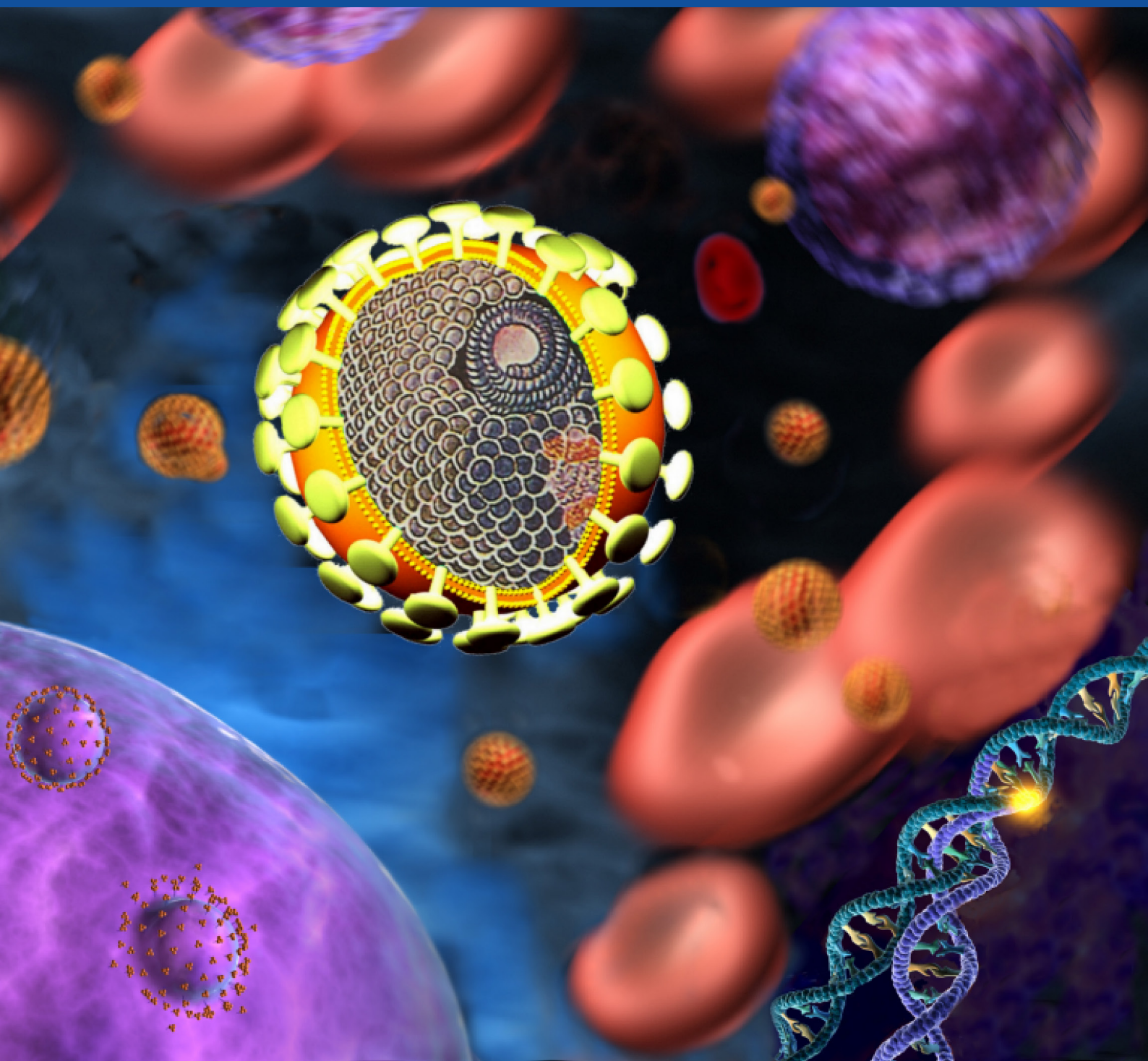


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VOLUME OF ABSTRACTS

THE 17th CONFERENCE OF THE ROMANIAN ASSOCIATION OF LABORATORY MEDICINE

27-29 May 2026, Targu Mures, Romania



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C1. REGULATING QUALITY FROM WITHIN: ADMINISTRATIVE REQUIREMENTS AND STANDARDS FOR LABORATORY INTERNAL QUALITY CONTROL

Radu Ilinca, Ionuț Adrian Chiriac

UMF "Carol Davila", Bucuresti, Romania

Introduction: Internal quality control (IQC) represents a core requirement in medical laboratories and is routinely implemented in accredited settings. However, in everyday practice, the conceptual distinctions between IQC, calibration, metrological traceability and proficiency testing (PT) may not always be explicitly articulated, as these processes are often applied operationally rather than analyzed comparatively. This can lead to overlaps in interpretation, especially when aligning technical practices with administrative requirements.

Methods: A conceptual and normative analysis was conducted based on ISO 15189:2022 requirements and CLSI C24 guidelines. The analysis focused on defining and differentiating the roles of calibration (in the medical laboratory context), metrological calibration and traceability, IQC, and PT. Emphasis was placed on how these concepts are positioned within the laboratory quality management system and how they relate to ensuring valid examination results.

Results: ISO 15189 establishes IQC as an essential component for ensuring the validity of examination results, requiring continuous monitoring of analytical performance. CLSI C24 further defines IQC as a statistical process designed to detect deviations from stable system performance and to reduce the risk of reporting erroneous patient results. Calibration supports alignment with reference measurement systems, while metrological traceability ensures linkage to higher-order standards. PT provides periodic external assessment of laboratory performance across interlaboratory comparisons. These elements operate at different levels: IQC within the analytical process, calibration and traceability at the measurement system level, and PT at the external evaluation level.

Conclusions: IQC should be understood as a continuous, internal control mechanism distinct from calibration and PT. A clearer conceptual delineation supports consistent implementation, strengthens compliance with ISO 15189, and contributes to improved reliability and clinical confidence in laboratory results.

Keywords: internal quality control, ISO 15189:2022, metrological traceability, proficiency testing

R2. NOVEL STATISTICAL METHODOLOGIES, WITH PARTICULAR EMPHASIS ON BAYESIAN APPROACHES TO QUALITY CONTROL AND THEIR APPLICATION IN ENHANCING EFFICIENCY WITHIN MEDICAL LABORATORIES

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Quality control (QC) in medical laboratories is often constrained by limited data, lack of extensive calibration phase, and the need for timely decisions. These challenges can reduce the effectiveness of traditional QC approaches, particularly in dynamic environments.

This presentation introduces novel statistical QC methodologies based on the Bayesian paradigm, offering a coherent framework that can be used for both Internal QC (IQC) and External Quality Assessment (EQA). By incorporating prior information and enabling sequential updating, Bayesian methods support real-time inference without requiring lengthy calibration phases, allowing more adaptive monitoring of analytical performance.

The talk outlines the core principles of the Bayesian framework and presents a Bayesian QC tool, the Predictive Control Chart (PCC). The PCC enables probability-based monitoring and improved detection of deviations, thereby enhancing efficiency in medical laboratory practice.

Keywords: bayesian, external quality assessment, internal quality control, predictive control chart

R3. A METROLOGICAL REASSESSMENT OF SYSTEMATIC ERROR COMPONENTS IN CLINICAL LABORATORY QUALITY CONTROL

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Introduction: Long-term quality control (QC) in metrology and clinical laboratories relies on statistical assumptions that frequently ignore the time-dependent behaviour of systematic error. Traditional error models treat the standard deviation derived from long-term QC data as an estimator of random error, assuming normally distributed long-term data. This study aims to clarify the structure of systematic error by distinguishing its constant and variable components and to evaluate their impact on QC interpretation.

Methods: Extensive computer simulations using multiple bias patterns (constant, linear drift, stepwise calibration-related variation, and sinusoidal change). The relationships between repeatability standard deviation (SD) (s_r), long-term SD (s_{RW}), and the SD of the variable systematic component (s_{VCSE}) were analysed.

Results: The analysis demonstrates that s_{RW} is a composite of random error and time-dependent systematic variability. Simulated QC datasets showed pronounced non-Gaussian behaviour, substantial variability in s_{RW} , and unstable long-term means when bias cycles were incomplete. Only s_r reliably estimated the true random error.

Conclusions: Long-term QC data are not normally distributed, and s_{RW} should not be used as an estimator of random error. Only the constant component of systematic error can be efficiently corrected, and QC decision limits based on s_{RW} must be reevaluated.

Keywords: systematic measurement error, random measurement error, repeatability, quality control

C4. SIGNIFICANT BUT NEGLECTED ERROR SOURCES IN THE CLINICAL LABORATORY

Atilla Barna Vandra

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Introduction: Correcting an error of unknown origin is only a cosmetic operation, not a solution. The study draws attention to four error sources that cause problems for specialists in the clinical laboratory due to their seemingly uncorrectable nature: the measurement error in calibration, the error in the value of the control material or calibrator, and the rounding error. These are neglected or minimized in the literature.

Methods: The study is a theoretical one, based on a 'bottom-up' analysis. The author tested the proposed solutions in his four decades of work.

Results: Although calibration is a measurement, because it is a corrective action, many studies (including the Westgard rules-based QC system) start from the assumption of a "perfect calibration". The coefficient of variation of the calibration factor cannot be smaller than the coefficient of variation determined in repeatability. Therefore, a smaller bias than a standard deviation measured in repeatability conditions is incorrigible. Why must we detect it? The conclusion calls for redefining the type I (α) error and the false alarms. The measured reference materials do not have their nominal value. Five causes are described: (1) nominal value error, (2) reconstitution error, (3) stability error, (4) homogenization error, and (5) sample temperature errors. Only the last three are avoidable human errors. Reconstitution error involves two volume measurements.

Conclusions: The consequences of the control value errors are false errors, but they lead to erroneous decisions, while in the case of calibrators, the errors are real and influence patient results. Due to the cumulative effect, seemingly negligible rounding errors for patient results may become significant error sources in statistical determinations (standard deviation, limit of quantitation, linearity, etc.). The analyzer should be set to use 1-2 more decimal places than those used for patient results.

Keywords: calibration, inherent error, nominal value, reconstitution, rounding

C5. THE DEFICIENCIES OF THE WESTGARD RULES-BASED QC SYSTEM

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Introduction: The Westgard rules are only correctly applied if the design of the Levey-Jennings graphs is based on the Gaussian parameter σ , or its correct estimator, s_r , the standard deviation determined under repeatability conditions. Otherwise, different rules are applied than intended. J. O. Westgard himself points out that the Westgard rules are inapplicable on graphs based on s_r . In light of the recent findings (the existence of uncorrectable biases, the non-Gaussian distribution of long-term control data, s_{RW} , the standard deviation determined under reproducibility within laboratory conditions is not the correct estimator of the Gaussian parameter σ the study aims at a mathematical reassessment of the Westgard rules.

Methods: The study is a theoretical evaluation, based on mathematical statistical methods and probability calculations. Westgard recommends two criteria for evaluating Type I and Type II errors (false and missed alarms): P_{fr} (probability of alarms in the absence of bias) and P_{ed} (probability of detecting critical systematic errors). The existence of uncorrectable systematic errors imposes a redefinition of the false alarm, which necessitates the replacement of P_{fr} with more stringent criteria, namely P_{ur} (probability of unnecessary rejection, in the case of uncorrectable biases $B < 1s_r$) and ARL_{ur} (average number of control runs without unnecessary alarms).

Results: While the Westgard criteria suggest “perfect” rules and cannot explain the inapplicability of Westgard rules on s_r -based graphs, P_{ur} explains the phenomenon. Other rules with extended decision limits are needed.

Conclusions: The Westgard recommendation (graph design based on s_{RW}) addresses the issue of unnecessary alarms; however, the proposed solution can significantly compromise the efficiency of error detection. In the case of small s_{RW}/s_r ratios (~ 1.5), the solution is still effective; unfortunately, this ratio varies. As the ratio increases, the intra-run rules ($R1-3S$ and $R2-2S$) lose their effectiveness. As alternative solutions, $R1-4s_r + R2-3s_r$, a rule based on the mean deviation (also proposed by Asberg and Bolann) $Rra-3s_r$, supplemented with decisions based on bias estimation, and the application of different rules in different decision-making situations are proposed.

Keywords: decision limits, false alarms, incorrigible errors, type I errors, Westgard rules

C6. AN ALTERNATIVE, COMPUTER-ASSISTED, AND PREVENTIVE QC SYSTEM

Atila Barna Vandra

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Introduction: The Westgard method is a corrective quality control system. The role of internal quality control is to discover variations in systematic errors that, between human interventions, are predictable. Consequently, in most cases, they can be discovered before they occur, and preventive actions can be applied.

Methods: The proposed solution is based on: (1) the percentage expression of the results (2) which allows the representation of the critical systematic error on graphs (3) graphs with a design based on s_r (4) computer-assisted calculation of decision limits, starting from the conditions of avoiding type I and II errors. (5) Different rules in four different decision situations, defined by the different bias variation dynamics: a) immediately after calibration b) repeated application of the rule in case of stable reagent, c) if the reagent is unstable, and d) rules for detecting trend changes. In cases b) and c), the bias is predictable, can be estimated, and decisions based on computer-assisted estimation have increased accuracy. The applied rules are based on: the mean deviation of control results in a run, the moving average of the last control runs, and the estimated bias (by computer-assisted dynamic estimation of the bias variation equation).

Results: Computer simulations suggested that although the number of alarms/calibrations did not increase, in only 2 cases out of 10,000 (0.02%) the critical bias value was reached. Real-life examples of the application of the proposed quality control system are presented. In cases where the reagent or control material changes frequently, the complementary rules based on the moving average and the estimated bias cannot be applied, so the system can only be applied partially. The method cannot be applied only if the design of the graphs is based on s_r (on graphs using the manufacturer's SD or s_{RW} , not).

Conclusions: The proposed system is more efficient in both detecting errors and avoiding unnecessary alarms. The increased accuracy is due to the reduction of the standard deviation by calculating the averages.

Keywords: corrective action, preventive action, mean rule, moving average, bias estimation

C8. HARMONIZATION OF REFERENCE INTERVALS FOR LEUKOCYTES

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Introduction: Leukocyte reference intervals (RIs) are influenced by both population characteristics and analytical methodology. Differences between hematology analyzers may affect reference limits and, consequently, clinical interpretation. Establishing harmonized RIs across platforms requires a structured statistical approach.

Methods: A cohort of 299 apparently healthy adults was initially enrolled. After exclusion of individuals with elevated C-reactive protein (CRP>5mg/L) and other conditions potentially affecting hematological parameters, 270 participants were included in the final reference population. Complete blood count parameters were measured on two automated hematology analyzers (Alinity h and Sysmex XN-1000). RIs were estimated using the non-parametric method (CLSI EP28-A3c), with 90% confidence intervals. Right-sided limits were applied for skewed parameters. Analyzer-specific partitioning was assessed using the Harris-Boyd method. Inter-analyzer agreement was evaluated using Bland-Altman analysis and Passing-Bablok regression, and bias was interpreted against biological variation-derived specifications.

Results: No analyzer-specific partitioning was required for most leukocyte parameters, as observed bias remained within acceptable limits. Basophils were the only parameter requiring analyzer-dependent interpretation. For eosinophils, targeted exclusion of four individuals with elevated IgE levels resulted in a reduction of the upper reference limit (right-sided) from 0.37 to $0.32 \times 10^9/\mu\text{L}$ (N=266). Harmonized RIs were defined for parameters meeting both statistical and analytical criteria and showed good agreement with published data, although narrower limits were observed.

Conclusions: Harmonized leukocyte reference intervals can be derived across hematology analyzers when supported by appropriate statistical validation and analytical performance criteria. One-sided limits are suitable for skewed leukocyte subsets, while low-count parameters may remain method-dependent.

Keywords: hematology analyzers, leukocyte reference intervals, method comparison, statistical harmonization

C9. ONE HEALTH – ONE QUALITY. THE LABORATORY PERSPECTIVE

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While the principles date back over a century, the concept "One Health" is used today to describe the interlinked health of humans, animals, and their shared environment, focused on zoonotic diseases. This is "a collaborative, multisectoral, and transdisciplinary approach—working at the local, regional, national, and global levels" as is formally recognized by Center for Diseases Control.

At the same time, quality-related concepts such as quality control, quality assurance, quality management and total quality control have gained increasing importance, and have been introduced even in the medical laboratory field.

Despite the technological progress recorded in each sector in recent decades, a limitation in strengthening the collaboration between them was quickly highlighted due to gaps or delays in standardisation or harmonisation of testing, quality control and reporting of results (including differences in units of measurements).

A high level of reproducibility and traceability—beyond metrological traceability alone—is essential for the effective analysis and interpretation of the large volumes of data generated across the three domains and consolidated within shared databases. These data include information on the global, regional, and local circulation of microorganisms among humans, animals, and the environment, as well as patterns in the spread of antimicrobial resistance and the transmission of virulence and resistance genes.

For this reason the common approach "One Quality" for improving the performance and achieving the highest quality level is the way to overcome the aforementioned limitations.

If "One Health – One Quality" will be successful, probably the next step will be the extension of the concept from the domain of the pathogenic microorganisms to the chemical pollutants which affect all (heavy metals, nano and microplastics, radionuclides, etc.).

Keywords: antimicrobial resistance, microorganisms, One Health, One Quality, pollutants

R10. LABORATORY-CLINICIAN COMMUNICATION: CHALLENGES AND STRATEGIES FOR IMPROVEMENT

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Despite the obvious progress (from manual techniques to automation, from manual registration to Laboratory Informatic System etc), laboratory medicine practitioners still face many challenges: increased workload, implementation of new tests and methods, time consuming paperwork. Also, communication between laboratory and clinicians is sometimes ineffective.

This presentation tries to analyse the main difficulties at the interface between laboratory staff and clinicians and to identify ways for improvement. Laboratory staff's major complaints about the clinicians are: not requesting the appropriate tests, repeatedly requesting unnecessary tests, not checking the availability of tests, not providing relevant information about the patients, not knowing the correct collection and transportation procedures, and not trusting the lab results.

Key points for improvement might include a more proactive attitude of laboratory staff regarding consultations about test selection and interpretation of complex results. Interdisciplinary meetings and a tighter collaboration between lab specialists and clinicians would result in better medical decisions, and improved patients' outcome.

Keywords: clinicians, communication, laboratory specialists

C11. RECENT ADVANCES IN CEREBROSPINAL FLUID ANALYSIS USED IN THE DIAGNOSIS AND PROGNOSIS OF MULTIPLE SCLEROSIS PATIENTS

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Recent advances in cerebrospinal fluid (CSF) analysis have transformed the diagnostic and prognosis of multiple sclerosis (MS). The 2024 McDonald diagnostic criteria now include kappa free light chains (κ -FLC) as an alternative to oligoclonal bands for demonstrating intrathecal immunoglobulin synthesis, with comparable sensitivity and specificity of approximately 90%. The κ -FLC index (cutoff ≥ 6.1) offers advantages including quantitative results, cost-effectiveness, and rater-independence, with higher values predicting greater disease activity.

Neurofilament light chain (NfL) has emerged as the most validated biomarker for monitoring disease activity and treatment response. While CSF NfL measurement was historically limited by invasiveness, highly sensitive fourth-generation assays now enable reliable blood-based quantification. CSF and serum NfL levels correlate with clinical and radiological activity, predict disability worsening, and decrease with high-efficacy therapies. Meta-analyses demonstrate that CSF NfL is significantly elevated in MS compared to controls and is particularly elevated during relapses versus remission.

Beyond traditional markers, multiplex proteomic approaches have identified novel CSF biomarker panels. Glial fibrillary acidic protein and chitinase-3-like protein 1 show promise for monitoring progressive disease biology independent of acute inflammation.

These advances position CSF biomarkers as essential tools for personalized MS management.

Keywords: cerebrospinal fluid biomarkers, kappa free light chains, multiple sclerosis, neurofilament light chain

C12. PRECISION MEDICINE IN ALLERGOLOGY: THE ROLE OF COMPONENT-RESOLVED DIAGNOSIS IN ALLERGY DIAGNOSIS

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The landscape of allergy diagnosis has undergone a paradigm shift with the advent of precision medicine, moving beyond extract-based testing toward a molecularly defined understanding of IgE sensitization. Component-Resolved Diagnosis (CRD) represents a cornerstone of this transformation, enabling clinicians to identify specific allergenic molecules responsible for an individual patient's sensitization profile rather than relying solely on whole allergen extracts.

Traditional allergy diagnostics, while clinically valuable, are limited by cross-reactive carbohydrate determinants and co-sensitization patterns that can obscure the true clinical relevance of a positive test. CRD addresses these limitations by distinguishing between genuine primary sensitization and cross-reactive responses—a distinction with profound implications for patient management, risk stratification, and therapeutic decision-making.

Through multiplex platforms such as ISAC (Immuno Solid-phase Allergen Chip) and singleplex ImmunoCAP assays, CRD allows simultaneous profiling of hundreds of allergenic molecules from a single serum sample. This approach has demonstrated particular clinical utility in complex polysensitized patients, in predicting the risk of severe systemic reactions—especially in food and venom allergy—and in identifying optimal candidates for allergen-specific immunotherapy (AIT).

This presentation will examine the molecular basis of major allergen families, the clinical interpretation of CRD results across key allergic conditions including respiratory, food, and hymenoptera venom allergy, and the integration of CRD into a precision medicine workflow. Special emphasis will be placed on how CRD-guided decision-making improves diagnostic accuracy, enhances patient safety, and optimizes the selection and outcome of immunotherapy.

As allergology enters the era of personalized medicine, CRD stands not merely as a diagnostic refinement, but as an essential tool for delivering individualized, evidence-based care to the allergic patient.

Keywords: Component-Resolved Diagnosis, precision medicine, IgE sensitization, molecular allergens, allergen-specific immunotherapy, polysensitization, cross-reactivity

R13. CLINICAL RELEVANCE OF PIVKA-II IN LIVER PATHOLOGY: COMPARATIVE INSIGHTS WITH AFP AND LABORATORY MARKERS

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Introduction: Protein induced by vitamin K absence-II (PIVKA-II) is an important biomarker for hepatocellular carcinoma (HCC), the most common primary liver cancer. Its clinical utility is often evaluated alongside alpha-fetoprotein (AFP) and other biochemical markers. This study aimed to assess the diagnostic performance of PIVKA-II and eight liver-related parameters in HCC, viral hepatitis, and cirrhosis.

Materials and Methods: A total of 69 adult patients admitted for the first time to "Sf. Spiridon" County Emergency Hospital in Iasi were included after applying selection criteria, excluding recent vitamin K administration. PIVKA-II levels were measured using ARCHITECT chemiluminescence. Due to non-normal distribution, Spearman's correlation was used to assess associations between PIVKA-II and 41 laboratory parameters. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic accuracy of eight biomarkers, calculating the area under the curve (AUC) and statistical significance.

Results: PIVKA-II showed strong diagnostic performance for HCC (AUC=0.815; $p<0.001$). AFP was more predictive for viral hepatitis (AUC=0.744; $p<0.001$). Cirrhosis was best indicated by AST (AUC=0.911) and ALT (AUC=0.839). PIVKA-II moderately correlated with AFP ($R=0.432$) and RDW ($R=0.488$), and strongly with direct bilirubin ($R=0.576$), INR ($R=0.591$), and prothrombin time ($R=0.59$). Negative correlations were observed with prothrombin activity ($R=-0.55$), lymphocyte count ($R=-0.46$), and sodium ($R=-0.42$).

Conclusions: The studied biomarkers provide complementary, not redundant, diagnostic information. PIVKA-II and AFP demonstrated the highest accuracy for HCC detection, while transaminases (AST, ALT) were most effective for cirrhosis. Lower PIVKA-II elevation in viral hepatitis compared to AFP suggests improved specificity in HCC screening. These findings support the combined use of biomarkers for accurate diagnosis and disease monitoring.

Keywords: PIVKA-II, hepatocellular carcinoma, biomarkers, liver disease, ROC analysis

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C14. BIOMARKER PROFILES IN CARDIAC RESYNCHRONIZATION THERAPY: TRANSCARDIAC GRADIENTS AND LONGITUDINAL CHANGES

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Introduction: Cardiac resynchronization therapy (CRT) improves outcomes in selected patients with heart failure and electrical dyssynchrony; however, a substantial proportion exhibit suboptimal response. Inflammation and myocardial remodeling may contribute to this variability, yet their modulation following CRT remains incompletely characterized.

Methods: Thirty-seven patients undergoing CRT implantation at the Institute of Cardiovascular Diseases and Transplant in Târgu Mureș between February 2023 and March 2024 were included. Five biomarkers – interleukin-1beta (IL-1b), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-a), soluble ST2 (ST2), and galectin-3 – were first measured at implantation (baseline) in peripheral blood and in the coronary sinus, and subsequently post-CRT (follow-up) in peripheral blood. Non-parametric statistical analyses (paired Wilcoxon and Friedman tests) with Bonferroni correction were applied.

