. A modest association was observed for the VKORC1 variants. The current body of evidence requires further studies to elucidate whether VKORC1 polymorphisms have a clinically meaningful role in bone health.

Oral health-related quality of life, dental aesthetics and dental anxiety evaluation – an online questionnaire study

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Introduction. As reported in scientific literature, a person's quality of life is impacted by factors such as oral health, dento-facial aspect or perceived level of anxiety. The purpose of the present study is to evaluate the oral health-related quality of life (OHRQoL), self-perceived dental aesthetics and dental anxiety, in a general sample.

Methods. Observing a cross-sectional design, the current study involved a sample, consisting of medical, non-medical students and employed persons (n=108). Initially, all respondents filled in a statement of informed consent. Google forms was employed to administer the following indices: the Romanian versions of OHIP-49, PIDAQ, MDAS, RSES, alongside a demographical data questionnaire. Each item was restricted to a single compulsory answer. Data organizing was succeeded by questionnaire subscale and overall score calculations. Score variance, in respect to the medical study status, occupation and gender, were assessed, by the means of t-test and one-way ANOVA. Pearson's correlations evaluated the associations between self-assessed general oral health, self-esteem, dental aesthetics and dental anxiety.

Results. Highest average subscale scores encompassed: for OHIP-49, functional limitation=7.7 and pain=9.35; for PIDAQ, social impact=32. The overall MDAS score was 9.87. Non-medical students reported marginally worse non-significant oral health and dental anxiety levels. Statistically significant correlations were obtained between: OHRQoL subscale and dental aesthetics subscale scores (functional limitation and psychological impact r=0.38, p=0.001; physical disability and social impact r=0.39, p=0.001); OHRQoL subscale (physical disability) and dental anxiety scores r=0.31, p=0.001.

Conclusion. The present study emphasized statistically significant relations between the patients' self-reported OHRQoL, dental aesthetics, and dental anxiety. Non-statistical score differences regarding medical studies were also reported.

Comparative evaluation of 1:1 assisted training versus video instruction in the application of three occlusal modeling techniques

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Introduction. Direct restorations are an essential component of clinical training in restorative dentistry. The improvement of occlusal modeling techniques and proper training contributes significantly to the development of operative precision and the reduction of working times. The main objective of the present study was to evaluate the technical performance, morphological accuracy and temporal efficiency in occlusal modeling, using two distinct training methods applied to students in the preclinical stage.

Methods. The study was analytical, observational, with a qualitative and quantitative component, carried out on a sample of 20 students of the third year of study.

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Participants were randomly assigned to two equal groups: Group 1 (assisted training) and Group 2 (individual video training). Each participant performed three restorations on lower molars with class I cavities 3D printed, using three occlusal modeling techniques: Cusp by Cusp, Essential Lines and Progressive Tracing. The completion of the fillings was individually timed.

Results. The morphological quality of the restorations was assessed under a microscope by three calibrated observers. Eight evaluation criteria were applied, awarding grades from 1 to 5. The scores awarded were later correlated with the execution times. For the comparative analysis of the three modeling techniques, ANOVA tests with repeated measurements and T-Student tests were used. The threshold of statistical significance was set at $p < 0.05$. The data were collected, centralized and processed through specific statistical programs, and the interobservational agreement coefficient was also calculated.

Conclusion. The study design allows the comparison of efficiency and precision between training methods and occlusal modeling techniques, providing a basis for optimizing the preclinical training process in restorative dentistry.

Clinical applications and advantages of Polytetrafluoroethylene (PTFE) tape in modern dental practice

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Introduction. Polytetrafluoroethylene (PTFE), commonly known as Teflon tape, has transitioned from industrial applications to a valuable adjunct in contemporary dental practice. Its unique properties - biocompatibility, chemical inertness, hydrophobicity, and easy manipulation - have encouraged widespread use across restorative, prosthetic, implant, and endodontic dentistry. This review aims to summarize the current evidence on the clinical applications and advantages of PTFE tape in dental procedures compared to traditional materials.

Methods. A systematic literature search was conducted across PubMed, Scopus, and Web of Science databases using keywords PTFE tape, Teflon tape, dental isolation, implant access sealing, restorative dentistry, and gingival retraction. Data were extracted and synthesized regarding usage domains, procedural benefits, limitations, and clinical outcomes.

Results. The reviewed literature indicates that PTFE tape offers significant clinical benefits across multiple dental specialties. In restorative and adhesive dentistry, it ensures effective gingival and interproximal isolation, reduces contamination, and prevents adhesion to composites. In prosthodontics and implantology, it serves as a non-stick spacer for sealing screw access channels, preventing cement entrapment, and stabilizing matrices. In endodontics, it acts as a temporary spacer and improves moisture control, while in gingival retraction it produces less tissue trauma than conventional cords with adequate displacement.

Conclusion. PTFE tape represents a versatile, inexpensive, and biocompatible adjunct in dental practice. Its broad range of applications contributes to cleaner procedures, improved precision, and predictable outcomes. The evidence supports its integration as a standard auxiliary material in restorative, prosthetic, and endodontic dentistry, reflecting a trend toward simplified and more controlled clinical workflows.

Assessment of gingival retraction efficiency using Polytetrafluoroethylene (PTFE) tape

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Introduction. Accurate exposure of the cervical margin is essential for obtaining precise impressions in both direct and indirect prosthetic restorations. Traditional gingival retraction methods, such as using cotton cords or impregnated pastes, may cause tissue irritation, allergic reactions, or leave debris in the sulcus. Polytetrafluoroethylene (PTFE -Teflon) tape offers a promising alternative due to its adjustable thickness, non-traumatic handling, and hydrophobic properties. It allows clean removal without leaving particles or causing soft tissue damage. This study aims to compare PTFE tape with conventional retraction cords and evaluate the benefits of introducing PTFE for clinical use.

Methods. The study was conducted on study models with artificial gingiva, which were impressed using addition silicone. The sulcus width was measured before and after the insertion of the retraction material - cotton cord and PTFE tape, respectively. Measurements were performed using a CAD scanner to accurately quantify the changes in sulcus width produced by each method. For each prepared tooth, four reference points were evaluated: distal, vestibular, mesial, and oral.

Results. Statistical analysis was performed using a paired t-test to compare sulcus width changes between cotton and PTFE (Teflon) retraction materials. The results showed a statistically significant difference between the two methods ($t = –2.24$, $p = 0.041$). PTFE tape produced a slightly smaller but more consistent sulcus widening compared to cotton cords, indicating better control and reduced tissue impact.

Conclusion. Within the study's limitations, PTFE tape appears to be a reliable and minimally invasive alternative to conventional cotton retraction cords. It provided consistent sulcus widening with no residue, supporting the use of PTFE as an effective option for gingival retraction in dental practice.