Results: ST2 demonstrated a significant transcardiac gradient, with higher concentrations in peripheral blood compared to the coronary sinus ($p=0.007$; $r=0.856$). IL-6 decreased significantly at follow-up versus baseline (median change -2.77 pg/mL; $p=0.033$; $r=0.544$). Longitudinal analysis in the subgroup with complete serial data confirmed statistically significant variation for IL-6 and ST2 across timepoints ($p<0.01$).

Conclusions: Our data suggests the association of CRT with selective modulation of the inflammatory biomarker profile, with a significant reduction in IL-6 and a baseline transcardiac ST2 gradient. These findings point to biologically distinct roles for cytokines and myocardial stress markers in patients undergoing CRT, warranting validation in larger cohorts.

Keywords: biomarkers, cardiac resynchronization therapy, inflammation, myocardial remodeling

R15. ASSESSMENT OF 25(OH) VITAMIN D STATUS: COMPARABILITY BETWEEN METHODS AND CLINICAL IMPLICATIONS

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Introduction: The routine evaluation of 25(OH) Vitamin D status requires quantification of the analyte using a range of immunoassay platforms. However, variability among these immunoassays may affect analytical consistency and clinical interpretation.

Methods: This study used 83 serum samples to measure 25(OH)Vitamin D using three different instruments: Cobas e801 (based on the ECLIA principle) and Liaison XL and Maglumi X6 (both based on the CLIA principle). To evaluate the comparability of these methods, we used Passing-Bablok regression and Bland-Altman analysis. Clinical agreement was determined by Cohen's kappa coefficient at a sufficiency threshold of 20 ng/mL, and the reclassification rate was checked at both 20 ng/mL and 12 ng/mL, the threshold for severe deficiency. Mean bias from DEQAS data and TAE were calculated and compared against recommended analytical performance specifications (APS).

Results: Analytical agreement between methods was generally acceptable. However, in the clinically relevant 10-30 ng/mL range, Passing-Bablok showed systematic differences, and Bland-Altman confirmed method-dependent bias. The ECLIA instrument consistently measured lower concentrations than CLIA, leading to significant disagreement and high reclassification at the 20 ng/mL threshold, with minimal reclassification at 12 ng/mL, suggesting good agreement at this level.

Conclusions: Differences between immunoassays and the high rate of reclassification at clinically relevant thresholds demonstrate that results across automated platforms are not interchangeable, and vitamin D results should be interpreted carefully.

Keywords: 25 (OH)-Vitamin D, method agreement, method comparison

C16. INFLUENCE OF VDR, CYP2R1, AND GC POLYMORPHISMS ON SEASONAL 25(OH)D VARIATION

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Introduction: Vitamin D deficiency is a global challenge, especially in Central and Eastern Europe where genomic data is scarce. Despite adequate seasonal UVB exposure, wide inter-individual variation suggests an inherited non-response phenotype. Polymorphisms in VDR, CYP2R1, and GC genes influence vitamin D metabolism, but their combined role in seasonal dynamics has not been studied in this region. We investigated gene-environment interactions in a Romanian cohort and developed a predictive model of seasonal non-response.

Methods: We enrolled 250 adults, genotyped for VDR rs731236, CYP2R1 rs10741657, and GC rs2282679. Serum 25(OH)D was measured in March (low UVB) and September (high UVB). Anthropometrics, BMI, and self-reported sun exposure were recorded. Seasonal variation was analyzed by paired t-tests and ANOVA. A Genetic Risk Score (GRS, 0-6) was calculated, and logistic regression combining GRS, BMI, and baseline 25(OH)D was evaluated with ROC analysis.

Results: Serum 25(OH)D rose significantly post-summer (mean Δ +29 ng/mL, $p < 0.001$). However, carriers of risk genotypes (VDR CC, CYP2R1 GG, GC CC) remained below sufficiency (< 30 ng/mL). A clear genotype hierarchy persisted (wild-type > heterozygote > risk homozygote). Self-reported sun exposure showed negligible effect compared with genotype and season (interaction $p > 0.24$). The predictive model identified non-responders ($\Delta 25(OH)D < 10$ ng/mL) with excellent accuracy (AUC=0.91, 95% CI: 0.86–0.96). GRS ($\beta = -0.30$) and BMI ($\beta = -0.56$) were strong negative predictors, while baseline 25(OH)D modestly increased response likelihood ($\beta = +0.16$). Heatmap analysis revealed cumulative effects, with triple-risk carriers showing the weakest gains ($\Delta \approx 20$ ng/mL).

Conclusions: This first Romanian genomic study demonstrates a genetically locked insufficiency phenotype persisting despite UVB exposure. By integrating an under-represented population into global genomic research, we expand diversity and emphasize genotype-guided supplementation as a pillar of precision public health. The sun shines equally, but genomes decide who remains deficient.

Keywords: genetic polymorphisms, predictive modeling, seasonal variation, vitamin D deficiency

P1. LIQUID BIOPSY IN CANCER

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Introduction: Cancer is the second leading cause of death worldwide and represents a major public health problem worldwide. Early detection and appropriate therapeutic management are essential pylons in improving the prognosis and survival rates of oncological patients.

Methods: A literature review study using the databases PubMed and Hinari has been performed. In the search process, the keywords "liquid biopsy", "cfDNA", "miRNAs" and "biomarkers" have been used.

Results: Liquid biopsy (LB) has become an indispensable tool in oncology, facilitating the transition to precision medicine. Clinical applications include non-invasive genotyping, early-stage disease monitoring, assessment of treatment resistance, and early cancer detection. From a comparative perspective, LB represents a viable alternative or complementary to tissue biopsy, having an essential role in screening programs. Recent research indicates that blood remains the most investigated biological fluid in the field of liquid biopsy, with the main analytes studied being cell free DNA (cfDNA), circulating tumor cells (CTCs), and microRNAs (miRNAs). Clinical data highlights a direct correlation between elevated serum cfDNA levels and pancreatic adenocarcinoma, with a decrease observed post-therapeutically. Simultaneously, a vast literature confirms the critical role of CTCs in metastatic dynamics and neoplastic progression. Circulating miRNAs also emerge as promising biomarkers in radiotherapy stratification and prediction of immunotherapy-related toxicities.

Conclusions: Liquid biopsy has become a fundamental component of precision oncology, offering non-invasive, real-time tumor profiling that has transformed cancer management. However, its full clinical potential depends on achieving standardization, adapting to evolving therapies, and integrating emerging technologies such as artificial intelligence.

Keywords: cfDNA, liquid biopsy, miRNAs

P2. CHARACTERIZATION OF TUMOR-INFILTRATING LYMPHOCYTES AND THE CD4/CD8 RATIO IN COLORECTAL CANCER BY FLOW CYTOMETRY

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Introduction: Tumor-infiltrating lymphocytes (TILs) represent an important component of the local immune response in colorectal cancer (CRC) and are correlated with a favorable clinical prognosis. Flow cytometry enables the characterization of the heterogeneity of the immune infiltrate within tumor tissue, contributing to the identification of cellular subpopulations and to understanding their role in the antitumor immune response.

Methods: The study included 17 patients with colorectal cancer (CRC) in advanced stages (II–III and III), who underwent surgical resection between January and December 2025. Tumor tissue samples and histologically normal tissue adjacent to the tumor (NAT) were collected, transported, and kept in RPMI 1640 culture medium. TILs were isolated and evaluated by flow cytometry, using the Navios EX cytometer (Beckman Coulter), and the data were processed with Kaluza C software. T, B, and NK lymphocyte subpopulations were evaluated with an immunophenotypic panel that includes the markers CD45, CD3, CD4, CD8, CD20, CD56, and CD14.

Results: Flow cytometry acquisition ranged between 58,000–400,000 events/tube, without compromising the evaluation of cellular population distribution. The tumor immune infiltrate highlighted a predominance of T (CD3⁺) lymphocytes (49–97%), especially the CD4⁺ subset (27–80%), compared to CD8⁺ (6–41%). B (CD20⁺) lymphocytes showed variable proportions (4–50%), while NK cells (CD56⁺) were poorly represented (0–3%). The CD4/CD8 ratio was higher in tumor tissue (0.7–6.6) compared to NAT (0.2–3.0). Available data suggests that patients with a favorable therapeutic response present, on average, a higher CD4/CD8 ratio (~1.7 vs ~1.23).

Conclusions: Flow cytometry highlights immune heterogeneity in CRC, distinct from that observed in NAT. The CD4/CD8 ratio may be a promising biomarker of the immune infiltrate, useful for evaluating and stratifying therapeutic response. The small size of the studied cohort does not allow for definitive statistical conclusions; therefore, patient enrollment and biological sample collection are ongoing.

Keywords: colorectal cancer, flow cytometry, TILs

Acknowledgements: Research funded under the National Research Project (2024–2027), within the State Program „Intratumoral microbiome and local immunity in colorectal cancer: mediating the response to specific therapy”, Code 100101.

P3. MULTIDISCIPLINARY MANAGEMENT AND THE ROLE OF TUMOR MARKERS IN TESTICULAR EMBRYONAL CARCINOMA FOR AN ADOLESCENT

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Introduction: Mixed germ cell tumors represent a diagnostic and therapeutic challenge in pediatric oncology and urology. Embryonal carcinoma, the predominant component in this case, is an aggressive form of non-seminomatous cancer characterized by a high proliferation rate and rapid metastatic potential, requiring close correlation between histopathology and laboratory parameters. We aimed to present the clinical and laboratory management of an adolescent patient with a left testicular neoplasm, highlighting the importance of histological risk factors in adjuvant therapeutic decision-making, even in the presence of normal serum tumor markers.

Methods: We present the case of a patient aged 15 years and 11 months, diagnosed in February 2025 with a left testicular tumor mass. The following clinical and paraclinical investigations were performed: clinical examination, imaging (ultrasound, MRI, chest-abdomen-pelvis CT), surgical intervention (inguinal orchiectomy), detailed histopathological examination, dynamic monitoring of tumor markers (AFP, β -HCG, LDH), and biochemical/hematological parameters during 4 cycles of adjuvant EP chemotherapy (Etoposide and Cisplatin).

Results: Histopathological examination confirmed a mixed germ cell tumor composed of 90% embryonal carcinoma, yolk sac tumor, and mature teratoma, with invasion of the rete testis (pT2 cN0 M0, Stage IB). Although tumor markers (AFP: 2.15 IU/mL, β -HCG: 0.10 mIU/mL) remained within normal limits postoperatively, the histological aggressiveness necessitated the administration of 4 cycles of chemotherapy. Biological monitoring in August 2025 demonstrated a stable post-therapeutic status, with preserved renal function (Creatinine: 0.82 mg/dL) and hepatic function (ALT: 26 U/L, AST: 29 U/L), and the absence of imaging signs of recurrence.

Conclusions: The high percentage of embryonal carcinoma (90%) and rete testis invasion represent major risk factors that justify adjuvant chemotherapy, independent of normal postoperative serum marker levels. The medical analysis laboratory is essential not only for the initial diagnosis but also for long-term surveillance to ensure early detection of any potential recurrence.

Keywords: adjuvant chemotherapy, mixed germ cell tumors, testicular embryonal carcinoma, tumor markers

P4. CRITICAL FACTORS IMPACTING ON THE SENSITIVITY OF DETECTION OF RARE CELLULAR SUBSETS IN POST-THERAPEUTIC MONITORING OF MULTIPLE MYELOMA PATIENTS

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Introduction: Hemodilution of bone marrow aspirate represents a major limitation in the performance of measurable residual disease (MRD) tests in hemato-oncology, as it reduces the proportion of relevant cellular subsets, decreases technical sensitivity, and consequently leads to underestimation of tumor burden, potentially resulting in false-negative outcomes.

Methods: Between 2023 and 2025, a total of 226 MRD tests were performed by flow cytometry in 159 patients with multiple myeloma (MM) at the Regional Institute of Oncology (IRO) Iasi. Detection sensitivity was calculated for each test, based on the lower limit of quantitation (LLOQ) and the limit of detection (LOD), defined as 50, respectively, 20 cells divided by total number of analyzed events. Retrospectively, with the aim of implementing into routine practice of a novel technical parameter relevant to sample quality, BMQI = Bone Marrow Quality Index was calculated using percentages of myeloid precursors and nucleated red cells (Oskarsson et al., 2023). The strategy currently used in the department for assessing hemodilution is based on bone marrow aspirate cellularity, mast cell and B lymphoid precursor frequency.

Results: Detection sensitivity of MRD testing by FCM ranged as follows: LLOQ – 2.94×10^{-6} to 6.94×10^{-5} and LOD – 1.18×10^{-6} to 2.78×10^{-5} . Based on the obtained BMQI values, sample quality was retrospectively classified as follows: 15.5% adequate quality samples (category 1, $\text{BMQI} \geq 2.5$), 33.6% moderate hemodilution (category 2, $1.4 \leq \text{BMQI} < 2.5$), 30% considerable hemodilution (category 3, $0.5 \leq \text{BMQI} < 1.4$), and 20.7% severe hemodilution (category 4, $\text{BMQI} < 0.5$). When BMQI values were compared with quality-related remarks extracted from validated test reports, the following discrepancies were observed: in category 1 (adequate quality), 8.6% of tests included remarks indicating hemodilution or reduced cellularity; in categories 2, 3, and 4 (hemodilution), 85.5%, 86.8%, and 40.4% of tests, respectively, did not include any mention of hemodilution in the reports. These discrepancies may be partially explained by several factors: (1) selective loss of the erythroid compartment during cellular enrichment procedures (Bulk Lysis), resulting in the underestimation of BMQI; (2) absence of erythroid-specific markers in the MRD_MM panel, with potential overlap between cellular debris and erythroid cells (both CD45-negative); (3) misinterpretation of hemodilution in the context of hypocellular bone marrow aspirates following therapy; and (4) decreased frequencies of myeloid precursors and erythroid cells during disease relapse, leading to consequent underestimation of the BMQI.

Conclusions: The implementation of the BMQI index may be useful for identifying cases with moderate and considerable hemodilution (where most discrepancies were observed), demonstrating superiority in assessing bone marrow aspirate quality. However, given the frequent occurrence of unexplained discrepancies, the parameters already in use (e.g. mast cell and B lymphoid precursor percentage) remain relevant for the evaluation of bone marrow aspirate sample quality.

Keywords: bone marrow hemodilution, Bone Marrow Quality Index (BMQI), flow cytometry, measurable residual disease, multiple myeloma

P5. MARKED LEUKOERYTHROBLASTIC REACTION DURING RETICULOCYTE CRISIS: DIAGNOSTIC CHALLENGES IN PERNICIOUS ANEMIA

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Introduction: Severe pernicious anemia can present as global bone marrow failure, mimicking malignant pathologies. Diagnosis becomes challenging during the initial treatment phase, when the "unblocking" of erythropoiesis can generate atypical peripheral patterns due to the breach of the blood-marrow barrier.

Methods: We report the case of a 71-year-old female patient, diagnosed with Pernicious Anemia (positive anti-gastric parietal cell antibodies), initially presenting with severe aregenerative pancytopenia: Hb: 7 g/dL, MCV: 101 fL, WBC: 1,720/ μ L, PLT: 47,000/ μ L and reticulocytes: 1.02% (absolute value: 20,100/ μ L). One month after initiating injectable vitamin B12 replacement therapy, the patient developed an explosive marrow response characterized by a massive reticulocyte crisis (reticulocytes: 10.01%, absolute value: 232,200/ μ L). The blood count, including the reticulocyte count were performed with the Sysmex® XN-1000 analyzer, and the blood smear (May-Grünwald-Giemsa staining) was interpreted according to the recommendations of the ICSH.

Results: Flow cytometry analysis of reticulocyte indices revealed intense regenerative activity, with an immature reticulocyte fraction (IRF) of 27.89% (fraction of reticulocytes with medium fluorescence—MFR: 17.3%, fraction of reticulocytes with increased fluorescence—HFR: 10.5%). This rapid marrow expansion was accompanied by a transient leucoerythroblastic reaction in the peripheral blood, showing 4% blasts, 1% myelocytes, 1% metamyelocytes and 3% orthochromatic erythroblast with a "ragged appearance". Peripheral blood smear morphology was remarkable, revealing pathognomonic elements of forced erythropoiesis: Cabot rings, Pappenheimer bodies, basophilic stippling, and marked poikilocytosis (macroovalocytes, dacryocytes). The value of reticulocyte Hb content (Ret-Hb) at the lower limit (28.1 pg) signaled the onset of a functional iron deficiency, secondary to the accelerated rhythm of hemoglobin synthesis.

Conclusions: The case highlights the need to recognize the phenomenon of malignant mimicry during recovery from severe vitamin B12 deficiency. Rigorous interpretation of next-generation reticulocyte indices and identification of specific morphological markers are essential to differentiate a benign leucoerythroblastic reaction from myelodysplastic syndrome, thus avoiding invasive investigations during a period of a hematological instability with a favorable prognosis.

Keywords: leucoerythroblastic reaction, pancytopenia, pernicious anemia, reticulocyte crisis, vitamin B12

P6. MicroRNA EXPRESSION IN POLYCYTHEMIA VERA, ESSENTIAL THROMBOCYTHEMIA AND PRIMARY MYELOFIBROSIS

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Introduction: Myeloproliferative neoplasms (MPNs) are biologically heterogeneous disorders in which inflammatory signaling, clonal architecture, and thrombotic burden contribute to clinical outcomes. MicroRNAs are plausible integrators of these processes, but their association with phenotype, driver mutations, and survival remains incompletely defined across the main MPN subtypes. We aimed to evaluate the expression levels of miR-125b and miR-223 in a group of patients diagnosed with polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF).

Methods: In the study, 216 unrelated patients with MPN were enrolled. The blood samples from both patients and healthy controls were collected in EDTA (ethylenediaminetetraacetic acid) tubes. The total RNA was extracted from the preserved peripheral whole blood samples using the mirVana miRNA Isolation Kit with phenol. We used the TaqMan MicroRNA Reverse Transcription Kit and TaqMan miRNA primers to obtain complementary DNA (cDNA). Quantitative real-time PCR (RT-PCR) was performed using the 7500 Fast Dx Real-Time PCR System with TaqMan™ Fast Advanced Master Mix and specific TaqMan™ assays for hsa- miR-125b-5p and hsa- miR-223-3p.

Results: No statistically significant differences in miR-125b-5p or miR-223-3p expression were observed between MPN subtypes and healthy controls ($p > 0.05$). We observed a statistically significant association between JAK2 status and miR-125b-5p expression in PV.

Conclusions: This divergence suggests that while miR-125b-5p and miR-223-3p may reflect disease biology and mutation signaling, their baseline expression alone does not supersede established clinical prognostic determinants in predicting overall survival within this cohort. Future studies integrating dynamic longitudinal miRNA changes, larger mutation-stratified subgroups, and multi-marker panels may clarify whether composite molecular signatures can add prognostic resolution beyond age and systemic disease burden.

Keywords: miRNA, miR-125b-5p, miR-223-3p, myeloproliferative neoplasms

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P7. SOLUBLE 4-1BB AND PD-L1 AS NON-INVASIVE INDICATORS OF FIBROSIS SEVERITY IN CHRONIC HEPATITIS C

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Introduction: Hepatitis C virus (HCV) persists in 70-80% of cases by inducing T-cell exhaustion through continuous antigenic stimulation. This process involves upregulating inhibitory receptors such as programmed death-1 (PD-1), cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), and T-cell immunoglobulin and mucin-domain containing-3 (TIM-3), alongside dysregulated co-stimulatory molecules like CD137 (4-1BB). Identifying reliable, non-invasive biomarkers for immune dysfunction remains a clinical priority. Soluble immune check-point proteins (sICPs) in peripheral blood may serve as accessible indicators of T-cell exhaustion and subsequent liver fibrosis.

Methods: This cross-sectional study analyzed 176 treatment-naïve patients with chronic hepatitis C (CHC) from the LIVE(RO)2-EST cohort. Participants were stratified by fibrosis stage and hepatocytolysis status. Plasma sPD-L1 and 4-1BB levels, measured via multiplex Luminex assay, were evaluated against fibrosis severity, non-invasive scores (FIB-4, APRI), biochemical markers of liver injury and serological parameters.

Results: Plasma 4-1BB levels moderately correlated with fibrosis severity ($r=0.387$, $p<0.001$), FIB-4 ($r=0.348$), APRI ($r=0.335$), and AST ($r = 0.305$). These concentrations were significantly higher in advanced fibrosis (F2–F4) compared to early stages (F0–F1) ($p<0.001$). Conversely, sPD-L1 showed a weaker link to fibrosis ($r=0.213$, $p=0.038$) than with AST ($r=0.357$) and APRI ($r=0.313$). Notably, neither marker correlated with virological or serological parameters.

Conclusions: Our findings indicate that circulating sICPs correlate with fibrosis severity and liver injury markers, but not with virological parameters. This suggests these molecules reflect host immune dysregulation from chronic antigenic exposure rather than active viral replication. Notably, 4-1BB demonstrated a stronger correlation with fibrosis than sPD-L1, highlighting the distinct roles of co-stimulatory versus inhibitory pathways in disease progression. Consequently, sICPs, particularly 4-1BB, act as promising non-invasive biomarkers of immune-mediated liver damage. Integrating these markers into clinical practice could significantly improve risk stratification and personalized management for patients with CHC.

Keywords: chronic hepatitis C, hepatic fibrosis, soluble immune checkpoints, 4-1BB, sPD-L1

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P8. DIAGNOSTIC PERFORMANCE OF THE GAAD SCORE IN HEPATOCELLULAR CARCINOMA

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Introduction: Early detection of hepatocellular carcinoma (HCC) remains a major clinical challenge, highlighting the need for accurate, non-invasive diagnostic tools. This study aimed to evaluate and compare the diagnostic performance of alpha-fetoprotein (AFP), PIVKA-II, and the GAAD score in detecting HCC.

Methods: A retrospective longitudinal study was conducted over 24 months, including 135 patients (95 male and 40 female) admitted to the IRGH "Prof. Dr. Octavian Fodor" Cluj-Napoca, diagnosed with HCC and/or chronic liver disease. Serum AFP and PIVKA-II levels were assessed, and the GAAD score was calculated for each patient. Diagnostic performance was evaluated using receiver operating characteristic (ROC) curve analysis.

Results: AFP showed moderate sensitivity but good specificity, limiting its utility as a standalone screening tool. In contrast, PIVKA-II demonstrated high sensitivity but lower specificity. The combined use of AFP and PIVKA-II improved overall diagnostic performance by addressing their individual limitations. The GAAD score exhibited excellent sensitivity (>90%) and good specificity (70%), outperforming both biomarkers when used independently.

Conclusions: The GAAD score is a robust, non-invasive diagnostic tool for HCC, offering superior sensitivity and favorable specificity. Its strong diagnostic performance supports its potential role in routine clinical practice, particularly for early detection.

Keywords: AFP, biomarker, GAAD, hepatocellular carcinoma, PIVKA-II

P9. RELATIONSHIP BETWEEN CALLY, HALP, AND FIB-4 INDICES IN PATIENTS WITH VIRAL HEPATITIS B

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Introduction: Non-invasive methods such as transient elastography and Fibrosis-4 (FIB-4) or FIB-5 scores have become first-line tools in fibrosis evaluation, providing an effective and affordable alternative to liver biopsy. The aim of the study was to evaluate the relationship between the immuno-metabolic indices CALLY and HALP with the degree of fibrosis assessed with the FIB-4 index in patients with chronic liver disease with chronic viral hepatitis B.

Methods: This retrospective study examined results from SIL for both the CALLY and HALP indices in patients who were tested positive for anti-HBc antibodies and admitted to the Târgu Mureș County Emergency Clinical Hospital between July 2024 and July 2025. The correlation between immuno-metabolic indices and liver fibrosis, as assessed by FIB-4, was also analyzed.

Results: Of the 222 patients with positive anti-HBc antibodies, 46.19% were women and 53.81% were men. HBs antigen was positive in n=74 (33.33%) and negative in n=148 (66.66%) of patients. CALLY indices (OR=0.85; 95% CI: 0.78-0.92), p=0.0001, and HALP (OR=1.016; 95% CI: 1.008-1.025), p<0.001 were found as independent predictors for advanced fibrosis (FIB-4 $\geq$ 3.25), after adjustment for C-reactive protein. The model's ROC curve and AUC was 0.795 (95% CI: 0.735-0.846), indicating a relatively good ability of the model to identify advanced fibrosis.

Conclusions: The results of the study suggest that the CALLY and HALP indices calculated from routine biological parameters can provide useful complementary information for the assessment of immuno-metabolic status, including in patients with chronic hepatitis B, being identified as independent predictors for the severity of liver damage and the presence of liver fibrosis.

Keywords: CALLY, chronic hepatitis, FIB-4, HALP, liver fibrosis, viral hepatitis B

P10. BIOLOGICAL PROFILE AND PRECANCEROUS LESION PROGRESSION IN ATROPHIC GASTRITIS: COMPARISON BETWEEN *HELICOBACTER PYLORI* AND AUTOIMMUNE ETIOLOGY

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Introduction: Chronic atrophic gastritis evolves along two main etiological pathways—*Helicobacter pylori* (*H. pylori*) infection and autoimmune mechanisms—with distinct biological profiles and histological progression potential. Identifying laboratory differences and the rate of precancerous lesion evolution is essential for developing etiology-specific surveillance strategies.

Methods: A single-center retrospective study enrolled patients with histologically confirmed atrophic gastritis, stratified into two groups: *H. pylori*-associated antral and corporal atrophic gastritis (AAG+CAG) and autoimmune corporal atrophic gastritis (CAG). The two populations (95 patients: 43 *H. pylori*, 52 autoimmune) were assessed for clinical, endoscopic, histopathological, and laboratory parameters (hemoglobin, mean corpuscular volume—MCV, serum iron, triglycerides, cholesterol, fibrinogen, INR). A longitudinal subcohort of patients with at least two upper endoscopies at $\geq$ 12-month intervals was analyzed for precancerous lesion progression according to the updated Sydney System.

Results: *H. pylori* pangastritis patients showed significantly lower triglyceride (p=0.018) and cholesterol (p=0.029) levels compared to the autoimmune group; multivariate regression identified low triglycerides as the sole independent predictor of *H. pylori* pangastritis (p=0.04). Hematological parameters did not reach statistical significance, though trends toward lower hemoglobin and MCV were noted in the *H. pylori* group. In the longitudinal subcohort (median follow-up 60 months), autoimmune gastritis demonstrated significantly higher overall progression rates than *H. pylori* disease (63.5% vs. 36.9%, p=0.003), with atrophy prevalence increasing by 48.1 percentage points versus 15.2. Intestinal metaplasia (IM) regression was virtually absent in autoimmune gastritis, in contrast with modest regression following *H. pylori* eradication.

Conclusions: The two etiologies of atrophic gastritis present distinct biological profiles, particularly in lipid metabolism, and fundamentally different longitudinal behaviors. Autoimmune gastritis follows a more aggressive and largely irreversible progression pathway, highlighting the need for etiology-specific endoscopic surveillance protocols informed by the patient's biological profile.

Keywords: atrophic gastritis, autoimmune gastritis, *Helicobacter pylori*, histological progression, precancerous lesions

P11. CORRELATION BETWEEN TREC /KREC QUANTIFICATION AND IMMUNOPHENOTYPING IN PRIMARY IMMUNODEFICIENCY

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Introduction: X-linked agammaglobulinemia (Bruton's disease) is a rare primary immunodeficiency characterized by blocked B-lymphocyte maturation, severe hypogammaglobulinemia, and increased susceptibility to recurrent infections. The differential diagnosis of primary immunodeficiencies requires sensitive methods for assessing T- and B-lymphocyte development. T-cell receptor excision circles (TREC) and kappa-deleting recombination excision circles (KREC) are molecular markers of lymphocyte neogenesis and allow assessment of the maturation of the T and B compartments.

Methods: A 36-year-old male patient was investigated following referral for immunological and genetic evaluation due to suspected Bruton agammaglobulinemia. The assessment included lymphocyte immunophenotyping by flow cytometry and quantitative real-time polymerase chain reaction analysis for TREC and KREC levels, expressed per 10^6 leukocytes.

Results: Immunophenotyping revealed severe B-cell depletion (CD19: 0.2%; $0.0022 \times 10^3/\mu\text{L}$), marked hypogammaglobulinemia (IgG: 3.20 g/L; IgA: 0.25 g/L; IgM: 0.25 g/L), and imbalance of T-cell subsets with reduced T-helper lymphocytes and a CD4/CD8 ratio of 0.67. Molecular analysis demonstrated significantly reduced KREC values ($419.21/10^6$ leukocytes), consistent with a major defect in B-cell maturation, together with decreased TREC levels ($17,835.13/10^6$ leukocytes), indicating concomitant T-cell impairment. Correlation of immunophenotypic and molecular findings allowed exclusion of classical Bruton agammaglobulinemia.

Conclusion: The integrated immunophenotypic–TREC/KREC profile supports the diagnosis of a primary combined immunodeficiency, highlighting the concordance between severe B-cell depletion and KREC reduction, as well as the involvement of the T compartment through TREC reduction. The integrative approach increases the accuracy of the diagnosis and demonstrates the clinical utility of TREC/KREC quantification both in the differential diagnosis of complex cases and as a valuable tool in neonatal screening programs.

Keywords: combined immunodeficiency, KREC, primary immunodeficiency, TREC

P12. BIOMARKERS FOR EARLY DETECTION OF INTRAUTERINE GROWTH RESTRICTION

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Introduction: Intrauterine Growth Restriction (IUGR), also referred to as fetal growth restriction, represents a leading cause of adverse perinatal outcomes. Its early identification remains challenging due to the late onset of clinical symptoms and ultrasonographic manifestations. Increasing evidence supports the role of circulating biomarkers of placental dysfunction as potential tools for early detection of IUGR.

Methods: A systematic literature review was performed using PubMed, targeting studies published between 2022 and 2025. Selection criteria included the detection and measurement of angiogenic and placental biomarkers with demonstrated relevance for early prediction and diagnosis of IUGR.

Results: Among the investigated biomarkers, Placental Growth Factor (PlGF), Soluble fms-like tyrosine kinase-1 (sFlt-1) and Pregnancy-Associated Plasma Protein-A (PAPP-A) demonstrated the highest clinical relevance. IUGR is characterized by decreased circulating levels of PlGF and increased levels of sFlt-1, reflecting an imbalance in angiogenic signaling pathways. The sFlt-1/PlGF ratio has shown robust diagnostic and prognostic performance in identifying placental insufficiency. Furthermore, reduced first-trimester PAPP-A levels are associated with an increased risk of subsequent IUGR. The correlation of these biomarkers with Doppler ultrasonography enhances early risk stratification.

Conclusions: Angiogenic and placental biomarkers represent a promising adjunct in early detection of IUGR. Combined with imaging techniques, they improve diagnostic accuracy and facilitate risk-adapted clinical management. Future research should focus on multi-biomarker models and their inclusion into precision medicine frameworks.

Keywords: angiogenesis, biomarkers, intrauterine growth restriction, PlGF, placental dysfunction, sFlt-1

P13. KEY GENES ASSOCIATED TO PATHOGENESIS OF INTRAUTERINE FETAL GROWTH RESTRICTION

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Introduction: Intrauterine fetal growth restriction (IUGR) is a multifactorial condition characterized by impaired fetal growth and failure to achieve the genetically determined potential size, often resulting in increased perinatal morbidity and long-term health consequences. Genetic and epigenetic factors play a crucial role in the pathogenesis of IUGR by influencing placental development, nutrient transport, angiogenesis, and fetal metabolism.

Methods: A literature review on the subject was performed using the PubMed platform, including articles published between 2020 and 2026 (95 articles).

Results: Insulin-like growth factor (IGF) pathway genes—including IGF1, IGF2, IGF1R, and IGF2R—are central regulators of cellular proliferation and differentiation, and polymorphisms or aberrant methylation within these loci have been strongly associated with reduced fetal growth. Similarly, genes involved in placental angiogenesis and vascular remodeling, such as VEGFA, FLT1, and ENG, exhibit altered expression in IUGR pregnancies, potentially compromising uteroplacental blood flow and oxygen delivery. Nutrient transport genes—SLC2A1 (GLUT1), SLC38A1 (SNAT1) and SLC38A2 (SNAT2)—have been found to be down-regulated in IUGR placentas, limiting the transfer of glucose and amino acids required for fetal growth. Genes regulating oxidative stress and mitochondrial function, including SOD1, GPX1, and PGC-1 α , may also contribute by modulating cellular resilience to hypoxic and stress conditions within the placenta. Increasing attention has been given to epigenetic modifications and imprinting disorders—notably in H19 and CDKN1C—which alter gene expression without changing the DNA sequence, providing a mechanistic link between environmental factors and genetic susceptibility.

Conclusions: These findings underscore the complex genetic architecture underlying IUGR, but further integrative genomic and functional analyses are essential to elucidate the molecular networks driving IUGR and to develop predictive biomarkers for early diagnosis and potential therapeutic interventions.

Keywords: bioinformatic analysis, intrauterine fetal growth restriction, IUGR genes

P14. METHYLXANTHINES: THE CLINICAL-BIOLOGICAL IMPACT OF CAFFEINE IN MEDICAL PRACTICE IN A GROUP OF PREMATURE PATIENTS

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Introduction: Methylxanthines are the first-line medications in apnea of prematurity. Their serum concentrations show marked variability due to immature hepatic metabolism and drug interactions. This study aimed to evaluate preterm infants diagnosed with apnea of prematurity and to highlight the role of therapeutic drug monitoring in preventing complications related to overaccumulation.

Methods: This prospective observational clinical study was performed on 325 preterm infants, divided into a study group with serum caffeine citrate titer >50 $\mu\text{g/mL}$ (SG, n=25) and a control group with serum titer <50 $\mu\text{g/mL}$ (CG, n=50) and a comparison group that did not receive caffeine citrate (CoG, n=250). CoG required pulmonary ventilation, while SG and CG received both pulmonary ventilation and the standard dose of caffeine citrate. Serum caffeine citrate titer was monitored in dynamics.

Results: Major complications in the caffeine group were intracranial hemorrhage (5.33%) and convulsions followed by death (4.00%), while CoG demonstrated fewer adverse outcomes and a more favorable clinical course.

Conclusions: Intermittent administration of standard doses of methylxanthines or adjustment of therapeutic doses, guided by serial monitoring of serum caffeine citrate titer, may improve clinical outcomes in critical cases, reduce adverse drug effects, and support safer and individualized therapeutic management of apnea of prematurity.

Keywords: apnea of prematurity, hypoxia, methylxanthines, therapeutic drug monitoring

P15. OXIDATIVE STRESS AND ANGIOGENIC BIOMARKERS IN PREECLAMPSIA: A COMPARATIVE ANALYSIS OF GPX1, SOD1, VEGF-A, sFlt-1 AND PLGF

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Introduction: Preeclampsia is characterized by endothelial dysfunction, oxidative stress, and altered angiogenic signaling. Our study examined antioxidant and angiogenic biomarkers in preeclampsia and compared their profiles with those in normotensive pregnancies.

Methods: A comparative analysis was conducted on samples from women with preeclampsia and normotensive controls. Group comparisons used unpaired t-tests. The analyzed biomarkers included GPX1, SOD1, VEGF-A, sFlt-1, PlGF, and the sFlt-1/PlGF ratio. Multiple linear regression was also performed within the preeclampsia group to identify predictors of sFlt-1 levels.

Results: The study included 20 controls and 45 women with preeclampsia. Maternal age did not differ significantly between groups, while preeclampsia was associated with higher pre-pregnancy BMI and higher BMI during pregnancy. Compared with controls, the preeclampsia group showed significantly lower GPX1 levels (342.6 vs 829.5, $p<0.0001$), lower SOD1 levels (1397 vs. 1766, $p<0.0001$), and lower PlGF levels (351.5 vs. 646.2, $p<0.0001$). In contrast, VEGF-A was significantly increased in preeclampsia (578.3 vs. 135.1, $p<0.0001$), as was the sFlt-1/PlGF ratio (61.44 vs. 20.00, $p<0.0001$). sFlt-1 levels alone did not differ significantly between groups (1233 vs. 1222, $p=0.9404$). In the regression analysis restricted to preeclampsia cases, neither the angiogenic model nor the oxidative stress model significantly predicted sFlt-1 levels, although the angiogenic model showed a better fit than the antioxidant model ($R^2=0.125$ vs. 0.002).

Conclusions: Preeclampsia was associated with reduced antioxidant defense, reflected by lower GPX1 and SOD1, together with a marked angiogenic imbalance characterized by lower PlGF, higher VEGF-A, and a markedly elevated sFlt-1/PlGF ratio.

Keywords: angiogenic biomarkers, antioxidant enzymes, oxidative stress, preeclampsia, sFlt-1/PlGF ratio

P16. PROTEIN BINDING TO POROUS SILICA NANOPARTICLES FOR LABELLING IN LATERAL FLOW IMMUNOASSAY

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Introduction: Worldwide, myocardial infarction (MI) is a leading cause of morbidity and mortality, with heart failure being a serious complication post MI. Cardiac troponin I (cTnI) and T (cTnT) are specific cardiac biomarkers of myocardial injury. The objective of this study is to develop a sensitive lateral flow immunoassay (LFIA) for quick detection of cTnI antibodies (anti cTnI).

Methods: The detection of the bioconjugate with anti cTnI and gold nanoparticles (NPs) 40nm (nanoComposix, AUXR40), was done by assessing surface plasmon resonance shift at 520nm on a UV spectrometer. To increase the number of binding sites and thus the sensitivity of the antibody-antigen reaction, our partners (The University Politehnica of Bucharest) obtained bifunctionalized mesoporous silica composites incorporating gold nanoparticles (AuNPs) and silver/gold alloy nanoparticles (AgAuNPs). The bioconjugation reaction on these composite NPs is in initial phase, and was conducted with bovine serum albumin (BSA). Protein binding efficiency was quantified at 280nm as the difference between the protein added and free protein.

Results: The first result was the successful bioconjugation reaction between gold nanoparticles 40nm and cTnI antibodies, followed by the attempt to bind BSA on silica composite with gold and silver/gold alloy nanoparticles.

Conclusions: A method for quick identification of heart failure markers is essential for a fast treatment response. The present study shows results of cTnI bioconjugation and preliminary results of BSA reaction with silica composites with AuNPs and AgAuNPs. Further studies are necessary for cTnI detection and the LFIA device development.

Keywords: AgAu@mesoporous silica composite, cardiac troponin, LFIA

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P17. ANALYTICAL PERFORMANCE COMPARISON OF TWO IMMUNOASSAY PLATFORMS FOR TSH AND TACROLIMUS DETERMINATION

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Introduction: Thyroid-stimulating hormone (TSH) is an essential marker of thyroid function, while Tacrolimus is an immunosuppressive drug with a narrow therapeutic range requiring careful monitoring. Differences between immunoassay platforms may influence analytical results and their clinical interpretation.

Methods: A total of 30 samples were analyzed for TSH using Immulite (chemiluminescence immunoassay–CLIA) and Cobas (electrochemiluminescence immunoassay–ECLIA), and 33 samples for tacrolimus using Architect (chemiluminescent microparticle immunoassay–CMIA) and Cobas (ECLIA). Statistical analysis included Pearson correlation, paired t-test, mean bias, and Bland–Altman analysis.

Results: For TSH, a very strong correlation was observed ($r=0.989$), with no statistically significant differences ($p=0.19$) and a mean bias of 0.14 mIU/L. For Tacrolimus, correlation was also very strong ($r=0.989$), but the difference between methods was statistically significant ($p<0.001$), with Cobas reporting higher values (bias +0.75 ng/mL).

Conclusions: The evaluated platforms show good agreement for both analytes. TSH measurements are clinically comparable between methods, whereas for Tacrolimus, the observed differences require consistent use of the same analytical method for patient monitoring.

Keywords: correlation, immunoassay, tacrolimus, TSH

P18. PREVALENCE OF ANTI-THYROGLOBULIN ANTIBODIES IN PATIENTS WITH SYSTEMIC AUTOIMMUNE DISEASES COMPARED WITH CONTROLS

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Introduction: Autoantibodies directed against thyroid antigens are frequently detected in the general population, but their clinical significance outside overt thyroid disease remains unclear. The present study evaluated the prevalence of anti-thyroglobulin antibodies (anti-Tg) in patients with systemic autoimmune diseases and compared it with that of a control population, while also assessing their relationship with thyroid function.

Methods: A total of 357 individuals were included: 86 patients with systemic autoimmune diseases and 271 controls without known autoimmune or thyroid disorders. Serum anti-Tg antibodies were measured using a chemiluminescent immunoassay, with positivity defined as ≥ 4.11 IU/mL. Thyroid function was evaluated using TSH (Thyroid-Stimulating Hormone) and free T4 measurements. Prevalence rates were compared using contingency tables, and correlations with thyroid function parameters were assessed using Spearman analysis.

Results: Anti-Tg antibodies were detected in 16 of 86 patients with autoimmune diseases (18.6%) and in 48 of 271 controls (17.7%), showing no significant difference between groups. Anti-Tg prevalence was higher in women than in men in both cohorts (19.4% vs. 15.8% in the autoimmune group; 21.6% vs. 13.6% in controls). No significant correlations were observed between anti-Tg titers and TSH or free T4 levels. However, patients with systemic autoimmune diseases showed higher median TSH and lower free T4 levels compared with controls.

Conclusions: Anti-thyroglobulin antibody positivity was common in both cohorts and was not associated with systemic autoimmunity or thyroid function parameters. These findings suggest that isolated anti-Tg positivity may reflect background seropositivity rather than clinically relevant thyroid autoimmunity.

Keywords: anti-thyroglobulin antibodies, autoimmune diseases, fT4, TSH

P19. ADAPTING THE MOLECULAR BIOLOGY DEPARTMENT WITHIN THE MEDICAL ANALYSIS LABORATORY FOR SCREENING OF SPINAL MUSCULAR ATROPHY

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Introduction: Spinal muscular atrophy (SMA) is a severe, progressive genetic disorder characterized by muscle function loss and, in severe cases, life-threatening respiratory complications. Early diagnosis is essential for prompt treatment, with a major impact on prognosis and quality of life. The integration of SMA into the National Neonatal Screening Registry and the National Neonatal Screening and Prevention Program, starting February 27, 2026, represents a major step for public health in Romania. Neonatal screening has expanded from 3 to 22 conditions through the introduction of 19 new metabolic and genetic biomarkers, enabling the early detection of rare and severe diseases before irreversible damage occurs.

Methods: At the Molecular Biology Department within the Pediatrics Clinical Hospital Sibiu, the SMA assay was performed using a standardized protocol with the SALSA® MC002 SMA Newborn Screen Melt kit (MRC-Holland) to detect the exon 7 deletion of the SMN1 gene via real-time PCR on dried blood spot samples from newborns in Sibiu and Mediaș, between December 8, 2025, and March 30, 2026.

Results: During this period, 775 samples were processed (52% boys). All had the SMN1 gene, and 94.8% (n=735) had SMN2, with equal proportions between sexes in cases with absent SMN2. The absence of the SMN2 gene has no clinical consequences if SMN1 is present. For 4 patients (all boys), with both genes present but suspected mutation, MLPA testing was also performed, confirming the presence of the mutation.

Conclusions: After 4 months and the analysis of 775 samples, the methods demonstrated high sensitivity and specificity for rapid identification of SMN1 mutations. Equivocal results were few and resolved through retesting and molecular confirmation, enabling early detection and genetic confirmation of suspected cases, with minimal risk of error. The program aims to expand, optimize the methodology, and develop early intervention protocols, improving SMA management at a national level.

Keywords: early diagnosis, newborn screening, real-time PCR, SMN1 gene deletion, spinal muscular atrophy (SMA)

P20. HOW FAST IS POSITIVE? TIME-TO-POSITIVITY AS A MARKER OF PATHOGEN TYPE IN BLOOD CULTURES

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Introduction: Time-to-detection (TTD) in blood cultures is an essential diagnostic parameter reflecting microbial growth kinetics and bloodstream infection dynamics. It may provide early clues regarding the causative pathogen and support timely antimicrobial decisions.

Methods: A retrospective observational study was conducted between June 2025 and March 2026 in a tertiary care microbiology laboratory. Blood cultures were processed using the BACT/ALERT® VIRTUO automated continuous-monitoring system. TTD was defined as the interval (in days) between incubation and positivity signal. A total of 215 positive blood cultures were analyzed, and microorganisms were identified by MALDI-TOF mass spectrometry. Statistical analysis was performed using comparison of medians (Kruskal-Wallis test), with $p < 0.05$ considered statistically significant.

Results: The overall median TTD was 0.52 days (~12.5 hours), while the mean TTD was 0.89 days (~21.4 hours). The shortest TTD recorded was 0.13 days (~3.1 hours), observed in fast-growing Enterobacterales such as *Escherichia coli* and *Klebsiella pneumoniae*. These organisms also demonstrated the lowest median TTD values (0.37 and 0.32 days, respectively), followed by *Enterobacter cloacae* complex (0.22 days). Among Gram-positive cocci, *Staphylococcus aureus* and *Enterococcus faecalis* showed relatively rapid detection (median 0.41 days), while coagulase-negative staphylococci such as *Staphylococcus epidermidis* and *Staphylococcus hominis* exhibited longer detection times (0.77 and 0.68 days). Non-fermenting Gram-negative bacilli, including *Pseudomonas aeruginosa*, showed intermediate TTD values (0.50 days). Significantly prolonged TTD was observed for slow-growing organisms. *Corynebacterium* spp. reached median values up to 1.22 days, while rare microorganisms such as *Granulicatella adiacens* showed TTD around 1.12 days. The longest TTD recorded was 4.85 days, associated with *Cutibacterium acnes* (median 4.19 days). Other slow-growing organisms included *Burkholderia arboris* (3.04 days) and *Cronobacter sakazakii* group (3.39 days). A statistically significant difference in TTD distribution was observed between major microbial groups (Enterobacterales, Gram-positive cocci, non-fermenters, and slow-growing organisms) ($p < 0.001$).

Conclusions: TTD demonstrates a clear pathogen-dependent gradient, ranging from a few hours for Enterobacterales to several days for slow-growing organisms such as *Cutibacterium acnes*. Integration of TTD into routine interpretation may improve early pathogen prediction and optimize antimicrobial therapy.

Keywords: antimicrobial therapy, BACT/ALERT VIRTUO, blood cultures, Enterobacterales, time-to-detection

P21. FROM FUNDAMENTAL RESEARCH TO CLINICAL PRACTICE: A CRITICAL APPRAISAL OF THE LIMITATIONS OF IN VITRO EXPERIMENTAL MODELS FOR ASSESSING THE ANTIBIOFILM EFFICACY OF FUNCTIONALIZED MEDICAL DEVICES

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Healthcare-associated infections (HAIs) constitute a critical and escalating public health burden, carrying substantial attributable mortality and imposing considerable economic strain through the management of associated clinical complications. The epidemiological and economic ramifications of HAIs are neither static nor self-limiting; rather, they follow a progressive trajectory that is further compounded by the accelerating global emergence of antimicrobial resistance. Approximately 26% of HAIs have been attributed to polymicrobial biofilm formation on the surfaces of implantable medical devices, with multidrug-resistant strains—refractory to clinically approved antibiotic regimens—accounting for a disproportionately high share of these infections.

Bacterial communities encapsulated within the exopolysaccharide matrix of device-associated biofilms exhibit markedly elevated tolerance to both antibiotic therapy and host immunological clearance mechanisms, rendering conventional treatment strategies largely ineffective. In response, contemporary biomedical research has directed considerable effort toward the development of non-antibiotic antibiofilm strategies for the prophylaxis of device-associated nosocomial infections. Despite the substantial volume of preclinical experimental literature published over the preceding two decades, the number of antibiofilm-functionalized medical devices that have successfully transitioned into authorized therapeutic use remains exceedingly limited. The principal barriers to clinical translation of in vitro findings encompass static experimental configurations, the employment of non-biomimetic substrates, testing microenvironments that inadequately reflect the in vivo biological complexity, and pronounced heterogeneity in experimental methodologies—collectively undermining inter-study comparability and the reproducibility of reported outcomes.

The present work undertakes a critical appraisal of this translational gap between fundamental research and clinical application. By systematically identifying tractable methodological determinants and proposing evidence-based strategies for their rational optimization, this study aims to enhance the predictive validity of preclinical models and to establish a more robust scientific foundation for rigorous clinical evaluation of antibiofilm-functionalized medical devices.

Keywords: clinical translation, implantable medical devices, in vitro testing, polymicrobial biofilm

P22. ANTIMICROBIAL RESISTANCE TRENDS IN ENTEROCOCCUS SPECIES: A CLINICAL ISOLATE STUDY

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Introduction: Enterococcus species are commensal organisms of the gastrointestinal tract that can act as opportunistic pathogens, particularly in hospitalized patients. They are commonly involved in urinary tract infections, bloodstream infections, surgical site infections, and intra-abdominal infections. *E. faecalis* and *E. faecium* are the predominant clinical species, while *E. avium*, *E. casseliflavus*, and *E. gallinarum* are less frequent but clinically relevant. Increasing resistance to glycopeptides and oxazolidinones highlights the need for continuous surveillance.

Methods: A total of 125 *Enterococcus* isolates from hospitalized patients were analyzed between January and June 2025 at the Medical Analysis Laboratory of the "Prof. Dr. Octavian Fodor" Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca. Specimens included urine (43.2%), blood cultures (24.8%), wound exudates (17.6%), intra-abdominal fluids (8.8%), and catheter-related samples (5.6%). Identification was performed using MALDI-TOF MS (VITEK® MS), and antimicrobial susceptibility testing using VITEK® 2, interpreted according to EUCAST 2025 criteria.

Results: Species distribution showed a predominance of *E. faecalis* (48.8%) and *E. faecium* (41.6%), followed by *E. avium*, *E. casseliflavus*, and *E. gallinarum* (9.6%). *E. faecalis* was mainly associated with urinary and wound infections and remained highly susceptible to ampicillin (92%), vancomycin (88%), and linezolid (100%). In contrast, *E. faecium* was more frequently isolated from bloodstream and intra-abdominal infections and demonstrated high resistance to ampicillin (94%), moderate susceptibility to vancomycin (65%), and high susceptibility to tigecycline (96%) and linezolid (100%). VanC species showed intrinsic resistance to vancomycin but remained susceptible to ampicillin, linezolid, and daptomycin.

Conclusions: Significant interspecies differences were observed, with *E. faecium* displaying a multidrug-resistant phenotype and stronger association with severe infections. The presence of vanC species in invasive samples emphasizes the importance of accurate identification and careful interpretation of glycopeptide resistance. Continuous surveillance and EUCAST-based reporting remain essential for guiding therapy and infection control.

Keywords: antimicrobial resistance, clinical distribution, Enterococcus, EUCAST

P23. MOLECULAR INVESTIGATIONS AND ANTIBIOGRAM RESULTS IN SYSTEMIC INFECTIONS: PRELIMINARY RESULTS

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Introduction: Antimicrobial resistance in Gram-negative bacteria represents a critical threat to global health, with systemic infections caused by carbapenemase involved in sepsis organism associated with substantial mortality. Rapid identification of bacteria and resistance mechanisms is essential and useful for the subsequent initiation of therapy. The aim of this study is to evaluate the concordance between resistance genes identified in bacterial isolates using molecular methods and the susceptibility profile to antibiogram obtained using automated testing.

Methods: A retrospective analysis was conducted on 30 blood culture isolates in 2025 from patients with systemic infections at the Emergency University Hospital Bucharest. Bacterial identification and resistance genes were performed using the BCID2 panel and the BioFire Film Array system. Antibiotic susceptibility testing was performed using the NMIC panel and the BD Phoenix system.

Results: Among the included isolates, 30% of the bacteria were Gram-positive and 70% were Gram-negative. The most common bacterial species identified were: *Klebsiella pneumoniae* (20%), *Pseudomonas aeruginosa* (16.7%), and *Staphylococcus epidermidis* (16.7%). Resistance genes detected in Gram-negative bacteria by molecular diagnostic instruments accounted for 33.3%, with the most common being OXA-48 (16.7%). For Gram-positive bacteria resistance genes were Van A, Van B, mec/A. Among isolates with positive resistance genes, 80% showed a resistant phenotype by antibiogram, compared with 35% of isolates without genes. The odds ratio (OR) was 7.4 (Fisher's exact test, $p = 0.03$), indicating that the odds of resistance were more than sevenfold higher in samples with a positive rapid resistance gene result.

Conclusions: The sensitivity of the molecular diagnostic tool is limited by the existence of various resistance mechanisms, but also by the restricted range of detectable genes. The presence of resistance genes does not always correlate with phenotypic expression, some of which are in an inactive state. The BioFire Film Array allows in emergency situations regarding antimicrobial therapy, but for phenotypic assessment of susceptibility the antibiogram remains the gold standard.

Keywords: antimicrobial resistance, molecular diagnosis, systemic infections

P24. VARIATION IN THE ANTIBIOTIC RESISTANCE PROFILE OF *KLEBSIELLA PNEUMONIAE* STRAINS ISOLATED FROM URINE CULTURES, IN ADULT PATIENTS, BETWEEN 2019 AND 2023, IN A HOSPITAL UNIT

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Introduction: The discovery of antibiotics led to the saving of many lives, but their excessive or incorrect use has caused the emergence of a true antibiotic resistance crisis. This may determine an increased risk of mortality, a longer duration of hospitalization, complications and increased costs. For *Klebsiella pneumoniae*, the phenomenon of antibiotic resistance is worrying, with more and more cases of carbapenem resistance and multidrug resistance being reported.

Methods: The target group was represented by adult patients hospitalized in the medical and surgical departments of a hospital. The analyzed period was five years, starting with the year 2019, before the Covid-19 pandemic, and continued with the pandemic and post-pandemic period until 2023. The analyzed data was taken from the hospital information system and from the registers of the Medical Analysis Laboratory. The Vitek 2 Compact automatic analyzer was used for the identification of microorganisms and the testing of their susceptibility to antibiotics. The interpretation of the results was performed according to the CLSI guideline.

Results: During the five analyzed years, 2900 microorganisms were isolated and identified, 64% of them being represented by Gram-negative bacteria. The percentage of *Klebsiella pneumoniae* strains out of the total isolated Gram-negative bacteria was 14.3% (266 strains). The main biological products from which the *Klebsiella pneumoniae* strains were isolated were urine cultures, sputum and wound secretions. Regarding the *Klebsiella pneumoniae* strains isolated from urine cultures, 17% of them were extended-spectrum beta-lactamase producers (ESBL), 29.8% were multidrug-resistant (MDR), 20.5% were resistant to third- or fourth-generation cephalosporins, 23.4% were resistant to fluoroquinolones and 4% were resistant to carbapenems.

Conclusions: The results highlight increased percentages of multidrug-resistant *Klebsiella pneumoniae* strains, approximately 30%. Resistance to third- or fourth-generation cephalosporins is moderately increased, 20.5%. Resistance to carbapenems for the strains isolated from urine cultures is low, 4%. Dynamic monitoring of the antibiotic resistance profile is very important both for correct treatment and for resistance control.

Keywords: carbapenems, ESBL, *Klebsiella pneumoniae*, multidrug resistance

P25. EVOLUTION OF *KLEBSIELLA PNEUMONIAE* STRAINS PRODUCING CARBAPENEMASES FROM INVASIVE INFECTIONS BETWEEN 2021-2025 IN ELIAS UNIVERSITY HOSPITAL

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Introduction: The bacterium *Klebsiella pneumoniae* is a common cause of invasive infections. We aimed to analyse the evolution of *Klebsiella pneumoniae* strains producing carbapenemases isolated from blood cultures between 2021–2025 in Elias University Hospital.

Methods: From 4169 strains isolated between 2021–2025, 618 strains of *Klebsiella pneumoniae* were identified and analyzed, 281 (45.45%) were carbapenemase producers. Blood cultures were incubated in the BactAlert Virtuo system. Positive samples were cultured and/or processed in the Biofire system (BCID panel). Identifications were performed using automated methods or MALDI-TOF (Bruker), and antibiograms by broth microdilutions/automated systems and disk diffusion. The identification of the type of carbapenemase was performed molecularly or by immunochromatographic tests (NG-Test CARBA-5).

Results: The collected data show that from a total of 11,424 positive blood cultures in the last five years, 4,169 strains were isolated, of which 618 *Klebsiella pneumoniae*, 281 (45.5%) being carbapenemase producers. The distribution according to the type of carbapenemase is: 64 OXA48 (23%), 28 NDM (10%), 75 KPC (26%), 97 OXA48 + NDM (34.5%) and 17 KPC + NDM (6%). The annual analysis shows the evolutionary pattern of these strains, in which the rise of the NDM and OXA48+NDM types is particularly noticeable, from 0% in 2021 to 16% and 49% in 2025, respectively.

Conclusions: The collected data shows that, in an evolutionary pattern that preserves from year to year the proportion of *Klebsiella pneumoniae* strains producing carbapenemases out of the total number of isolates, spectacular changes are observed in the type of carbapenemase associated with them. The generated situation is critical, as these strains express high levels of antibiotic resistance, being XDR or PDR.

Keywords: blood culture, carbapenemases, evolution, *Klebsiella pneumoniae*

P26. ENTEROBACTERALES RESISTANCE AGAINST B-LACTAM ANTIBIOTICS IN THE INTENSIVE CARE UNIT OF THE SUCEAVA CLINICAL EMERGENCY COUNTY HOSPITAL DURING THE 2023-2025 PERIOD

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Introduction: Enterobacterales family represents a major cause of infection in the ICU elsewhere and emergence of multi resistant strains is a big challenge in critical patient management. Resistance survey, reports on its dynamics and the introduction of the antibiotic stewardship programme (ABS) are solutions for a better patient care.

Methods: Suceava Clinical Emergency County Hospital is a 1,300-bed, multispecialty and the biggest facility in Suceava county and North Eastern part of Romania. Our study series comprised 749 Enterobacterales strains, as follows: *Escherichia coli* (n=368) and *Klebsiella pneumoniae* (n=381), isolated from different clinical samples (blood cultures, endotracheal secretions, urine) between 1 January 2023–31 December 2025. Identification and sensitivity testing was done by MicroScan and Vitek systems, against the standard antibiotic panel.

Results: We analysed the resistance trends against the following antibiotics: for *E.coli* strains: Amoxicilin-Clavulanic acid (AMC), Cef-tazidime (CAZ), Meropenem (MEM) Piperacilin/Tazobactam (PTZ). The resistance ratio for AMC increased from 5% in 2023 to 8.22% in 2025; for CAZ from 13.48% in 2023 to 16.8% in 2025; for MEM was 1.08% in 2023 and 1.43% in 2025 and for PTZ decreased from 3.19 to 0% in 2025. For *K. pneumoniae* we analysed the following antibiotics : CAZ, MEM, PTZ and Ertapenem (ERT). The resistance ratio for CAZ increased from 59.6 % in 2023 to 63.25 % in 2025; for MEM was 61.4 % in 2023 and 47.73 in 2025; for PTZ decreased from 69.5 % to 59.37 in 2025 ; for ERT decreased from 74.19 % to 61.42 % in 2025.

Conclusions: Even if *E. coli* remains sensitive against the majority of the tested antibiotics , for *K. pneumoniae* the data is pessimistic. In this complex epidemiological situation, the solution is resistance monitoring and implementation of an efficient and effective ABS programme.

Keywords: antibiotic stewardship, beta lactam antibiotics, Enterobacterales, multiresistant strains

P27. LABORATORY DIAGNOSIS OF NON-TUBERCULOUS MYCOBACTERIA: SEARCH AND YOU WILL FIND

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Non-tuberculous mycobacteria (NTM) are a heterogenous group including species that can cause severe infections. Even if they are paid less attention compared to *Mycobacterium tuberculosis*, they represent a diagnostic and treatment challenge. Their presence is associated with immunocompromised status, cystic fibrosis or chronic lung disease. They can occur as lung, skin, bone or soft tissue infections or adenitis.

Different attempts for NTM classification were made according to criteria such as pigment production or generation time, but taxonomy is continuously changing. Infection diagnostic depends on infection site. Gold standard is represented by cultivation and species level identification. In the present, molecular tests allow even subspecies identification. These tests include hybridization, polymerase chain reaction (PCR) or sequencing. Main diagnostic difficulties include: high number and variety of species, genetic predisposition in different patient groups and a wide range of clinical manifestations.

In conclusion, because of the complexity, the diagnosis remains a true challenge for the medical team. In the last years, studies also point out the quality of NTM as nosocomial pathogens that can produce severe surgical infections. Transmission amongst cystic fibrosis patients of *Mycobacterium abscessus* was proved. According to these facts, NTM infections should be considered a diagnosis, research, as well as a public health problem.

Keywords: non tuberculous mycobacteria, polymerase chain reaction, subspecies

P28. CASE REPORT: COMPLICATIONS OF CMV INFECTION REACTIVATION IN PATIENTS WITH NON-HODGKIN LYMPHOMA

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Introduction: Patients with non-Hodgkin lymphoma (NHL) have an increased risk of cytomegalovirus (CMV) reactivation. They are immunocompromised, but chemotherapy is the main virus reactivation inducer. This reactivation may lead to different complications, including serious neurological ones such as encephalitis, radiculomyelitis, or peripheral neuropathies, and it can be difficult to distinguish it from other infectious or paraneoplastic etiologies.

Case presentation: We present the case of a patient with NHL, where neurological complications secondary to CMV reactivation following chemotherapy were suspected. A 52-year-old female patient, diagnosed with diffuse large B-cell NHL, underwent six R-CHOP chemotherapy sessions, which were well tolerated. Shortly after the treatment sessions, she developed neurological symptoms (diplopia, distal tetramelic paresthesias and dysesthesias, postural instability, and decreased muscle strength in the lower limbs). Imaging and paraclinical investigations excluded a bacterial/fungal infection and metastasis; electrophysiological studies did not support an autoimmune etiology. Cerebrospinal fluid (CSF) examination was paucicellular and revealed the presence of 89% mature B lymphocytes. The discrepancy between B-cell lymphocytosis in the CSF and imaging findings, as well as post-chemotherapy immunosuppression, raised suspicion of an infectious process involving the central nervous system (CNS). Subsequently, the patient developed recurrent febrile episodes, biological inflammatory syndrome, and worsening neurological symptoms. Viral screening revealed a CMV viremia of 154,000 IU/mL, for which treatment with valganciclovir was initiated. Subsequent intrathecal chemotherapy courses did not result in clinical improvement and were discontinued due to pancytopenia. A repeat CSF examination showed increased IgM levels and a reduced CMV load (58 IU/mL). Despite antiviral therapy, the patient's condition did not improve, and neurological symptoms persisted.

Conclusions: This case highlights the importance of PCR viral screening (viral panel for reactivation susceptible viruses) in hematological patients, prior to initiating chemotherapy. Early diagnosis based on laboratory findings and prompt initiation of antiviral treatment can significantly improve clinical outcomes and increase survival rate and chemotherapy efficacy. To document chemotherapy induced viral reactivation and complications, the laboratory recommends the baseline viremia measurement and periodic remeasurement when risk factors or symptoms develop.

Keywords: cytomegalovirus reactivation, non-Hodgkin lymphoma, PCR viral screening

R17. HOW ARTIFICIAL CAN BIOBANK INTELLIGENCE BE? A CONSERVATIVE APPROACH

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Introduction: Artificial Intelligence is discreetly or very obviously invading all areas of biomedical research. Biobanks are no exception to this phenomenon. The question is increasingly being asked whether artificial intelligence can support innovation without compromising ethics and compliance.

Methods: We conducted a retrospective study, analyzing the PubMed, Web of Science and Scopus databases, using search keywords. We also used additional bibliographic references, identified after consulting the articles initially found.

Results: The study focused on the “empty side of the glass”, namely the arguments that objectively call for caution and restraint in the enthusiastic approach to the scientific progress proposed by artificial intelligence in the field of biobanks. Following the Ten Commandments of Ethical Medical AI postulated by Heimo Müller and his collaborators in 2021, we analyzed those hot spots where artificial intelligence must be used with a sense of responsibility within biobanks: clear decision-making, transparent, explainable, repeatable and comprehensible decisions, identifiable AI-generated communication, insurance of ethical and legal responsibilities and adherence to standards, explanations based on scientific evidence, non-manipulated accuracy, avoidance of bias and discrimination and, above all, keeping AI oversight under human control. Leveraging the biobanking management system for the ethical integration of artificial intelligence is an essential component to address issues related to potential misuse of participant data and lack of transparency in consent management, bias in artificial intelligence algorithms, loss of control over data quality, transparency and accountability in research.

Conclusions: Artificial intelligence is already an integral part of the biobanking process, but a calculated approach and unhurried enthusiasm can ensure greater and more certain success.

Keywords: artificial intelligence, biobanking, caution, ethics

R18. TARGETED INTERVENTIONS ON THE HUMAN MICROBIOTA: POTENTIAL STRATEGIES TO COMBAT ANTIMICROBIAL RESISTANCE

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Antimicrobial resistance is a major threat to global public health. Consistent implementation and continuous improvement of actions within the One Health approach are essential to limit the spread of antimicrobial resistance: antimicrobial stewardship, adequate diagnosis, surveillance of drug-resistant organisms, vaccination, and improved infection prevention and control. A growing body of evidence suggests that interventions targeting the human microbiota may help in reducing the impact of drug-resistant organisms.

The human microbiota is a key modulator of both humoral and cellular immune responses. The diversity and composition of gut microbiota are correlated with various health conditions, including susceptibility to infections, and with immune response to vaccines. Microbiota characteristics also drive the risk of mucosal colonisation by multidrug-resistant organisms. The intestinal microbiota is the main reservoir for antibiotic resistance genes, which can be transferred horizontally within or between species through mobile genetic elements such as plasmids, integrative conjugative elements, or bacteriophages. Several factors shape the diversity and composition of gut microbiota, including modifiable factors such as type of delivery (for newborns), feeding method (for infants), duration and type of antibiotic exposure, and diet.

Interventions targeting the gut microbiota may improve humoral and cellular immune responses, thereby reducing susceptibility to infections, increasing vaccine efficacy, and consequently decreasing the need for antibiotic treatments, thus limiting the selection pressure for antimicrobial resistance. Overall, these preventive or therapeutic interventions could represent potential complementary strategies to combat antimicrobial resistance.

Keywords: antimicrobial resistance, antimicrobial stewardship, gut microbiota, One Health

C19. FROM ANTIBIOGRAM TO ANTIBIOTIC SELECTION: A PRACTICAL APPROACH TO MULTIDRUG-RESISTANT GRAM-NEGATIVE BACILLI (MDR-GNB) INFECTIONS

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The impact of antimicrobial resistance (AMR) transcends borders, affecting countries across all regions and income levels. The global proliferation of multidrug-resistant Gram-negative bacilli (MDR-GNB) poses a significant challenge to public health systems. The presentation provides current clinical guidance for managing MDR-GNB infections, with a specific focus on updated antibiotic selection.

This presentation is based primarily on the most recent MDR-GNB treatment guidelines from the Infectious Diseases Society of America (IDSA) and the Brazilian Society of Infectious Diseases (SBI).

The discussion focuses primarily on infection site-specific treatment for key pathogens – including Enterobacterales, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Stenotrophomonas maltophilia*, and *Burkholderia cepacia* – all of which exhibit diverse antibiotic resistance mechanisms.

In the dynamic landscape of AMR, this material provides the tools necessary to improve the management of these challenging healthcare-associated infections within an antimicrobial stewardship strategy.

Keywords: antibiotic resistance, antibiotic stewardship, multidrug-resistant Gram-negative bacilli, Infectious Diseases Society of America

C20. SURVEILLANCE OF ANTIBIOTIC RESISTANCE OF STRAINS ISOLATED FROM ONCOLOGY PATIENTS IN IRO IASI: TRANSFORMATION OF LABORATORY DATA INTO CLINICAL ACTION

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Introduction: Infections are a frequent cause of mortality in hemato-oncological patients. Knowledge of the local resistance profile can guide empirical therapy, the clinical cumulative antibiogram being an important tool in the correct and efficient use of antibiotics, with an impact also in preventing the development of antibiotic resistance.

Methods: Bacterial strains isolated in 2025, within the IRO hospital, were analyzed. Bacterial identification was performed by MALDI-TOF, antibiograms were performed in the MICRONAUT automated system (minimum inhibitory concentration). Isolates were tested for carbapenemases production with an immunochromatographic test. Antibiogram analysis was performed using the WHONET program.

Results: During the analyzed period, out of a total of 18,984 cultures for bacteriological examination, 2,625 samples had positive results (14%). Identical isolates repeated in the same patient were not analyzed. 20% were isolated from the ICU section, 16% from Hematology, 15% from Medical Oncology. The most frequent positive cultures were urine cultures (37%), followed by purulent secretions (29%), blood cultures (19%) and sputum/BAL (7%). The isolates were represented by *Escherichia coli* (31%), *Klebsiella pneumoniae* (16%), *Staphylococcus aureus* (10%), and *Pseudomonas aeruginosa* (8%). *E. coli* strains do not pose a problem for therapy with 80% sensitivity to cephalosporins, 75% to quinolones and 100% to carbapenems, compared to *K. pneumoniae* with 40%, 45%, and 64%, respectively, 36.7% being multi-drug resistant strains, this percentage being higher in the critical care ICU (49.4%) and Hematology (54.2%) departments. As a mechanism of resistance, 56% of the *K. pneumoniae* multi-drug resistant isolates were producers of OXA48+NDM type carbapenemases.

Conclusions: Knowing the resistance profile by department provides the clinician with useful information for choosing the most appropriate antibiotic in the first-line therapy of infections in the critically ill hemato-oncological patient.

Keywords: antimicrobial resistance, carbapenemase production, cumulative antibiogram, oncology

R21. MICROBIOLOGICAL TRENDS AND PREDICTIVE RISK FACTORS IN BURN PATIENTS

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Introduction: Infections are among the most common complications in extensive burn patients and frequently involve multidrug (MDRO) or even extensively drug resistant organisms (XDRO), which contribute to mortality increase and prolonged hospitalisation. The aim of this study was to describe the local patterns of antimicrobial resistance in a burn unit (BU) and to identify risk factors associated with the acquisition of XDRO.

Methods: We conducted a one-year, observational, retrospective cohort study including all burn patients with at least one positive culture, admitted to BU during 2024. Routine microbiological diagnostic tests were used in order to identify pathogens and perform antibiograms. A multivariable logistic regression model was used to identify XDRO risk factors.

Results: Among the 180 total admissions, 128 (71.1%) had at least one positive microbiological culture, resulting in 643 bacterial isolates out of 559 samples. The most frequently identified were *A. baumannii*, *P. aeruginosa*, *S. aureus*, and *K. pneumoniae*. We isolated MDRO in 59.37%, and XDRO in 26.56% of patients during hospitalisation. Three independent predictors for the XDRO acquisition were identified: a higher Abbreviated Burn Severity Index score (aOR 6.12; $p = 0.001$), hospital length of stay (aOR 1.02; $p = 0.030$), and the number of bacterial species identified per sample, representing polymicrobial growth (aOR 5.91; $p = 0.001$). The results obtained were interpreted in light of previous studies conducted by our team at the same BU.

Conclusions: Burn patients presenting the risk factors mentioned are at increased risk for the XDR infections acquisition. In clinical practice, empirical antibiotic treatment should be tailored to local resistance patterns. At the same time, antimicrobial stewardship and infection control measures remain essential for the preservation of the limited therapeutic options available.

Keywords: burn unit, MDRO, risk factors, XDRO

R22. INTEGRATED LOW-COST DIAGNOSTIC MODEL FOR URINARY TRACT INFECTIONS: COMBINING MICROBIOLOGICAL DATA, HOST RESPONSE, AND RISK STRATIFICATION IN RESOURCE-LIMITED LABORATORIES

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Introduction: Urinary tract infections (UTIs) remain among the most common bacterial infections, while antimicrobial resistance (AMR) complicates diagnosis and treatment. Conventional microbiological approaches rely mainly on urine culture and susceptibility testing but fail to capture host response and recurrence risk. We aimed to propose an integrated, low-cost diagnostic model combining microbiological findings, host-derived indicators, and clinical context to improve diagnostic accuracy and clinical decision-making in resource-limited laboratories.

Methods: A conceptual and practical algorithm was developed based on standard microbiological techniques (urine culture, identification, antimicrobial susceptibility testing), supplemented by host-response indicators (urinalysis, inflammatory markers) and clinical risk factors. A composite scoring system (UTI-Integrated Score) was proposed to stratify infection severity and recurrence risk.

Results: The model integrates three diagnostic axes: (1) infection activity, (2) antimicrobial resistance, and (3) persistence risk (including biofilm formation). The proposed scoring system enables classification into colonization, uncomplicated infection, and complicated/persistent infection. The approach enhances interpretative value without requiring advanced technologies.

Conclusions: An integrated diagnostic approach can significantly improve UTI management in resource-limited settings by transforming routine laboratory data into integrated clinically actionable insights. This model bridges the gap between advanced microbiological concepts and real-world laboratory practice.

Keywords: antimicrobial resistance, biofilm, integrated diagnostics, resource-limited laboratories, risk stratification, UTI

C23. HUMAN CRYPTOSPORIDIOSIS IN WESTERN ROMANIA

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Cryptosporidium is a zoonotic parasite with global distribution, affecting both the human population and numerous animal species, regardless of climatic, socio-economic, or demographic conditions. This protozoan causes cryptosporidiosis, a disease that may occur in subclinical or sporadic forms, but also as epidemic outbreaks with major public health impact. Clinically, cryptosporidiosis manifests as a severe diarrheal syndrome, characterized by watery diarrhea, nausea, vomiting and abdominal pain. Typically, the infection is self-limiting, with diarrhea lasting sometimes up to two weeks in adults and up to three weeks in children. In immunocompromised individuals this parasitic infection may become chronic and debilitating. In Romania, screening for the detection of Cryptosporidium is not routinely conducted and standard parasitological examinations often fail to detect this protozoan in clinical laboratories. Therefore, there is limited information regarding this zoonotic infection in humans from Romania.

Recent studies revealed a cryptosporidiosis prevalence of 6% in hospitalized patients and epidemiological surveys assessed for the first time the risk factors associated with human infection in Romania, with a higher rate of infection in urban areas. Moreover, using molecular techniques we detected Cryptosporidium canis and Cryptosporidium ryanae for the first time in Romanian patients, with significant zoonotic implications. Experimental infection in mice with Cryptosporidium isolated from humans demonstrated that mice could represent a potential source of infection for other animal species, including humans, suggesting a possible role in the life cycle of the parasite.

Results of the studies conducted in Western Romania, including epidemiological, molecular and experimental investigations of cryptosporidiosis are presented.

Keywords: cryptosporidiosis, prevalence, risk factors, zoonotic disease

C25. EXPERIENCE IN USING THE GENIUS DIGITAL SCANNING SYSTEM FOR LIQUID-BASED CERVICOVAGINAL CYTOLOGY (THINPREP)

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Introduction: Liquid-based cervicovaginal cytology (ThinPrep) represents the current standard in screening for cervical lesions. The integration of digital technologies and automated scanning systems, such as the Genius Digital Diagnostics System, authorized by the FDA in 2024, brings new perspectives in optimizing workflow and increasing diagnostic accuracy in pathology.

Methods: In the pathology department of the central Regina Maria laboratory in Bucharest, the Genius system was implemented for scanning ThinPrep slides. The implementation was carried out progressively in routine practice, initially by evaluating a limited number of cervicovaginal cytology cases both through conventional microscopy and assisted digital assessment. Evaluation time, image quality, and ease of identifying cellular lesions were compared.

Results: The use of the Genius system reduced evaluation time by facilitating rapid identification of relevant fields. The quality of digital images was comparable to that obtained through conventional microscopy and was sufficient for accurate assessment of morphological details, including cellular uniformity and clarity. Additionally, the system contributed to improved detection of cytological abnormalities, particularly in cases with subtle lesions. The implementation of digital scanning in cervicovaginal cytology brings significant benefits to routine practice, including standardization of evaluation to reduce interobserver variability, as well as the possibility of case archiving and review. However, there are challenges related to familiarization with the system, interpretation of automatically preselected fields, adaptation to digital evaluation, and full integration into the workflow.

Conclusions: The Genius system is a valuable tool in modern cytological diagnosis, contributing to increased efficiency and accuracy in the evaluation of liquid-based cervicovaginal cytology samples (ThinPrep). Our experience supports its utility in routine pathology practice.

Keywords: cervical screening, cervicovaginal cytology, digital pathology, image analysis, ThinPrep

C26. CLINICAL RELEVANCE OF SILENT AND NULL ALLELES IN SOLID ORGAN AND BONE MARROW ALLOTRANSPLANTATION

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Introduction: The HLA (Human Leukocyte Antigen) system exhibits extreme polymorphism and plays a central role in the immune response. In addition to alleles with normal expression, there are specific genetic variants: null alleles (marked with the suffix "N"), which do not produce detectable proteins on the cell surface, and silent alleles, which differ by synonymous nucleotide substitutions. The presence of these "invisible" variants can generate discrepancies between the genetic genotype and the protein phenotype, influencing post-transplant clinical outcomes. This paper evaluates the impact of these alleles on the success of solid organ and hematopoietic stem cell transplantation. It aims to optimize donor-recipient selection to prevent humoral rejection and graft-versus-host disease (GvHD) by identifying situations where a mismatch at the DNA level does not imply a real antigenic incompatibility.

Methods: The analysis is based on high-resolution molecular typing techniques, such as NGS (Next-Generation Sequencing) and SBT (Sequence-Based Typing). These methodologies allow for the scanning of non-coding regions and the detection of frameshift mutations or premature stop codons that can functionally inactivate an allele.

Results: Research indicates that monitoring null and silent alleles provides benefits in transplant management. In solid organ cases, a null allele in the donor may allow for a safe transplant even if the recipient has antibodies (false DSA). In stem cell transplantation, a null allele in the recipient may reduce the risk of GvHD, as the antigen is not physically expressed.

Conclusions: The accurate identification of null and silent alleles represents an important step in refining immunological selection. This approach helps avoid the unjustified exclusion of donors and prevents unforeseen immune reactions, contributing to the long-term survival of the graft.

Keywords: graft-versus-host disease, human leukocyte antigen, next-generation sequencing, null alleles

C27. THE IMPORTANCE OF ALLELIC MATCHING IN ALLOGENEIC BONE MARROW TRANSPLANTATION: IMPACT ON LONG-TERM POST-TRANSPLANT SURVIVAL

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Introduction: Allogeneic hematopoietic stem cell transplantation remains the only curative therapeutic option for numerous malignant and non-malignant hematological conditions. Allelic HLA compatibility between donor and recipient profoundly influences the incidence of graft-versus-host disease (GvHD), the risk of graft failure, and overall long-term survival, representing the central prognostic factor of the procedure. This study evaluates the impact of the degree of HLA allelic compatibility at 10 loci on overall and event-free survival in patients undergoing bone marrow allotransplantation, analyzing the specific contribution of each locus to GvHD risk and mortality.

Methods: The study cohort included bone marrow transplant patients treated between 2022–2024. High-resolution HLA typing was performed for the HLA-A, -B, -C, -DRB1, -DQB1, and -DPB1 loci. Patients were stratified by the number of allelic mismatches, and survival was calculated using the Kaplan-Meier method with the log-rank test.

Results: Overall survival at 1 and 2 years was significantly higher in 10/10 matched pairs compared to those with at least one mismatch ($p < 0.05$). Mismatches at HLA-B and HLA-DPB1 were significantly associated with an increased incidence of grade III-IV acute GvHD. The risk of severe GvHD increased proportionally with the total number of identified allelic mismatches.

Conclusions: Full allelic compatibility at 10 HLA loci remains the gold standard in bone marrow allotransplantation. Mismatches at HLA-B and HLA-DPB1 significantly increase the risk of acute GvHD, although their independent impact on overall survival varies depending on the protocol and the prophylaxis strategy used. High-resolution HLA typing is mandatory in donor selection for bone marrow allotransplantation.

Keywords: allogeneic hematopoietic stem cell transplantation, graft-versus-host disease, high-resolution HLA typing, human leukocyte antigen

C28. THE ROLE OF mRNA IN BLADDER CANCER

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Introduction: Bladder cancer is characterized by a high recurrence rate, requiring repeated, costly, and invasive endoscopic monitoring. Identifying non-invasive molecular biomarkers in urine, such as specific tumor messenger RNAs (mRNAs), represents a priority for improving early diagnosis and effective surveillance of urological oncology patients. This paper evaluates the performance of mRNA expression analysis via the GeneXpert platform in urine samples, compared to conventional urinary cytology, for the diagnosis and monitoring of bladder cancer.

Methods: The study included patients with suspected or confirmed bladder cancer evaluated between 2024–2025. Urine samples were analyzed using GeneXpert to assess the expression of 5 mRNAs. The results were validated through histopathological examination and cystoscopy, in comparison with conventional urinary cytology.

Results: The sensitivity of GeneXpert diagnostic was significantly higher than that of urinary cytology ($p < 0.05$). Molecular detection of tumor recurrences occurred several weeks prior to cystoscopic confirmation in approximately one-third of the cases. A direct correlation was observed between the expression levels of molecular markers and the degree of tumor aggressiveness, with GeneXpert maintaining a high negative predictive value even in low-grade lesions.

Conclusions: Assessing mRNA expression via GeneXpert offers a superior alternative to conventional cytology. Combining these markers increases diagnostic accuracy and can significantly reduce the frequency of cystoscopies, improving the quality of life for patients with urothelial neoplasms. The implementation of this non-invasive monitoring protocol allows for more precise risk stratification, optimizing healthcare resource allocation by increasing the intervals between endoscopic check-ups for patients with a stable molecular profile.

Keywords: bladder cancer, GeneXpert, mRNA expression, urinary cytology

C29. MicroRNA-150 AS A PROMISING BIOMARKER IN THE MINIMALLY INVASIVE DIAGNOSIS OF MELANOMA

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Introduction: Melanoma is one of the most aggressive forms of skin cancer, with increasing incidence worldwide. Early diagnosis significantly improves survival rates. In recent years, microRNAs have emerged as promising molecular biomarkers for cancer detection and monitoring. Among them, miR-150 has been suggested to play a role in tumor development and progression. The aim of this study was to evaluate the diagnostic sensitivity and specificity of miR-150 in blood and tissue samples from melanoma patients.

Methods: This study included a cohort of 50 patients diagnosed with melanoma stages I–IV. Biological samples consisted of peripheral blood and tumor tissue collected at the time of diagnosis. Total RNA was extracted from both blood and tissue samples. The expression of miR-150 was analyzed using reverse transcription polymerase chain reaction (RT-PCR). Expression levels detected in blood were compared with those identified in tumor tissue samples. Diagnostic performance was evaluated by calculating sensitivity and specificity, and correlations between circulating and tissue miR-150 levels were assessed.

Results: miR-150 expression was detected in both blood and tumor tissue samples in a significant proportion of patients. The analysis showed an overall sensitivity of approximately 84% and a specificity of 89% for the detection of melanoma using circulating miR-150. Increased expression levels were observed more frequently in patients with advanced melanoma stages (III–IV). A positive correlation was identified between miR-150 expression levels in blood samples and those in corresponding tumor tissue.

Conclusions: miR-150 demonstrates promising diagnostic potential as a circulating biomarker in melanoma patients. The significant correlation between blood and tissue expression supports its potential use as a minimally invasive tool for melanoma detection and disease monitoring. Further studies with larger cohorts are needed to validate these findings.

Keywords: biomarker, miR-150, melanoma, skin cancer

C30. A NEW BIOMARKER IN THE MONITORING OF RENAL TRANSPLANT PATIENTS

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Introduction: Renal transplantation is the therapy of choice for end-stage renal disease; however, monitoring graft integrity remains a continuous challenge. Conventional monitoring methods—serum creatinine and renal biopsy—have significant limitations in the early detection of graft injury, with creatinine demonstrating nearly random discriminatory power for active rejection. This study evaluates the clinical utility of dd-cfDNA as a non-invasive tool for monitoring renal transplant patients, analyzing its ability to detect rejection episodes early compared to serum creatinine and renal biopsy.

Methods: Renal transplant patients were followed prospectively over a 24-month period. dd-cfDNA levels were quantified via next-generation sequencing from peripheral blood samples. The results were correlated with histopathological data from protocol and indication biopsies, as well as the evolution of renal function.

Results: An increase in dd-cfDNA preceded the rise in serum creatinine in approximately 80% of histologically confirmed acute rejection episodes ($p < 0.05$). The sensitivity for antibody-mediated rejection was significantly higher compared to serum creatinine ($p < 0.05$). Persistently elevated baseline dd-cfDNA values correlated significantly with chronic graft dysfunction at 12 months, supporting its prognostic value.

Conclusions: dd-cfDNA represents a non-invasive biomarker superior to serum creatinine for the early monitoring of the renal graft, featuring high negative predictive values that allow for the exclusion of active rejection with high probability. Its integration into post-transplant surveillance protocols, alongside conventional markers, may reduce the need for renal biopsies and optimize individualized therapeutic management for transplant patients.

Keywords: dd-cfDNA, end-stage renal disease, next-generation sequencing, renal graft rejection

C31. THE MONITORING OF ANTI-HLA IMMUNIZATION POST RENAL TRANSPLANT: CASE STUDY

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Introduction: Monitoring anti-HLA antibodies is part of the HLA laboratory activity, the detection of donor-specific antibodies being associated with an increased risk of humoral rejection. By identifying HLA antigens with an essential role in allorecognition recipient and donor, the risk of rejection is reduced and graft survival is increased. The aim of the study is to emphasize the importance of complete testing of the HLA loci, including the associative DR51/DR52/DR53, which are expressed at lower levels compared to DRB1, and the detection of donor-specific antibodies directed against them can be associated with rejection.

Case presentation: This is the case of a 24-year-old patient at the time of transplantation with a related donor (mother), performed in 2023 (compatibility 7/12), who during of 2025 presented increases in serum creatinine values of 2.1 mg/dl, proteinuria of 1 g/24 h, raising the suspicion of possible rejection. Post-transplant serum monitoring was requested at INTS. The patient did not present antibodies in pretransplant, and the viral marker profile was absent. Detection of de novo immunization in post-transplant was performed by the LUMINEX technique, which facilitated the identification of class I (ABC) and class II antibodies with DRB1/DQB1/DQA1/DPB1/DPA1/DRB3/DRB4/DRB5 specificities. The specificities of anti-HLA antibodies post transplant were evaluated on the mean fluorescence value MFI >1000 for the analyzed loci. Anti-HLA class I antibodies were absent, and class II antibodies were present with the specificities anti DR52 (DRB3*02:02/DRB3*03:01) possible donor specific with MFI=7729, resp. 6037, anti DR53 (DRB4*01:01) at MFI=2598, DQA1*05:01 at MFI=2258 and DP1 at MFI=4496. The patient and the donor were tested for DR52(DRB3*) and DQA1 by SSP technique. Anti-DR52(DRB3*02:02) antibodies post transplant were donor specific. Laboratory data were correlated with the graft biopsy and according to the BANFF classification chronic humoral rejection was identified, along with cellular rejection.

Conclusions: DR52/DR53/DR51 testing is validated in accordance with their association with the DRB1 locus. Detection of anti-DR52/53/51 immunization requires complete testing of the associative loci. Dynamic monitoring of donor-specific antibody MFI is essential for monitoring graft.

Keywords: anti-HLA antibodies, donor-specific antibodies, humoral rejection, LUMINEX

R32. MODULATION OF THE INFLAMMATORY RESPONSE IN CHILDREN WITH LEUKEMIA IN THE CONTEXT OF GINGIVO-PERIODONTAL ALTERATIONS

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Introduction: The literature reports an increased incidence of gingivo-periodontal alterations as common oral manifestations in children diagnosed with leukemia. Reflecting periodontal homeostasis, gingival crevicular fluid (GCF) becomes an inflammatory exudate under pathological conditions, and its components include key mediators of periodontal inflammation, such as cytokines, matrix metalloproteinases, and oxidative stress markers. The aim of this study was to correlate the oral health status of children with leukemia, with certain biochemical indicators: IL-1 (interleukin 1), IL-6, IL-17, and TGF-β1 (transforming growth factor beta) in order to explore the potential for early assessment of the relationship between these biomarkers and the severity of gingivo-periodontal alterations.

Methods: The study included 97 children divided into two groups (leukemia group: n=47; control group: n=50 children without leukemia). Oral health status was evaluated using the OHI-S (Oral Hygiene Index-Simplified) and GI (Gingival Index). Samples of gingival crevicular fluid and plasma were collected and analyzed for biomarker levels using ELISA (enzyme-linked immunosorbent assay) techniques.

Results: IL-6, IL-17α, and TGF-β1 recorded higher values in children with leukemia, both in GCF and plasma, compared to the control group.

Conclusions: Elevated levels of IL-1β in GCF, as well as IL-6, IL-17α, and TGF-β1, both systemically and locally in the gingival crevicular fluid of children with leukemia, are associated with oral hygiene status and the degree of gingival inflammation. All inflammatory biomarkers displayed a tendency to increase proportionally with worsening oral hygiene and the severity of gingival inflammation. Among these, IL-1β levels in GCF and plasma, IL-6 in plasma, and IL-17α in GCF exhibited a stronger association with gingival inflammation.

Keywords: children, gingivo-periodontal alterations, inflammatory biomarkers, leukemia

C34. EVOLUTION OF PROINFLAMMATORY MARKERS IN PATIENTS WITH ATRIAL FIBRILLATION AND TYPE II DIABETES MELLITUS

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Introduction: Atrial fibrillation (AF) is the most common sustained arrhythmia in medical practice. People with type II diabetes (T2DM) have a higher incidence of AF compared to those without T2DM. The neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), monocyte-lymphocyte ratio (MLR), systemic immune-inflammation index (SII) and systemic inflammatory response index (SIRI) are potential markers in assessing the level of inflammation in non-valvular AF. The aim of the study was to investigate proinflammatory markers in patients with AF and those with AF associated with T2DM.

Methods: The study included 90 patients of the same age and gender, who were randomized into 3 groups: study group I (SG I: 30 patients with AF), study group II (SG II: 30 patients with AF and type II DM), and control group (CG: 30 healthy individuals). The results of NLR, PLR, MLR, SII and SIRI and the receiver operating characteristic (ROC) curves were analyzed.

Results: The results of NLR, PLR, MLR, SII and SIRI were significantly higher in patients in SG II than in SG I and CG (all $p < 0.01$). SIRI offered the best balance between sensitivity and specificity (AUC=0.55; sensitivity 80%; specificity 30%). NLR and MLR reached the level of the curve (AUC=0.52; sensitivity 66%; specificity 46.0%) and (AUC=0.50; sensitivity 43%; specificity 63.0%). SII and PLR demonstrated very poor differentiation capacity.

Conclusions: Analyzing the results obtained, we can confirm that the proinflammatory markers in the study can be used to assess the severity and prognosis of AF in combination with T2DM.

Keywords: atrial fibrillation, type II diabetes mellitus, systemic inflammatory response index

C35. UNTARGETED METABOLOMICS IN PREDIABETES: PREDICTIVE BIOMARKERS, METABOLIC MEDIATORS, AND IMPLICATIONS FOR PRECISION MEDICINE

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Prediabetes is not a homogeneous entity — glycemic subtypes of isolated impaired glucose tolerance (IGT) and IGT combined with impaired fasting glucose (IFG) exhibit distinct pathophysiological mechanisms and variable response to lifestyle interventions. Untargeted metabolomics offers the opportunity to characterize this heterogeneity at the molecular level, with potential for personalized therapeutic stratification.

The methodology of untargeted metabolomics — from data preprocessing (batch correction, normalization, scaling) to predictive models and longitudinal analyses — is discussed in the context of identifying therapeutic response biomarkers in prediabetes, with emphasis on the concept of dissociation between baseline predictors and longitudinal mediators of therapeutic response.

Current literature identifies acylcarnitines as markers of mitochondrial beta-oxidation capacity, with a role in predicting metabolic response to intervention, particularly in subtypes with complex energy metabolism dysfunction. Odd-chain lysophosphatidylcholines reflect hepatic phospholipid metabolism and membrane remodeling associated with weight loss. Secondary bile acids, as markers of the gut microbiome-hepatic metabolism axis, show subtype-specific associations with intervention response. The predictor-mediator dissociation concept — whereby a biomarker predicts baseline response without changing in parallel with the outcome — has direct implications for the clinical interpretation of metabolomic profiles.

Integration of untargeted metabolomics into laboratory medicine enables progression beyond classical glycemic classification of prediabetes through characterization of the underlying biological mechanisms. Identification of subtype-specific biomarkers — mitochondrial in IGT+IFG, entero-hepatic in isolated IGT — supports a stratified therapeutic decision model, in which the baseline metabolomic profile may guide both the intensity of lifestyle intervention and the optimal timing of pharmacological therapy initiation.

Keywords: acylcarnitines, lysophosphatidylcholines, precision medicine, prediabetes, untargeted metabolomics

R36. PROTEIN GLYCATION: FROM PHYSIOLOGICAL TO PATHOLOGICAL

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Protein glycation is a non-enzymatic post-translational modification resulting from reactions between reducing sugars (or reactive carbonyl species such as methylglyoxal) and amino groups of proteins, typically lysine and arginine residues.

In physiological conditions, glycation occurs at low levels and may function as a subtle regulatory signal within the broader network of post-translational modifications, contributing to cellular signaling and proteome diversity. Cells maintain glycativ homeostasis through detoxification systems, notably the glyoxalase pathway, and through protein turnover, which limits accumulation of modified proteins. Early glycation products (Schiff bases, Amadori products) are partially reversible and usually do not severely impair protein function. Under pathological conditions, especially hyperglycemia, oxidative stress, or aging, glycation is markedly accelerated, leading to the formation and accumulation of advanced glycation end products (AGEs). These are chemically heterogeneous, often irreversible structures that alter protein conformation, reduce enzymatic activity, and promote cross-linking, particularly in long-lived proteins such as collagen or lens crystallins.

AGEs exert pathogenic effects through multiple mechanisms. First, structural damage—protein crosslinking stiffens extracellular matrix and impairs tissue elasticity. Second, cell signaling dysregulation—binding to the receptor for advanced glycation end-products (RAGE) activates pro-inflammatory and pro-oxidant pathways, sustaining chronic inflammation. Third, oxidative stress amplification—AGEs formation and reactive oxygen species (ROS) generation reinforce each other in a vicious cycle.

In conclusion, clinically, excessive glycation is implicated in diabetes complications, cardiovascular disease, neurodegeneration, renal failure, and aging-related disorders. Protein glycation transitions from a controlled, low-level physiological modification to a pathological driver of molecular damage and chronic disease when carbonyl stress overwhelms cellular defense systems.

Keywords: advanced glycation end products, protein glycation, reactive oxygen species

C37. THE PROGNOSTIC ROLE OF COMPLETE BLOOD COUNT-DERIVED PARAMETERS IN PATIENTS WITH OBLITERATIVE ARTERIOPATHY WITH AND WITHOUT INFECTIOUS GANGRENE

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Introduction: Complete blood count-derived parameters have a potential prognostic role. Inflammation and infectious gangrene influence the evolution of arteriopathy. The aim of the study was to evaluate the prognostic role of blood count-derived markers in obliterative arteriopathy with and without infectious gangrene, the correlation between them, and the analysis of germs cultivated from pus and their resistance profile.

Methods: The research was carried out in the surgical departments of the County Clinical Hospital of Târgu Mureș on 99 patients with obliterative arteriopathy hospitalized during the coronavirus pandemic. Complete blood count was performed on Cell Dyn Ruby (Abbott Laboratories), the cultivation of germs from wet gangrene was carried out by classical microbiological methods. Statistics were made with the R program and GraphPad InStat3.

Results: The average age of participants was 68 years, 79% were men, 41% from urban environment, half diabetics. Neutrophil/lymphocyte ratio positively correlated with platelet/lymphocyte ratio, lymphocyte/monocyte ratio was negatively correlated with these two markers. Platelet count/mean platelet volume ratio was significantly higher in patients with infectious gangrene compared to those without this complication ($p=0.019$). Duration of hospitalization negatively correlated with lymphocyte/monocyte ratio, being significantly longer in those with pathological values of blood count-derived parameters compared to patients with normal results ($p=0.028$). The most frequently cultured germ from the pus was *Staphylococcus aureus* in 31%, followed by *Proteus* in 21%. Almost half of the Gram-negative isolates showed resistance to cephalosporins and only 16% to fluoroquinolones; multidrug resistance was present in 39% of the Gram-negative isolates. Among the isolated Gram-positive bacteria, 40% of the enterococcal strains were resistant to gentamicin and streptomycin.

Conclusions: Blood count-derived parameters are inexpensive, accessible and may be promising prognostic markers in arteriopathy. Antibiotic resistance occurs frequently in bacteria cultured from gangrene, treatment should be based on antibiogram, infections prolonging the period of hospitalization.

Keywords: antibiotic resistance, bacteria, complete blood count-derived markers, obliterative arteriopathy, wet gangrene

C38. DYNAMIC ASSESSMENT OF METABOLIC PARAMETERS AND INFLAMMATORY MARKERS IN DIABETIC AND NON-DIABETIC PATIENTS WITH PERIPHERAL ARTERIAL DISEASE UNDERGOING SURGICAL INTERVENTION

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Introduction: The evolution of peripheral arterial disease is aggravated by diabetes mellitus. In advanced stages, surgical interventions are required. The aim of the study was the perioperative assessment of some biochemical and inflammatory markers to reveal correlations and to evaluate their prognostic role.

Methods: The study was conducted at the County Clinical Hospital in Târgu Mureș, enrolling thirty-one patients with severe arteriopathy, hospitalized between 2020-2021 for surgery. Biochemical parameters were measured by photometry, C-reactive protein (CRP) was determined by turbidimetry (Architect c4000, Abbott Laboratories), fibrinogen by Sysmex CS 2500 (Sysmex Corporation). Proinflammatory cytokines (Interleukin-6 – IL-6, tumor necrosis factor alpha – TNF α) were assayed by fluorescence at the Center for Advanced Medico-Pharmaceutical Research on Flexmap3D (Luminex Corporation). Samples were collected before and 2 days after surgery. Statistical analysis was performed with SPSS28, GraphPad InStat3.

Results: We enrolled 2.45 times more men than women, with a mean age of 71 years, two-thirds with type 2 diabetes mellitus. 19 had preoperative hyperglycemia, over three-quarters of subjects had dyslipidemia on admission, and serum creatinine was elevated preoperatively in a quarter of the patients. Preoperative triglyceridemia correlates positively with cholesterolemia and glycemia. Preoperative CRP was increased in almost half of them, the values being double in diabetics compared to non-diabetics ($p>0.05$), with a mostly increasing trend after amputation. In diabetics there were double values of IL-6 preoperatively compared to non-diabetics ($p=0.09$), the difference being significant postoperatively ($p=0.04$). Positive correlation occurred between the preoperative values of CRP and IL-6 ($r=0.44$, $p=0.02$). The pre- and postoperative values of CRP, IL-6, TNF α and fibrinogen are positively correlated. Preoperative IL-6 >35 pg/ml proved to be a predictive factor for prolonged hospitalization.

Conclusions: Inflammation becomes more pronounced after amputation, a more intense phenomenon in diabetics. IL-6 could be a prognostic factor for the postoperative evolution of patients with arteriopathy.

Keywords: amputation, biochemical parameters, diabetes mellitus, inflammatory markers, peripheral arterial disease

C39. THE RELATIONSHIP BETWEEN THE ALBUMIN / CREATININE RATIO (ACR) AND URINE SEDIMENT: CORRELATIONS AND DISCREPANCIES IN THE EVALUATION OF RENAL PATHOLOGY

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Introduction: The albumin/creatinine ratio (ACR) and urine sediment analysis are essential tools in the evaluation of renal damage. While the ACR reflects glomerular permeability, the urine sediment provides information about inflammatory, infectious or degenerative processes in the urinary tract. The relationship between these two methods is not always concordant.

Methods: The study included 40 cases, distributed in four equal groups: 10 cases with normal ACR values and normal urinary sediment; 10 cases with normal ACR values and abnormal urinary sediment; 10 cases with abnormal ACR values and abnormal urinary sediment; 10 cases with abnormal ACR values and normal urinary sediment. The data were analyzed comparatively to highlight the concordance and discordance between the two parameters. These studies of urinary sediment were performed using both manual microscopy and automated methods (flow cytometry and digital microscopy) and the determination of urinary albumin was performed both quantitatively by immunoturbidimetric and semiquantitatively by screening with strips.

Results: Evaluation of the correlation between ACR values and changes in urinary sediment, as well as the identification of clinically relevant discordance situations. The results highlighted both cases of concordance and cases of discordance (ACR and urinary sediment). The presence of an abnormal urinary sediment in the conditions of a normal ACR suggests possible non-glomerular processes, while an increased ACR with normal sediment may indicate incipient glomerular damage.

Conclusions: ACR and urinary sediment provide complementary information in the evaluation of renal pathology. Their combined use increases the accuracy of diagnosis and may facilitate the early identification of renal diseases that could be missed by using a single parameter.

Keywords: albumin/creatinine ratio, correlation, kidney disease diagnosis, urinary sediment

R40. THE CENTRAL IMMUNOHEMATOLOGY LABORATORY OF THE NATIONAL INSTITUTE OF BLOOD TRANSFUSION "PROF. DR. C.T. NICOLAU": REACTIVATION, RESPONSIBILITIES AND PERSPECTIVES IN THE ERA OF PRECISION MOLECULAR MEDICINE

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The Central Laboratory of Immunohematology (LCI) of the National Institute of Blood Transfusion "Prof. Dr. C. T. Nicolau" (INTS) represents the top structure of the national blood transfusion network in Romania in the field of complex immunohematological diagnostics. Although this structure was nominally included within the institute, for about 15 years its activity was interrupted or inoperative for multiple organizational, administrative and human resource reasons.

This paper presents: (1) the legal and institutional context of the reactivation; (2) the full spectrum of LCI responsibilities; (3) the place of LCI in the architecture of the national transfusion network, in comparison with European reference models; and (4) the development prospects of the molecular biology sector that will become operational in the second half of 2026.

Keywords: blood transfusion, erythrocyte genotyping, immunohematology, INTS, molecular biology, NGS, reference laboratory

C41. THE MAJOR CLINICAL IMPORTANCE OF THE SIMPLEST LABORATORY ANALYSES IN TRANSFUSION MEDICINE: BEDSIDE BLOOD COMPATIBILITY TEST

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Blood typing performed at the patient's bedside is a critical stage of transfusion safety, performed just before the administration of red blood cell components, the aim being to prevent the most severe adverse reaction, acute intravascular hemolysis, of immunological cause, due to ABO blood group incompatibility.

WHO 1224/2006 requires the performance of the "last bedside check" which consists of verifying the patient's identity; checking the macroscopic appearance and integrity of the unit to be transfused; checking the compatibility between the selected blood unit and the patient: determining the ABO and Rh(D) blood group in the patient; determining the ABO and Rh(D) blood group at the unit to be transfused; checking the documentation; recording in the observation sheet. Blood grouping performed before transfusion has certain peculiarities, because it is a laboratory analysis performed outside the laboratory, performed by medical assistants, laboratory analysis supervised by a clinician, laboratory analysis performed on the ward, partially performed, being part of a method for determining the ABO blood group (Beth Vincent).

This analysis is performed systematically before each administration of red blood cell concentrate, having an essential role in transfusion safety. It seems very simple and is sometimes considered unimportant. The procedure for performing it must be strictly observed, and the steps for performing the last control at the patient's bedside must be followed rigorously, considering that any deviation constitutes a risk for the patient. Interpreting the result is easy at first glance, but can be difficult for many prescribing physicians.

Several clinical cases of performing and interpreting the blood group at the patient's bedside, as a last pre-transfusion control, followed by inappropriate decisions illustrate the importance of this simple laboratory analysis. Maximum responsibility, strictly respecting the procedure of the last pretransfusion control is critical for transfusion treatment. Even the simplest laboratory analysis hides complex medical aspects and has an essential importance in restoring the patient's health.

Keywords: blood grouping, transfusion security

C42. DETERMINATION OF ANTI-ERYTHROCYTE ANTIBODIES AS AN IMPORTANT STEP IN TRANSFUSION SAFETY: PARTICULARITIES OF THE POLYTRANSFUSED PATIENT WITH THALASSEMIA MAJOR

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Introduction: Blood transfusion can be a potentially immunizing event, and the investigation of anti-erythrocyte antibodies in a patient's serum is essential before selecting compatible red blood cell components. Screening for anti-erythrocyte antibodies is performed using a panel of test red blood cells with known antigenic configuration using complementary, antiglobulin, enzymatic and saline techniques. A positive result indicates the presence of one or more anti-erythrocyte antibodies and by using extended red blood cell panels their specificity can be identified. Patients with thalassemia major, through chronic transfusion regimen, are among the highest consumers of red blood cell components, therefore they represent a population at risk for developing anti-erythrocyte alloantibodies. In these patients, data from the literature indicate wide variations in the frequency of alloimmunization, from a minimum of 2% to a maximum of 37%.

Methods: The detection of anti-erythrocyte antibodies was performed using the column agglutination method- gel agglutination ID Microtyping BioRad. The study group consisted of 100 patients with thalassemia major undergoing a chronic transfusion regimen registered at the National Institute of Blood Transfusion.

Results: Patients with thalassemia major are transfused with leukocyte-depleted erythrocyte units at intervals of 14-21 days following immuno-hematological testing protocol- determination of irregular antibodies and cross-match tests before each transfusion. The frequency of alloimmunization is 5% in the study group, the specificity of alloantibodies being in the Rh and Kell systems, the most immunogenic ones. Once the specificity is identified, it is taken into account in the subsequent selection of the blood component. Transfusion-dependent thalassemia major is associated with a particular immune status, the abnormalities being caused by oxidative stress, posttransfusion hemochromatosis, splenectomy.

Conclusions: Chronic transfusions, through prolonged exposure to blood components, subjects polytransfused patients to associated risks. Adherence with pretransfusion testing protocols including irregular antibodies detection allows the identification of clinical significance alloantibodies, those that have the potential to trigger accelerated destruction of the erythrocyte carrying the corresponding antigen.

Keywords: alloantibody specificity, alloimmunization, thalassemia major

C43. SEROLOGICAL SCREENING STRATEGIES IN TRANSFUSION MEDICINE: RETROSPECTIVE ELISA ANALYSIS AND EVALUATION OF CHEMILUMINESCENT METHODS

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Introduction: Transfusion safety requires adherence to analytical standards and the use of technologies that meet the real needs of the laboratory. The study aimed to compare the performance of two automated chemiluminescent serological testing platforms, Elecsys (Roche) and Alinity S (Abbott), with the ELISA Evolis (Bio-Rad) system routinely used in the laboratory.

Methods: The analyzed platforms are based on different detection principles: Evolis uses ELISA with colorimetric detection, Elecsys is based on electrochemiluminescence (ECLIA), and Alinity S uses chemiluminescent microparticle immunoassay (CMIA). The evaluation for Elecsys included testing of 2317 samples from first-time donors, in parallel with Evolis, for HBsAg, HCV Ag/Ab, HIV Ag/Ab, HTLV Ab and *Treponema pallidum* Ab. For Alinity S, 1006 samples from first-time donors were analyzed, also in parallel with Evolis, for HBsAg, HIV Ag/Ab, HTLV Ab and *Treponema pallidum* Ab.

Results: The concordance between methods was very good, with all confirmed cases correctly identified. The donation deferral rate was similar between methods (2.63% for ELISA and 2.50% for Elecsys). Differences were minor and were mainly observed at the level of false reactive results, with a tendency toward reduction for chemiluminescent platforms. For the HIV marker, for example, 7 false reactive results were recorded with ELISA compared to 4 with Elecsys and 0 with Alinity S.

Conclusions: All three platforms demonstrated efficiency in screening for transfusion-transmissible infections, with no major differences in terms of test sensitivity and specificity. The level of safety and reliability is comparable, and the choice of the appropriate system depends on the specific context of each laboratory. ELISA remains a solid and validated option, while chemiluminescent platforms may provide additional benefits in settings where donor volume and operational requirements justify a higher level of automation.

Keywords: CLIA, ELISA, transfusion safety

C44. INFECTIONS TRANSMITTED THROUGH BLOOD TRANSFUSIONS IN ROMANIA

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Introduction: Transfusion-transmissible infections represent a significant risk to patient safety. In Romania, blood transfusion activities are coordinated by the National Institute of Blood Transfusion "Prof. Dr. C. T. Nicolau" from Bucharest and regulated by specific legislation to ensure the quality and safety of blood used for therapeutic purposes. The main objective is to prevent the transmission of infectious agents and protect public health.

Methods: All blood donations undergo strict screening for infections such as HIV, HBV, HCV, HTLV, and *Treponema pallidum*. Screening testing is performed using ELISA method and confirmation using CLIA (chemiluminescence), immunoblot, and nucleic acid testing (NAT) techniques. Seasonal screening for West Nile virus is also conducted. The hemovigilance system monitors the entire transfusion process, while "look-back" and "trace-back" procedures are used to investigate suspected transmission cases.

Results: In 2024, out of approximately 360,000 donations, positive cases for several infectious agents (HIV, HBV, HCV, HTLV, syphilis) were identified, highlighting the need for continuous screening.

Conclusions: In conclusion, blood transfusion remains vital for saving lives, and its safety depends on strict adherence to testing protocols, an effective hemovigilance system, and proper implementation of legal regulations.

Keywords: blood donation, ELISA (enzyme-linked immunosorbent assay), transfusion safety

C45. PREMATURETY DRIVES TRANSFUSION NEEDS: EVIDENCE FROM NEONATAL PRACTICE IN A REGIONAL CENTER

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Introduction: Neonatal transfusion practice remains a critical component of clinical management in transfusion medicine, particularly in premature patients with hematologic instability. In a regional center setting, understanding how gestational age influences transfusion burden and hemoglobin dynamics is essential for optimizing indications and product utilization.

Methods: A cross-sectional study included 42 neonates receiving a total of 239 transfusions. Variables analyzed were gestational age, hemoglobin prior to transfusion (Hb Pre), birth weight, postnatal age, and number of transfusions per patient. Non-parametric analyses were applied. Associations were evaluated using Spearman's correlation, while differences in Hb across gestational age categories were assessed using the Kruskal–Wallis test. Linear regression examined the effect of gestational age on pre-transfusion hemoglobin

Results: Gestational age correlated strongly with birth weight ($p = 0.861$, $p < 0.001$) and negatively with postnatal age ($p = -0.532$, $p < 0.001$). A moderate negative correlation was observed between gestational age and transfusion burden ($p = -0.48$, $p = 0.002$), indicating increased transfusion requirements in more premature neonates. Hemoglobin levels differed significantly across gestational age categories ($H = 61.84$, $p < 0.001$). Regression analysis confirmed gestational age as a significant predictor of pre-transfusion hemoglobin ($\beta = 0.139$, $p < 0.001$), with modest explanatory power ($R^2 = 0.156$). Prematurity is associated with increased transfusion needs and altered hematologic profiles, reflecting both physiological immaturity and clinical complexity. These findings highlight the central role of gestational age in guiding transfusion indications and tailoring product use in neonatal practice.

Conclusions: Gestational age is a key determinant of transfusion demand and hematologic status. These results support a stratified, clinically integrated approach to neonatal transfusion practice within regional transfusion medicine services.

Keywords: gestational age, hemoglobin, neonatal transfusion, prematurity

C46. WHEN RED BLOOD CELL TRANSFUSION BECOMES A CHALLENGE: AN IMMUNO-HEMATOLOGY CASE SERIES FROM THE BUCHAREST BLOOD TRANSFUSION CENTER

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Introduction: Immunization following red blood cell transfusion requires accurate detection and interpretation of immunohematological findings in order to identify clinically significant alloantibodies, which are frequently associated with hemolytic disease of the fetus and newborn (HDFN) and post-transfusion adverse reactions.

Methods: A retrospective analysis was conducted on 1035 cases referred to the Bucharest Blood Transfusion Center between January and August 2025. Irregular antibody screening (IAT) was performed in all cases, followed by antibody identification in positive samples. Antibody specificity was confirmed by extended erythrocyte phenotyping. The direct antiglobulin test (DAT) was used to support the investigation of hemolytic anemia, post-transfusion reactions, and autoimmune conditions.

Results: Overall, 32.46% of patients were immunized. Among these, 10.80% presented alloantibodies with defined specificity, 2.03% had specific autoantibodies, 4.87% showed both autoantibodies and nonspecific antibodies, and 14.76% exhibited non-specific antibodies. Clinical diagnosis contributed to interpretation only when documented. Case complexity required additional testing correlated with clinical data to reduce the risk of post-transfusion hemolytic reactions.

Conclusions: To sum up, correlation between autocontrol and DAT results may suggest the presence of autoantibodies or alloantibodies; however, confirmation requires further testing guided by transfusion history and relevant clinical and paraclinical data.

Keywords: alloantibodies, extended phenotyping, post-transfusion adverse reactions

C47. ALGORITHM FOR DIAGNOSIS AND MANAGEMENT OF LABORATORY TESTS FOR THE HEMATO-ONCOLOGY PATIENT WITH DISSEMINATED INTRAVASCULAR COAGULATION

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Introduction: To identify patients at risk of disseminated intravascular coagulation (DIC), predisposing conditions should be assessed (sepsis, trauma, malignancy, obstetric complications), along with complete clinical examinations to detect signs of microvascular thrombosis or hemorrhage. In acute promyelocytic leukemia (APL3), hyperfibrinolysis predominates, with an increased risk of severe bleeding. The role of ATRA (all-trans retinoic acid) in reducing tissue factor expression and stabilizing the leukemic cell membrane is essential in the management of this disease. In other hematological malignancies, the mechanisms are varied, requiring a personalized approach.

Methods: A total of 93 patients from the ICU department of IRO Hospital, Iași, were evaluated in 2025, through laboratory investigations for DIC, with complete blood count including platelet count, PT/INR, aPTT, fibrinogen, D-dimers and TEG (thrombelastogram with R, K, α , MA parameters).

Results: In patients from the pathological Group P, with hypocoagulability, TEG parameters (R and K) increased significantly by 49%, maximum clot amplitude (MA-TEG) decreased by over 30%, compared to the normal Group N. In patients with hypercoagulability, R-TEG increased by 32.31%, K-TEG increased by 38.90%, and MA-TEG decreased significantly by 17.17%, compared to Group N, and in those with secondary fibrinolysis, the increase was significant only for K (45.01%) compared to Group N. The increase in the R-TEG parameter correlated prolongation of aPTT and TQ, while decreased alpha-TEG and MA-TEG values correlated with reduced fibrinogen and thrombocytopenia levels leading to hypocoagulability and hemorrhagic syndrome. In secondary fibrinolysis, defibrination resulted from the combined action of DIC (which results in consumption of fibrinogen and plasma factors) and the lytic action of plasmin correlating with alpha and MA-TEG which showed significant increases compared to Group N.

Conclusions: Laboratory investigation results correlated with ISTH, JAAM or SIC scores depending on the clinical context enabled a targeted therapeutic approach to DIC. Personalized treatment based on the type of DIC (predominantly thrombotic vs. predominantly hemorrhagic) and continuous monitoring of coagulation parameters will allow for therapy adjustment in hemato-oncological patients with DIC.

Keywords: CID, hemato-oncology, leukemia, TEG

C48. JAK2 V617F CLONAL HEMATOPOIESIS AND EARLY DIAGNOSIS OF MYELOPROLIFERATIVE NEOPLASMS

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The activating *JAK2* V617F mutation is largely recognized as the most common driver of BCR::ABL1-negative myeloproliferative neoplasms (MPNs). At the same time, the mutation is found in healthy individuals generating clonal hematopoiesis of indeterminate potential (CHIP), a condition associated with an increased risk of myeloid neoplasm development, accelerated atherosclerosis, and thrombotic events.

By employing sensitive PCR methods, it is possible to detect *JAK2* V617F mutation in the peripheral blood granulocytes even when present at very low mutational load. Several cases of unexplained arterial and venous thrombosis with blood counts below the MPN diagnostic thresholds that were referred for *JAK2* V617F testing will be presented. A few of them were diagnosed with early polycythemia vera while others were considered *JAK2* CHIP requiring periodic monitoring.

The impact of MPN early diagnosis will be discussed along with the potential of therapeutic intervention with disease modifying drugs.

Keywords: clonal hematopoiesis of indeterminate potential, early diagnosis of myeloproliferative neoplasms, *JAK2* V617F mutation

C49. PRACTICAL DIAGNOSTIC APPROACH TO LYMPHOCYTOSIS IN ADULT PATIENTS

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Lymphocytosis is a hematologic abnormality frequently encountered in clinical practice. A critical step in lymphocytosis assessment is the distinction between reactive and malignant lymphocytosis. In this respect, morphologic examination of peripheral blood smear provides essential findings that should be correlated with the clinical data.

While the pleomorphic aspect of lymphocytes is suggestive for reactive lymphocytosis the presence of monomorphic cells of small/intermediate/large size, atypical nuclear shape either cleaved or convoluted, moderately condensed chromatin with prominent nucleoli, blastic features, villous cytoplasm or plasmacytoid appearance are indicative of neoplastic lymphocytosis.

Multiparameter flow cytometry represents the next step in characterization of lymphoid cells. Several cases of leukemic phase malignant lymphomas will be described, highlighting the key morphologic abnormalities. The condition of monoclonal B-cell lymphocytosis as a precursor of chronic lymphocytic leukemia will be also introduced.

Keywords: monoclonal B-cell lymphocytosis, multiparameter flow cytometry, reactive versus neoplastic lymphocytosis

C50. THE JOURNEY FROM INTERNATIONAL CONSENSUS TO ROUTINE HEMATO-ONCOLOGY LABORATORY TESTS

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Given the importance of monitoring measurable residual disease (MRD) for risk stratification and treatment guidance in acute myeloblastic leukemia (AML), it is necessary to make sure that international guidelines generated in multicenter studies are being implemented in the daily routine of flow cytometry laboratories by multicolor flow cytometry (MCF).

During 2025, 281 bone marrow aspirate samples from 126 patients with AML were evaluated for de measurement of MRD by MCF within the flow cytometry department of IRO Iasi. Current MRD_AML protocols are based on the strategy of tracking those LAIP (aberrant/leukemia-associated immunophenotypes) detected at diagnosis. Given the updated ELN (European Leukemia Net) recommendations for MRD testing in AML by MCF and molecular biology, including NGS (Cloos et al, 2025), it is necessary that the procedures currently used in our department be reconsidered, taking into account:

1. The panel (recommendation B3: it is recommended to use in all cases CD4, CD7, CD11b, CD13, CD14, CD15, CD33, CD34, CD36, CD38, CD45, CD56, CD64, HLA-DR, CD117, CD123, regardless of the LAIP identified at diagnosis);
2. Hemodilution: its assessment needs to be part of the MRD test by MCF and there are clear clinical recommendations for performing the aspiration with minimal risk of hemodilution (recommendations B7 and A4);
3. The optimal sensitivity level (recommendation B10: it is recommended to purchase at least 500 000 cells/tube);
4. The need to identify leukemic stem cells (LSCs) (recommendation B11 to use the following marker panel: CD45, CD34, CD38, CD45RA, CD123 and CLEC12A/ CD371);
5. Reporting method: a new category of MRD status is introduced = warning MRD/ MRD Low Level ($0.01\% < \text{MRD-LL} < 0.1\%$), with the mention that the prognostic impact of MRD-LL by MCF, including cut-off values, testing times, MRD kinetics and relevance for genetic risk groups, requires further clinical validation studies.

In conclusion, there is still a lack of clarity regarding what strategies to use for evaluating immunophenotypic profiles different from normal (DiffN), for identifying unstable LAIP, what is the level of sensitivity required for quantifying LSCs, how to report and define the MRD when multiple distinct potential AML clones are identified.

Keywords: acute myeloid leukemia, leukemia-associated immunophenotypes, multiparameter flow cytometry

C51. INTEGRATED IMMUNOPHENOTYPIC AND MOLECULAR STRATEGIES FOR MEASURABLE RESIDUAL DISEASE MONITORING IN ACUTE MYELOID LEUKEMIA

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Introduction: Measurable residual disease (MRD) assessment has become a cornerstone of response evaluation and treatment decision-making in acute myeloid leukemia (AML). Multiparameter flow cytometry (MFC), molecular detection of fusion genes, and next-generation sequencing (NGS) represent complementary approaches, each with distinct sensitivity, applicability, and turnaround time. The integration of these methods may enhance MRD monitoring accuracy, yet their concordance in routine clinical practice remains incompletely defined.

Methods: Starting January 2024, all newly diagnosed AML patients evaluated at our center were assessed at diagnosis using a standardized panel incorporating MFC-based immunophenotyping, RT-PCR/qPCR for recurrent fusion genes (RUNX2::RUNX2T2, CBFB::MYH22, PML::RARA, BCR::ABL2), and NGS for somatic mutations. Follow-up MRD evaluation was performed in patients achieving complete remission, applying one or more of the same methods defined at diagnosis.

Results: A total of 382 AML patients were analyzed at diagnosis using all three platforms. Of these, 102 patients underwent at least one post-remission MRD evaluation by MFC. A subset of 16 patients had concurrent MRD assessment by all three techniques, enabling preliminary cross-method comparison. Data analysis regarding concordance rates, discordant results, and clinical implications is currently ongoing.

Conclusions: This prospective single-center cohort demonstrates the feasibility of implementing a comprehensive, three-platform MRD monitoring strategy in routine AML care. Preliminary data suggest that integrating MFC, fusion gene quantification, and NGS provides broader patient coverage and potentially complementary prognostic information. Final concordance analysis will inform recommendations for optimized, risk-adapted MRD monitoring protocols.

Keywords: acute myeloid leukemia, measurable residual disease monitoring, multiparameter flow cytometry, risk-adapted MRD assessment.

C52. THE IMPACT OF NGS TECHNOLOGY ON THE DIAGNOSIS, PROGNOSIS, AND THERAPEUTIC MANAGEMENT OF MYELODYSPLASTIC SYNDROMES

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Introduction: Myelodysplastic syndromes (MDS) represent a heterogeneous group of myeloid neoplasms characterized by clonal hematopoiesis, cytopenias (anemia, neutropenia, and/or thrombocytopenia), and dysplastic cellular morphology, with a variable risk of transformation into acute myeloid leukemia. The incidence of MDS increases significantly with age, reaching 55.4 per 100,000 individuals in those over 80 years old. Advances in molecular genetics have shown that over 90% of MDS patients harbor somatic mutations in myeloid-associated genes. Next-generation sequencing (NGS) has enabled the identification of recurrent alterations in genes such as *SF3B1*, *SRSF2*, *TP53*, *DNMT3A*, *ASXL1*, and *TET2*. This study aims to evaluate the incidence and prognostic role of these molecular abnormalities in newly diagnosed MDS patients.

Methods: Bone marrow aspirates from 147 patients diagnosed with MDS (81 females, 66 males) between February 2024 and April 2026 at the Regional Institute of Oncology Iasi were analyzed using NGS (HEMEaccuTest™). The relationship between mutational status and clinical-biological characteristics, including IPSS-R, karyotype, progression to AML, and overall survival, was investigated.

Results: At least one mutation was identified in 86% of patients, of whom 37% had a normal karyotype. The most frequent mutations were: *ASXL1* (18.2%), *TET2* (12.2%), *SF3B1* (11.16%), *BCOR* (10.5%), and *DNMT3A* (9.9%).

Conclusions: NGS results are redefining MDS management by providing essential diagnostic clarity, particularly for patients with a normal karyotype or equivocal cytogenetic results. Characterizing the mutational landscape not only improves risk stratification through advanced molecular scores (such as IPSS-M) but also establishes the foundation for the transition toward precision medicine. Understanding the specific impact of each mutation on clinical evolution facilitates the implementation of targeted therapeutic strategies, thereby optimizing the long-term prognosis of patients.

Keywords: mutation, myelodysplastic syndrome, next-generation sequencing (NGS)

C53. EVALUATION OF MINIMAL RESIDUAL DISEASE IN ACUTE MYELOID LEUKEMIA THROUGH MOLECULAR BIOLOGY TECHNIQUES

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Identifying genetic anomalies is mandatory for the diagnosis, classification, and post-therapeutic monitoring of malignant hematological diseases. Molecular biology methods enable the establishment of a precise diagnosis and the development of a treatment specific to each individual patient. Among these, next-generation sequencing (NGS) stands out as one of the most comprehensive approaches currently available, simultaneously providing an extensive volume of data with diagnostic and prognostic relevance. However, the evaluation of minimal residual disease (MRD) requires high sensitivity, which is why combining multiple techniques remains the optimal strategy. The present study included 382 patients diagnosed with acute myeloid leukemia (AML), followed at the Regional Institute of Oncology in Iasi. MRD assessment was performed by correlating results obtained through RealTimePCR, QPCR, QF-PCR, MLPA, and NGS with data provided by conventional karyotyping and FISH. A comprehensive MRD evaluation in AML patients requires the use of high-resolution methods capable not only of detecting markers initially identified at diagnosis, but also of revealing additional markers present in minor clones—information that proves valuable for monitoring treatment efficacy and assessing prognosis.

Keywords: acute myeloid leukemia, minimal residual disease, next-generation sequencing, polymerase chain reaction

C54. CYTOLOGICAL AND IMMUNOPHENOTYPIC FEATURES OF A RARE VARIANT OF ACUTE PROMYELOCYTIC LEUKEMIA WITH BASOPHILIC DIFFERENTIATION: CASE REPORT

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Introduction: Acute promyelocytic leukemia (APL) is a myeloid neoplasm characterized by clonal proliferation of abnormal promyelocytes, caused by the translocation t(15;17)(q24;q21), with formation of the PML-RARA fusion gene, which leads to a block in granulocytic maturation at the promyelocyte stage. Among the frequent clinical manifestations is disseminated intravascular coagulation (DIC), associated with consumption of coagulation factors and spontaneous bleeding. APL with basophilic differentiation represents a rare variant of this disease, described in the literature as being associated with an increased risk of hemorrhagic manifestations and higher mortality. The differential diagnosis includes other acute leukemias with basophilic differentiation.

Case presentation: We present the case of a 55-year-old female patient, diagnosed with APL with basophilic differentiation, characterized from a cytological and immunophenotypic point of view. We also review data from the literature regarding the incidence, genetic profile, and prognosis of this rare variant. APL with basophilic differentiation is cytologically characterised by the presence of leukemic promyelocytes with abnormal granulations in May-Grünwald-Giemsa staining, strongly peroxidase-positive, some also showing basophilic granules, with metachromatic staining with toluidine blue. From an immunophenotypic point of view, the classical APL profile was observed: CD34 negative/low, HLA-DR negative, CD117 negative/low, CD33 strongly positive, CD13 with heterogeneous expression, CD9 positive, CD15 negative. In addition, expression of basophil-specific markers such as CD203c was identified. The diagnosis of APL was confirmed by the presence of the PML-RARA fusion gene.

Conclusions: The presented case highlights the aggressiveness of APL with basophilic differentiation and the diagnostic challenges, emphasizing that early recognition is essential for a favorable patient outcome.

Keywords: acute promyelocytic leukemia, basophilic differentiation, immunophenotyping, PML-RARA

C55. MOLECULAR DIAGNOSTICS IN SOLID TUMORS: INTEGRATING LABORATORY ANALYSIS INTO CLINICAL PRACTICE

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Introduction: The implementation of molecular diagnostic techniques in medical analysis laboratories highlights the importance and benefits of standardizing the methods of interpretation and reporting of results. The molecular profile obtained through the analysing of tumour DNA or RNA provides valuable information about diagnosis, prognosis and potential targeted therapies. Additionally, it offers further information about off-label therapy for specific molecular variants, as well as therapies available through clinical trials.

Methods: Samples from 431 patients diagnosed with colorectal cancer were analysed using molecular diagnostic techniques. In these cases, variants in the KRAS, NRAS and BRAF genes were evaluated using Real-Time PCR technology with the EasyPGX® system. Additionally, molecular analysis by Next-Generation Sequencing (NGS) was performed for patients diagnosed with one of the 3 types of neoplasia: non-small cell lung cancer (NSCLC), breast or ovarian cancer. The analysed samples consisted of formalin-fixed paraffin-embedded tissue (FFPE), and the NGS technique was performed using the Illumina platform. Gene panels of variable sizes, ranging from 78 to 500 genes, were employed.

Results: In the cohort of patients with colorectal cancer, the analysis of clinically relevant variants indicated that approximately 47% of patients harbour pathogenic variants in the KRAS gene, of which 64% are located at codon 12. The KRAS G12C variant was identified in 4% of patients; this finding is clinically relevant, as it may confer eligibility for participation in clinical trials. Clinically significant variants were also identified in the NRAS gene in 4% of patients and in the BRAF gene in 4% of KRAS and NRAS negative patients. Data analysis, performed using artificial intelligence algorithms, highlighted the presence of clinically significant variants in patients with non-small cell lung cancer (NSCLC), across the 78 genes included in the panel used. In breast cancer, the genetic analysis aimed to identify pathogenic variants in the 131 genes evaluated. For ovarian cancer, clinically significant variants were analysed using an extended panel covering 500 genes. The identified variants were classified into 5 categories according to their somatic or germline origin: (1) Oncogenic/Pathogenic, (2) Likely oncogenic/pathogenic (3) Variant of uncertain significance (VUS), (4) Likely benign, (5) Benign. Additionally, these variants were stratified according to the AMP/ASCO/CAP guidelines into the following class: Tier I (variants with strong clinical significance), Tier II (variants with potential clinical significance), Tier III (variant of uncertain significance), and Tier IV (Likely benign or benign).

Conclusions: The expansion use of NGS platforms in the molecular diagnosis of solid tumours has generated new analytical challenges for medical laboratories. One of the key aspects for molecular specialists is the standardization of the interpretation and reporting of variants identified in tumour sequences data. The analysis of NGS results in accordance with established guidelines supports informed therapeutic decision-making by enabling the identification of clinically relevant genetic variants.

Keywords: artificial intelligence, cancer, next-generation sequencing

C56. MORPHOLOGICAL RED FLAGS IN PERIPHERAL BLOOD AND BONE MARROW: INTRACYTOPLASMIC INCLUSIONS, MICROORGANISMS, AND CRYSTALLINE STRUCTURES IN INFECTIOUS CYTOPENIAS

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Introduction: Cytopenias are a frequent indication for hematological evaluation and may occasionally reveal infectious etiologies. Careful morphological examination of peripheral blood and bone marrow smears can provide essential diagnostic clues, particularly through the identification of intracytoplasmic inclusions. In addition, the direct visualization of microorganisms within leukocytes and the presence of intracytoplasmic crystalline structures (“death crystals”) may represent critical morphological warning signs associated with severe infection.

Methods: We report two cases referred for investigation of cytopenia in which morphological evaluation of May-Grünwald Giemsa stained peripheral blood and bone marrow smears played a key diagnostic role. The first case involved a patient presenting with severe thrombocytopenia. Peripheral blood smear examination revealed intracytoplasmic inclusions (morulae) within neutrophils, suggestive of *Anaplasma phagocytophilum* infection. The diagnosis was confirmed by molecular testing and antibiotic therapy led to rapid clinical and hematological recovery. The second case concerned a patient investigated for pancytopenia. Peripheral blood smear revealed rare intracytoplasmic inclusions within neutrophils, consisting of oval organisms with a nucleus and kinetoplast, suggestive of *Leishmania amastigotes*. Bone marrow aspirate showed numerous macrophages containing similar inclusions. The diagnosis of visceral leishmaniasis was confirmed by serological testing. Additionally, we present supplementary observations of rare cases showing microorganisms within circulating neutrophils, reflecting phagocytosed pathogens, as well as intracytoplasmic crystalline inclusions (“green crystals of death” or “critical green inclusions”), associated with sepsis, severe inflammation and adverse outcomes.

Results: Peripheral blood smear examination provided key diagnostic information in the first two cases. To our knowledge, morphological diagnosis of *Anaplasma phagocytophilum* infection on peripheral blood smear has not been previously documented in Romania.

Conclusions: Morphological evaluation remains a fast and cost-effective diagnostic tool. Recognition of pathogen-specific inclusions, microorganisms and crystalline structures in leukocytes may provide valuable diagnostic and prognostic information in infectious cytopenias.

Keywords: hematologic morphology, infectious cytopenias, intracytoplasmic inclusions

C57. B LYMPHOBLASTIC LEUKEMIA WITH KMT2A REARRANGEMENT: CASE REPORT

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Introduction: B lymphoblastic leukemia (B-ALL) with KMT2A rearrangement is defined by the presence of rearrangements between KMT2A and various fusion partners (over 90 different partner genes). A characteristic phenomenon for KMT2A is lineage switching, suggesting that these leukemias contain progenitors with lineage plasticity biologically related to MPAL. These leukemias frequently present de novo as MPAL. We present 2 cases of B-ALL with KMT2A rearrangement—diagnosis and evolution.

Methods: Bone marrow aspirate smears were stained using the May-Grünwald Giemsa technique. Following examination, immunophenotyping, cytogenetics, and molecular biology were recommended. Sample processing and labeling were performed according to EuroFlow recommendations; acquisition was carried out using the DxFlex flow cytometer and the Infinicyte analysis software was used.

Results: The morphological examination of the smears established the diagnosis of acute leukemia. The cases were classified by flow cytometry as B-ALL with an immunophenotype compatible with KMT2A rearrangement. In the first case, complete morphological and immunophenotypic remission was achieved after induction therapy. Subsequently, minimal residual disease (MRD) remained positive at values <0.01%, followed by relapse with the diagnostic phenotype. Remission was no longer achieved thereafter, with MRD repeatedly positive <0.01%. At the next relapse, two distinct blast populations were identified, and the case was classified as acute leukemia with mixed myeloid/B-lymphoid phenotype. Following treatment, the myeloid clone was eliminated, but the patient relapsed with the initial diagnostic clone. The second case remained in complete remission, both morphologically and immunophenotypically, and is currently transplanted.

Conclusions: Acute leukemia with KMT2A rearrangement generally has a poor prognosis compared to other genetic categories. The short-term course of the disease in our patients was significantly different, and the involvement of other factors in the evolution and prognosis of the disease is also possible.

Keywords: B lymphoblastic leukemia, KMT2A rearrangement, minimal residual disease

C58. VIRAL INFECTIONS IN PATIENTS WITH MALIGNANT DISEASES: ROLE AND RATIONALE OF THE MOLECULAR DIAGNOSIS AND THE VIRAL LOAD MEASUREMENT

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Infection is the leading cause of fever in malignant disease; it interrupts specific treatments, contributes to vital organ dysfunction, and may lead to unnecessary or inappropriate antibiotic therapy. Bacterial infections are investigated using specific protocols, while molecular biology remains the gold standard for viral diagnosis. Viral and bacterial infections may coexist. Fever related to therapy, cytokinemia, or malignancy itself is a diagnosis of exclusion.

In patients with malignant disease, infection represents the greatest risk. Certain stages of care and medical procedures carry a particularly high risk of infection. Bone marrow suppression and cytotoxicity associated with oncologic therapies frequently cause neutropenia, predisposing patients to pathogenic and opportunistic infections. During radiotherapy, persistent immunosuppression maintains a constant risk of infection. In chemotherapy, especially during induction with high-dose regimens, the nadir period (days 7–14) carries the highest risk of bacterial translocation and/or viral reactivation.

Latent viruses that may reactivate during immunosuppression include HBV and HCV, which may lead to hepatocarcinoma and fulminant hepatitis; CMV, associated with neurological disease; and Epstein-Barr virus (EBV), strongly linked to nasopharyngeal carcinoma, Hodgkin lymphoma, Burkitt lymphoma, and gastric cancers. Opportunistic viruses such as Herpes Simplex Virus, Varicella-Zoster Virus, EBV, and Human Herpesvirus 6 are major causes of severe illness.

Risk factors for HBV reactivation are assessed according to combinations of hepatitis markers detected by PCR, with specific viral loads used to define infection. Respiratory viruses of concern include Respiratory Syncytial Virus (RSV), Influenza, Parainfluenza, Adenoviruses, Rhinoviruses, and SARS-CoV-2. Other clinically relevant viruses include Polyomaviruses (BK virus, JC virus), Parvovirus B19, and Rotavirus. The epidemiological situation of HBV and HCV in Romania is presented, together with the early development of PCR testing at Coltea Hospital. The concept and applications of syndromic testing are discussed, including viral load assessment for Adenovirus, BK virus, CMV, EBV, Herpesviruses, and VZV.

In conclusion, immunocompromised patients are highly exposed to viral infections and unculturable bacterial pathogens. Definitive diagnosis often relies on PCR-based molecular testing. Positive viral screening results should be confirmed by molecular methods to reduce unnecessary antibiotic use and limit the selection of multidrug-resistant microorganisms. PCR also facilitates patient access to curative HCV therapy through the National Health Program.

Keywords: HBV and COVID-19 monitoring in hematologic malignancies, viral infections in immunocompromised patients, viral reactivation in chemotherapy-induced neutropenia

P29. MORPHOLOGICAL CHARACTERIZATION OF A LIPID NANOPARTICLE-mRNA PLATFORM FOR TAILORED MOLECULAR THERAPIES

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Introduction: The therapeutic potential of messenger RNA (mRNA) has become apparent following the widespread deployment of COVID-19 vaccines. Synthetic mRNA molecules require codon optimization and specific structural modifications at the 5' terminus and poly(A) tail, alongside incorporation of modified nucleosides. These alterations enable exogenous mRNA to maintain functionality within the cellular environment for extended durations. Modified mRNA is delivered via lipid nanoparticles (LNPs), which serve as efficient non-viral transfection vectors. LNPs typically comprise an ionizable lipid, helper lipids, cholesterol, and a polyethylene glycol-functionalized lipid. Variations in these components influence the structural integrity, stability, and persistence of the complex, potentially dictating preferential tissue accumulation. Transmission electron microscopy (TEM) remains the "gold standard" for the morphological characterization of LNP-mRNA complexes and represents a critical prerequisite for in vitro or in vivo evaluation. Here, we describe the assessment of an optimized LNP-mRNA platform via negative staining and cryo-TEM, designed for application in targeted therapeutics.

Methods: Synthesis of mRNA was performed via in vitro transcription, optimized for the generation of linear mRNA featuring a co-transcriptional 5' Cap-1 structure and poly(A) tail. For encapsulation, a modified lipid composition based on the Moderna vaccine formulation was selected. For cryo-TEM, samples were vitrified by rapid immersion in liquid nitrogen-cooled ethane, using an automated vitrification system. Frozen grids were transferred to a Talos F200C TEM, equipped with a 4kx4k camera. Particle fields were evaluated at 200 keV, at doses below $4 \text{ e}^-/\text{\AA}^2$. Images were acquired at a specimen-level resolution of $<1\text{\AA}$. For negative staining, 3 μL of sample was placed onto copper grids, followed by incubation with uranyl acetate and TEM visualization.

Results: LNP-mRNA particle fields had relatively homogeneous, spherical morphology and diameters of 80-120 nm. Particles showed minimal aggregation, and no contaminants were identified. For reference, the Spikevax and BNT162b2 COVID-19 vaccines were analyzed, showing similar morphology.

Conclusions: TEM analysis demonstrates that this optimized formulation generates LNPs with homogeneous morphology and high purity, suitable for efficient delivery of mRNA in personalized molecular therapies.

Keywords: electron microscopy, lipid nanoparticles, mRNA, personalized medicine, tailored therapies

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P30. ELECTRICAL ISOFOCUSING: AN ESSENTIAL METHOD FOR ADVANCED PROTEIN ANALYSIS

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Introduction: Electrical isoelectric focusing (IEF) is an extremely high-resolution isoelectric point (pI) protein separation technique capable of distinguishing proteins that differ by a single electrical charge. In laboratory medicine, IEF represents the standard for oligoclonality analysis, isoenzyme characterization and identification of rare protein variants, significantly exceeding the sensitivity of conventional electrophoresis.

Methods: The presentation is based on the literature and established applications of IEF in the clinical laboratory. The supports used (IPG gels, capillaries), the types of ampholytes, and the physicochemical principles that determine the migration and focus of proteins in the pH gradient are discussed. IEF is made in a stable pH gradient, where proteins migrate until they reach pI. Three major approaches are analyzed: IPG gel IEF—immobilized, stable pH gradient with excellent resolution; allows fine separation of proteins and is frequently used in CSF and gammopathy analysis. In situ generated gradient IEF—uses mobile ampholytes for gradient formation during electrophoresis; provides flexibility in optimizing separation. Capillary Isoelectric Focusing (cIEF)—automated technique with integrated optical detection, high reproducibility, and the possibility of integration into advanced proteomic flows. The role of immunofixation as a confirmatory method for identifying the specificity of the bands is mentioned.

Results: According to data from the literature, IEF allows: detection of oligoclonal bands with superior sensitivity, precise differentiation of gammopathies, identification of hemoglobin variants and characterization of isoenzymes. High resolution is essential in situations where classical electrophoresis does not provide diagnostic clarity.

Conclusions: IEF is an indispensable technique in the modern laboratory, providing critical information for differential diagnosis. In-depth understanding of methodological principles and variants allows optimal integration of IEF into diagnostic algorithms and increases the accuracy of clinical interpretation.

Keywords: isoelectric focusing, pH gradient, protein separation

P31. DESIGN OF A NEW METHOD FOR DIRECT ELECTROCHEMICAL DETECTION OF RESPIRATORY VIRUS DNA

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Introduction: Respiratory infections represent a major cause of morbidity and mortality globally, requiring rapid, sensitive, and specific diagnostic methods for the identification of the pathogens in complex biofluids. In this context, a new innovative electrochemical method was developed, coupled with the isothermal method Recombinase Polymerase Amplification (RPA) for the detection of Influenza A and B, from human samples.

Methods: This new method is based on the detection of double-stranded DNA (dsDNA) resulted from reverse transcription and amplification by the RPA technique. For the impedimetric detection of dsDNA, screen-printed sensors with a gold working electrode are used, a mixed thiol self-assembled layer (SAMs) containing thiolated oligonucleotides was immobilized on the surface, these functioning as a capture agent for the dsDNA sequences obtained by RPA. The model design for Influenza A and B detection was carried out in accordance with the European legislation, Regulation (IVDR) no. 746/2017.

Results: The following were performed: 1) RNA extraction and reverse transcription by classical methods, 2) primer design for viral dsDNA amplification by RPA method, 3) sensor design for detection of amplicons resulting from amplification, and 4) the stages of preparation and obtaining the biosensor.

Conclusions: The implementation of the method aims at ultra-rapid detection (≤ 30 min) of a panel of respiratory viruses, in pharyngeal and nasal exudate samples, with applicability in fields such as health, public safety, and economy.

Keywords: respiratory infections, RPA, Electrochemical biosensors

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P32. CLINICAL AND BIOCHEMICAL PROFILE OF LIVER CIRRHOSIS: A COMPARATIVE STUDY

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Introduction: Follow-up recommendations in patients with cirrhosis include routine laboratory testing, endoscopic surveillance for varices, and screening for hepatocellular carcinoma, with intervals varying according to disease stage and control of etiology.

Methods: In this retrospective single-center study, we compared features between 54 patients with liver cirrhosis and 101 controls without liver disease investigated on endoscopy to identify clinical, hematological, and biochemical possible predictors for advanced liver conditions in the endoscopic population.

Results: Cirrhotic patients had a higher prevalence of smoking (29.17% vs. 12.87%, $p=0.0224$, $OR=2.78$), cardiovascular disease (79.63% vs. 58.42%, $p=0.0082$, $OR=2.78$), history of anemia (55.56% vs. 37.62%, $p=0.0415$, $OR=2.07$), chronic kidney disease (25.93% vs. 9.90%, $p=0.0111$, $OR=3.18$), and pulmonary disease (37.04% vs. 20.79%, $p=0.036$, $OR=2.24$). Among symptoms, epigastric pain, heartburn, and nausea/vomiting were significantly less frequent in cirrhotic patients (all $p<0.05$). Regarding laboratory parameters, cirrhotic patients had lower hemoglobin (10.85 vs. 12.8 g/dL, $p<0.0001$), lower total cholesterol (3.315 vs. 4.74 mmol/L, $p<0.0001$), and lower albumin levels (3.16 vs. 4.05 g/dL, $p=0.0012$), alongside higher INR (1.28 vs. 1.02, $p<0.0001$), liver enzymes (AST: 51.5 vs. 20 U/L; ALT: 25 vs. 16 U/L; GGT: 95 vs. 25 U/L; all $p<0.0001$), alkaline phosphatase (295 vs. 180.5 U/L, $p<0.0001$), and bilirubin levels (total bilirubin: 1.3 vs. 0.6 mg/dL, $p<0.0001$). No significant differences were observed in serum iron or triglyceride levels, or in endoscopic evidence of esophageal varices or features of portal gastropathy. Spearman correlation analysis demonstrated that liver cirrhosis correlated positively with INR, liver enzymes, and bilirubin, and negatively with albumin and hemoglobin.

Conclusions: Liver cirrhosis presents a distinct clinical and biochemical profile characterized by increased comorbidity burden and laboratory abnormalities, rather than endoscopic characteristic features, highlighting the importance of integrated clinical-laboratory assessment in patients referred for endoscopy.

Keywords: advanced liver conditions, liver cirrhosis, portal gastropathy

P33. COBAS E801 vs ALINITY i vs MAGLUMI X6: VITAMIN B12 METHOD COMPARISON

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Introduction: High-volume clinical laboratories frequently use multiple immunology platforms, which requires a comparability assessment of the results obtained between different analyzers. The aim of this study is to evaluate the comparability of vitamin B12 on 3 immunology platforms (Alinity i, Cobas e801 and Maglumi X6) and to identify systematic differences and inter-method variability.

Methods: 84 plasma samples obtained from apparently healthy individuals (49 women, 35 men; aged between 18 and 65 years) were measured. Statistical analysis included descriptive statistics (box-plot), normality test (D'Agostino-Pearson), non-parametric comparison (Friedman test) and comparability analysis using Passing-Bablok linear regression and Bland-Altman method, according to CLSI EP09.

Results: Vitamin B12 values demonstrated a non-Gaussian distribution on Cobas e801 and Alinity i and a Gaussian distribution on Maglumi X6. Differences between medians were statistically significant ($p<0.05$). Passing-Bablok analysis showed the presence of systematic bias between methods. Bland-Altman analysis confirmed a significant systematic bias with wide limits of agreement: Alinity–Maglumi bias 30.9% (–5.1% to 66.8%), Cobas–Maglumi 47.2% (21.2% to 73.2%) and Cobas–Alinity 16.9% (–9.6% to 43.3%), along with the presence of outliers. Observed bias exceeded analytical performance specification based on biological variation (EFLM), where the minimum accepted bias is 14.1%.

Conclusions: The identified systematic differences indicate limited comparability between platforms, with both statistical and clinical significance. Therefore, they cannot be used interchangeably for vitamin B12 measurements. These results underline the necessity of careful interpretation of values, particularly in context of long-term patient monitoring and transitions between different analytical platforms.

Keywords: immunology analyzer, method comparison, vitamin B12

P34. PREVALENCE OF VITAMIN B9 AND B12 DEFICIENCY IN THE PEDIATRIC POPULATION

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Introduction: Vitamin B9 and vitamin B12, water-soluble vitamins, act as coenzymes and are effective in the formation of a healthy nervous system and erythrocytes. Their deficiency can cause serious signs and symptoms such as macrocytic anemia, cognitive delay, irreversible neurological damage, and depression. Vitamin B9 deficiency occurs in a diet poor in green vegetables and in gastrointestinal disorders. Vitamin B12 deficiency can occur in the following situations: pernicious anemia, gastrointestinal diseases with inflammation and a strictly vegan diet. The aim of this retrospective study was to evaluate the prevalence of hypovitaminosis B9 and B12 among the pediatric population.

Methods: A retrospective study was carried out, analyzing 394 pediatric samples in the period 2023-2024, and the data analysis was carried out on several age groups: 0-12 months, 1-3 years, 3-5 years and >5 years. Determination of the serum level of vitamin B9 and B12 from samples collected in a closed system and analyzed by chemiluminescence on the Diasorin Liaison XL automatic analyzer.

Results: In the age group 0-12 months, a 14% decrease in vitamin B9 concentrations was revealed ($p=0.007$) and there was no vitamin B12 deficiency. In the age group 1-3 years, the deficit was 7.4% for vitamin B9 and 39% for vitamin B12 ($p=0.001$). In the age group 3-5 years, the deficit is 16% for vitamin B9, 23% for vitamin B12 ($p=0.004$). In patients over 5 years, the deficit was 24% for vitamin B9 and 48% for vitamin B12 ($p=0.005$).

Conclusions: No vitamin B12 deficiency was recorded in children under 12 months. In children over 5 years of age, the greatest deficiency of vitamin B9 and B12 was recorded. Vitamin B9 and B12 deficiency increases with age. In order to avoid the pathologies associated with vitamin B9 and B12 deficiency, periodic dosing and their supplementation through prophylaxis programs is necessary.

Keywords: hypovitaminosis prevalence, pediatric population, vitamin B9 deficiency, vitamin B12 deficiency

P35. ESTABLISHMENT OF SERUM CREATININE REFERENCE INTERVALS IN AN ADULT POPULATION

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Introduction: Establishing reference intervals (RIs) for serum creatinine (SCr) is essential for the accurate interpretation of laboratory results. The aim of this study was to establish RIs for SCr using two analytical methods.

Methods: A total of 121 men and 159 women, aged 18-63 years, apparently healthy, from Mureș County, without known pathologies and treatment, were included. Subjects with BMI ≥ 30 kg/m² and users of creatine supplements were excluded. SCr was measured on Alinity and Cobas proB. Reference intervals were established using the non-parametric method, according to CLSI C28-A3. Method comparison was performed using Wilcoxon/t-test, Bland-Altman and Passing-Bablok, and the Harris-Boyd test for the need of partitioning. Differences were compared with the intra-individual biological variation (BV) of SCr (4.4%).

Results: The differences between methods were 1.6% in women CI (-11.6%, 14.8%) and 4% in men CI (-5.7%, 13.6%). In both groups, Bland-Altman intervals exceeded BV. Passing-Bablok analysis did not show deviation from linearity, and the Harris-Boyd test did not indicate the need for statistical partitioning. However, analytical differences justified the practical separation of RIs. The reference intervals were 0.58-0.94 (Alinity) and 0.54-0.94 mg/dL (Cobas) in women, respectively 0.73-1.23 and 0.73-1.17 mg/dL in men. Compared to manufacturer values, the RIs were generally narrower; however, for Cobas in women, the upper limit was slightly higher.

Conclusions: Differences between methods suggest the need for method-specific reference intervals. The obtained RIs, generally narrower than those of the manufacturer, highlight population characteristics.

Keywords: analytical methods, reference intervals, serum creatinine

P36. LIPOPROTEIN(A) AND APOLIPOPROTEIN B: EMERGING ATHEROGENIC BIOMARKERS IN PERSONALIZED MEDICINE

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Introduction: Personalized medicine represents a critical trend in the evolution of clinical practice. There is notable interindividual variability in clinical presentation, such that patients with similar lipid profiles may exhibit different outcomes: some develop atherosclerotic disease, while others do not. This divergence is largely determined by levels of Lipoprotein(a) [Lp(a)] and Apolipoprotein B (Apo B).

Methods: A systematic review of the scientific literature was conducted using PubMed, Scopus, and Web of Science databases. Original research articles, meta-analyses, and relevant clinical guidelines focusing on Lp(a) and Apo B were included.

Results: In earlier approaches to assessing atherothrombotic risk, measuring total cholesterol was considered sufficient; subsequently, LDL cholesterol became the primary focus. Today, scientific understanding has advanced with the evaluation of novel biomarkers—key components of lipoprotein particles: Lp(a) and Apo B. Lp(a) is primarily genetically determined and minimally influenced by therapeutic interventions. It contains a structure homologous to plasminogen and contributes to plaque destabilization, increasing the risk of myocardial infarction or cerebrovascular accident even in individuals with otherwise “normal” laboratory results. Following the International Consensus Statement in Brussels advocating for expanded testing and management of Lp(a) as part of cardiovascular health strategies, recent guidelines have recommended a one-time measurement of Lp(a) to identify individuals with a genetic predisposition to atherosclerotic cardiovascular disease. Apolipoprotein B is present in all atherogenic lipoprotein particles and is increasingly used to assess cardiovascular risk, gradually superseding LDL cholesterol. To evaluate atherogenic potential and optimize therapy in patients receiving lipid-lowering treatment, direct quantification of Apo B-containing particles is valuable, as it provides a more precise assessment of particles capable of promoting atherosclerotic deposition.

Conclusions: Lp(a) is officially recognized as a significant risk modifier, and repeated measurement may be necessary for accurate cardiovascular risk stratification. Apo B is becoming the gold standard for evaluating the risk of myocardial infarction and stroke and serves as a therapeutic target within the lipid profile. Understanding the clinical significance of these biomarkers enables a more vigilant approach to personalized treatment.

Keywords: atherogenic biomarkers, Apo B, cardiovascular risk, Lp(a)

P37. CATHEPSIN S, B, AND CYSTATIN C IN THE ASSESSMENT OF ATHEROSCLEROTIC BURDEN AND DISEASE PROGRESSION IN CAROTID ARTERY STENOSIS AND PERIPHERAL OBLITERATIVE ATHEROSCLEROSIS

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Introduction: Cathepsins are cysteine proteases involved in the development, progression, and destabilization of atherosclerotic plaques. Cystatin C, a ubiquitary low-molecular-weight protein, acts as an endogenous inhibitor of these enzymes. Increased circulating levels, tissue accumulation of cathepsin B (Cat B) and S (Cat S), and cystatin C (Cys C) depletion have been associated with arterial wall inflammation, extracellular matrix degradation, and plaque destabilization.

Methods: In the first study, we analyzed the variations of Cat S and Cys C in 90 patients with obliterative atherosclerosis, in relation to clinical stage, functional and laboratory parameters. In the second study, serum cathepsin B and cystatin C levels, as well as their local expression, were comparatively evaluated in another 27 patients—16 with carotid atherosclerosis and 11 with femoral atherosclerosis—indicated for thrombectomy, immediately prior to surgery.

Results: Cys C and the Cat S/Cys C ratio were associated with ankle-brachial index (ABI) scores <0.4 in univariate and multiple regression models. Cys C was elevated, while the Cat S/Cys C ratio was significantly lower in subjects with polyvascular atherosclerotic disease. In the second study, groups with carotid and femoral atherosclerosis showed no differences in serum Cat B and Cys C concentrations. Multivessel disease did not significantly affect the levels of the two proteins. In atherosclerotic plaques, the expression pattern was relatively different, with higher Cat B/Cys C ratios in carotid stenosis patients. At the level of the fibrous cap, Cys C expression showed a significant negative correlation with that of Cat B ($r=-0.46$, $p=0.039$).

Conclusions: Cys C and the Cat S/Cys C ratio may be useful in stratifying the biological stages of obliterative peripheral atherosclerosis and assessment of atherosclerotic burden. The Cat B/Cys C ratio shows a wide range distribution and relatively different patterns in carotid and femoral atherosclerosis.

Keywords: atherosclerosis, cathepsin B, cathepsin S, cystatin C

P38. LABORATORY MONITORING OF CARDIAC FUNCTION IN PATIENTS WITH DIABETES MELLITUS: ROLE OF BIOMARKERS

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Introduction: Diabetes mellitus represents a major cardiovascular risk factor, accelerating atherosclerosis and increasing the incidence of silent myocardial ischemia and heart failure. Cardiac involvement in diabetic patients is often underdiagnosed due to atypical or absent symptoms. The aim of this study was to evaluate the role of laboratory parameters in monitoring cardiac function and cardiovascular risk in patients with diabetes mellitus, with emphasis on their utility in early detection and risk stratification.

Methods: The study was conducted on a group of patients admitted to the Emergency County Clinical Hospital "Saint Apostle Andrei", Constanța, between 2024 and 2025, diagnosed with acute cardiac conditions, of whom a subgroup had diabetes mellitus. The study group was analyzed according to the presence of cardiovascular risk factors, with diabetes mellitus considered a major associated factor. Laboratory investigations included glycemic control markers (blood glucose, HbA1c), lipid profile (LDL, HDL, triglycerides), inflammatory markers (CRP), renal function (urea, creatinine), and cardiac biomarkers (troponin T). Microalbuminuria was also assessed as an early indicator of endothelial dysfunction and cardiovascular risk.

Results: Diabetes mellitus was associated with an increased cardiovascular risk profile, characterized by dyslipidemia, chronic inflammation, and endothelial dysfunction. Elevated HbA1c levels were correlated with a higher incidence of cardiovascular events, confirming its role as a predictive marker for cardiac complications. Microalbuminuria proved to be an early and strong indicator of cardiovascular risk, reflecting both renal and vascular impairment.

Conclusions: Inflammatory markers such as CRP and alterations in the lipid profile indicate the progression of atherosclerosis and an increased risk of cardiac events. Troponin T remained essential for detecting myocardial injury, including in patients with atypical clinical presentation.

Keywords: biomarkers, cardiovascular risk, diabetes mellitus, HbA1c, microalbuminuria

P39. GLYCATION OF SMALL PROTEINS vs GLYCATED HEMOGLOBIN: NOVEL CANDIDATE MARKERS AS INDICATORS OF METABOLIC STATUS IN PATIENTS WITH TYPE 1 AND TYPE 2 DIABETES

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Introduction: An increasing body of research indicates that protein glycation—a non-enzymatic post-translational modification—plays a significant role in the onset, progression, and development of various pathologies associated with metabolic diseases, including vascular and neurodegenerative disorders. In this study, we present molecular evidence demonstrating that glycation of certain small hemoproteins is a kinetically prior process to hemoglobin glycation.

Methods: To investigate protein glycation, hepatic mitochondria, cytochrome c, and hemoglobin (monomeric and tetrameric forms) were incubated with 40 mM sugars (glucose, galactose, fructose, and ribose) and methylglyoxal at 37 °C for three days. Proteins were analyzed by phenylboronic acid electrophoresis, with and without trypsin digestion. Samples were also subjected to fluorescence, Raman, and FTIR spectroscopic analyses.

Results: Cytochrome c and monomeric hemoglobin (PDB: 5TY3, 1ECA) were exposed to glycation, and the resulting data were compared with clinically used glycated hemoglobin standards (Roche Diagnostics, USA). Electrophoretic analysis, with and without enzymatic digestion, revealed increased spot affinity for the dye, consistent with exposure of hydrophobic amino acids characteristic of the Amadori reaction. Spectroscopic data confirmed extensive glycation through a decrease in histidine and arginine signals (known glycation targets). Kinetic studies further assessed functional effects by measuring the intrinsic peroxidase activity of hemoproteins, which decreased logarithmically as glycation progressed. These alterations were also observed in mitochondrial suspension studies.

Conclusions: Electrophoretic, spectroscopic, and kinetic analyses demonstrated that the tested hemoproteins are more susceptible to glycation than human hemoglobin and to subsequent structural modifications, which may play a key role in the onset and progression of vascular diseases.

Keywords: cytochrome c, hemoproteins, metabolic disease biomarkers, protein glycation

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P40. DIABETES AND CARDIOVASCULAR COMORBIDITIES: WHAT LIES WITHIN THE ROUTINE BLOOD TESTS

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Introduction: Cardiovascular (CV) complications represent the one of the leading causes of mortality among individuals with diabetes. Persistent hyperglycaemia and insulin resistance contribute to inflammatory responses and vascular injury, thereby elevating CV risk. Recent studies demonstrate that standard blood test markers are reliable indicators of these risks in both type 1 (T1DM) and type 2 diabetes (T2DM), as they reflect underlying metabolic status and systemic inflammation.

Methods: Samples from 8,092 diabetes patients (2019-2023), with (DM+sCVD) or without symptomatic cardiovascular diseases (DM), were collected and inflammatory and composite metabolic biomarkers were calculated, such as SIRI (systemic inflammatory response index), NLR (neutrophil-to-lymphocyte index), MLR (monocyte-to-lymphocyte ratio), MHR (monocyte-to-HDL ratio), PLR (platelet-to-lymphocyte ratio), THR (triglyceride-to-HDL ratio) and TyG (triglyceride/glucose index). Group comparisons and analyses of sub-cohorts, including patients with sCVD, were performed using appropriate statistical methods.

Results: Statistically significant differences ($p < 0.001$) were found between the DM and DM+sCVD groups, except for TyG ($p = 0.101$), PLR ($p = 0.463$), and THR ($p = 0.373$). However, multivariate data analysis revealed that even though the differences were small, they might show statistically significant tendencies, as seen with TyG. Stratification according to diabetes type and sCVD revealed sub-population specific differences. Among patients with T2DM+sCVD higher odds of exceeding cut-off values were observed for MHR [1.443, CI95%: 1.234-1.688], MLR [1.360, CI95%: 1.154-1.602], and THR [1.424, CI95%: 1.234-1.643], with subunit odds ratios found for NLR and SIRI. The T1DM+sCVD subpopulation showed higher odds ratio only for MHR ($p < 0.05$). In the sCVD sub-cohort statistically significant differences were obtained only for SIRI and NLR in a symptomatic-dependent manner.

Conclusions: Routine blood tests provide valuable information regarding cardiovascular risk in people with diabetes. Analysing a range of haematological and metabolic biomarkers enhances clinical decision-making, especially for those with cardiovascular comorbidities.

Keywords: cardiovascular risk, diabetes mellitus, haematological biomarkers, multivariate data analysis

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P41. MODIFICATION OF THE INFLAMMATORY RESPONSE IN PATIENTS WITH PULMONARY TUBERCULOSIS ASSOCIATED WITH DIABETES MELLITUS

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Introduction: The association between diabetes mellitus (DM) and pulmonary tuberculosis (TB) represents a major global public health challenge, with diabetes being recognized as a significant risk factor for the development and progression of pulmonary tuberculosis. The present study analyzes in detail the immunological features of TB/DM comorbidity, highlighting the impact of diabetes on TB pathogenesis and on the mechanisms involved in the innate immune response.

Methods: This prospective observational study was conducted at the Institute of Pneumology “Chiril Draganiuc”, Chișinău, Republic of Moldova, during the period 2019–2024, and included 118 patients. Participants were divided into two subgroups: group L1—patients with TB without DM, evaluated before and after treatment under inpatient conditions, and group L2—patients with TB associated with DM, similarly evaluated before and after anti-tuberculosis treatment under inpatient conditions. All participants, who were sensitive to anti-TB treatment, were hospitalized for a period of one month. Diagnosis and monitoring were performed by measuring C-reactive protein (CRP) and the levels of pro-inflammatory cytokines.

Results: The serum level of IL-1 β showed a significant decrease of 15.6% during treatment, which was associated with a 30.4% reduction in IL-6. These cytokines, considered important triggering factors for CRP synthesis, also showed a decrease in group L1. Notably, the reduction in serum CRP levels was similar in both groups (47.8%). In contrast to the positive dynamics of IL-8 in group L1, this cytokine, also recognized for its chemokine properties, decreased by 42.6% in group L2 after treatment. Furthermore, TNF- β levels in patients with DM showed a more pronounced decrease compared to group L1 (52.9% vs. 14.28%).

Conclusions: In conclusion, TB/DM comorbidity is characterized by a more pronounced reduction in IL-6 and TNF- β compared to group L1 during anti-TB treatment, as well as by a significant decrease in IL-8, suggesting an attenuation of the inflammatory response.

Keywords: C-reactive protein, diabetes mellitus (DM), pro-inflammatory cytokines, pulmonary tuberculosis (TB)

P42. OXIDATIVE STRESS AND COMPOSITE INFLAMMATORY INDICES IN HEMODIALYSIS AND DIABETIC NEPHROPATHY PATIENTS

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Introduction: Oxidative stress and systemic inflammation are key features of advanced kidney disease, but the relationship between oxidative markers and combined inflammatory indices remains unclear. We compared AOPP and TBARS, along with CAR (the C-reactive protein-to-albumin ratio) and IBI (defined as C-reactive protein $\times$ neutrophil-to-lymphocyte ratio), between the hemodialysis (HD) and diabetic nephropathy (DN) groups, and examined their relationships with renal function.

Methods: We analyzed 50 HD and 50 DN patients. Between-group differences were mainly assessed with nonparametric tests; Pearson correlation, along with multiple linear regression, were used to explore the relationship between oxidative and inflammatory markers and estimated glomerular filtration rate, eGFR.

Results: eGFR was significantly lower in HD than in DN, with median values of 5.58 versus 56.75. Oxidative stress markers were notably higher in HD, with median AOPP at 25.53 compared to 9.51, and median TBARS at 8.69 versus 1.97. CAR and IBI also showed significant differences between groups, with median CAR at 1.06 versus 0.27 and median IBI at 147.2 versus 31.5 in HD and DN, respectively. Both CAR and IBI were strongly correlated in each group, especially in HD. However, neither AOPP nor TBARS demonstrated a significant correlation with eGFR, and CAR and IBI were not significantly associated with eGFR in either group. In multiple linear regression analysis, neither the AOPP plus TBARS model nor the CAR plus IBI model independently predicted eGFR in HD or DN, with low explained variance: $R^2=0.010$ and 0.009 in HD, and 0.018 and 0.046 in DN.

Conclusions: HD and DN exhibited distinct oxidative and inflammatory profiles, with increased oxidative stress in HD and notable differences between groups in CAR and IBI. However, neither oxidative stress markers nor the composite inflammatory indices independently accounted for renal function in this dataset, indicating limited usefulness as standalone predictors of eGFR.

Keywords: chronic kidney disease, diabetic nephropathy, hemodialysis, inflammatory indices, oxidative stress

P43. CHRONIC KIDNEY DISEASE AND ITS ASSOCIATED COMORBIDITIES

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Introduction: Chronic kidney disease (CKD) is a major public health concern worldwide, with prevalence steadily increasing, especially among the elderly and those with other chronic conditions. The main effects of CKD include anemia, malnutrition, bone, neurological, cardiovascular, and immune system disorders, which are particularly apparent in stages G4 and G5, although many start as early as stages G2–G3. This study aimed to examine the comorbidities associated with CKD.

Methods: The study involved 320 patients (181 women and 139 men) with CKD, stages G1–G5, all having at least one comorbidity. Urea, creatinine, eGFR, albuminuria, and renal ultrasound were used to evaluate the study participants.

Results: 73.125% of CKD patients had hypertension; 33.125% had ischemic heart disease; 31.875% had atherosclerosis; 71.125% were obese; 28.4375% had type 1 diabetes; 12.1875% had type 2 diabetes; 15.625% had neoplasms. 46.56% of patients were between 60 and 74 years old, 20.3125% were over 75, 18.4375% were between 45 and 59, 9.6875% were between 30 and 44, and 3.75% were under 30. Renal function analysis revealed changes in eGFR (below 60 mL/min/1.73 m²) in 80.3125%, low albumin (<3.4 g/dL) in 85%, elevated urea (>50 mg/dL) in 45.31%, and creatinine (>1.3 mg/dL) in 37.5%.

Conclusions: These changes indicate not only advanced kidney damage but also a metabolic disturbance linked to chronic inflammation, electrolyte imbalances, and multiple organ dysfunction. Since obesity and cardiovascular diseases are often associated with CKD, evaluating kidney function should be approached from an interdisciplinary perspective.

Keywords: albuminuria, chronic kidney disease, diabetes mellitus, hypertension, obesity

P44. MEDIUM MOLECULAR WEIGHT PEPTIDES AND URINARY ENZYMES: BIOMARKERS OF ENDOGENOUS INTOXICATION

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Introduction: Intoxication syndrome in tubulointerstitial nephropathies represents the totality of clinical and biological manifestations caused by the accumulation of toxic metabolic products in the body, as a result of impaired renal tubular function. The clinical importance of the intoxication syndrome lies in the fact that it reflects the severity of renal dysfunction and necessitates the initiation of appropriate treatment, which may include dietary measures, correction of metabolic imbalances, and, in severe cases, the initiation of renal replacement therapy, such as dialysis. We aimed to evaluate endogenous intoxication by determining medium molecular weight peptides (MMP) and certain urinary enzymes in patients with chronic tubulointerstitial nephropathies.

Methods: The study included 56 patients with chronic tubulointerstitial nephropathies in the latent phase (Group I), with a mean age of 51±7.1 years, and 52 patients with chronic tubulointerstitial nephropathies during exacerbation (Group II), with a mean age of 49±6.8 years. The control group consisted of 35 apparently healthy individuals with normal urinalysis results. The activity of MMP, urinary enzymes AAP, LDH, γ-GT, and NAG was assessed using spectrophotometric methods. In parallel, other biochemical parameters were also investigated.

Results: The measured level of MMP in serum reflected the intensity of endogenous intoxication, while urinary enzymes indicated the degree of renal impairment caused by this intoxication.

Conclusions: The simultaneous evaluation of urinary enzymes (N-acetyl-β-D-glucosaminidase, γ-glutamyltransferase, alanine aminopeptidase, and lactate dehydrogenase), along with serum medium molecular weight peptides allows the assessment of the severity and progression of the pathological process in chronic tubulointerstitial nephropathies. Thus, these values can be considered markers of endogenous intoxication.

Keywords: chronic tubulointerstitial nephropathies, medium molecular weight peptides, urinary enzymes

P45. COMPARABILITY OF URINARY PROTEIN AND ALBUMIN DETERMINATIONS IN ROUTINE URINALYSIS USING THE LABUMAT 2 AND ATELICA 1500 URINE ANALYZERS

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Introduction: Verification of the comparability of analytical results is one of the requirements of the SR EN ISO 15189:2023 that must be met by accredited laboratories when different equipment or methods are used for the same test. When results are comparable, the equipment or methods can be used interchangeably.

Methods: Urinary proteins and urinary albumin were determined in 20 urine samples collected from hospitalized patients. The samples were initially tested using the LabUMat analyzer with LabStrip U12 mALB/CREA urine test strips and subsequently analyzed on the Atellica 1500 (Cinitel Novus) using CLINITEK Novus PRO 12 cassettes. The weighted kappa test was used to assess the level of agreement between the two determinations performed using the two types of urine test strips. A Cohen's kappa coefficient (κ) ≥ 0.5 was considered acceptable for the determinations to be regarded as comparable.

Results: For urinary proteins, the κ value was 0.52, while for urinary albumin it was 0.67.

Conclusions: The results of urinary protein and urinary albumin determinations obtained using the LabUMat analyzer are comparable to those obtained using the Atellica 1500 analyzer.

Keywords: Cohen's kappa coefficient (κ), comparability, urinary albumin, urinary proteins

P46. IMPACT OF SAMPLE COLLECTION CONTROL ON PREANALYTICAL NON-CONFORMITIES: A COMPARISON BETWEEN PRIVATE AND PUBLIC LABORATORIES

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Introduction: The rejection of non-compliant samples represents a critical component of quality management in clinical laboratories, both private and public, ensuring the accuracy, precision, and reliability of laboratory results.

Methods: The study was conducted between March 26, 2024 and September 24, 2025, at Praxis Health Laboratory in Iași, Romania, based on the sample rejection criteria established by the ISO 15189. Samples collected for biochemistry, complete blood count (CBC), coagulation tests, and erythrocyte sedimentation rate (ESR) were included. Non-compliance rates were analyzed in comparison with those reported in the scientific literature for public laboratories. The evaluated non-conformities included coagulated samples, hemolyzed plasma, and insufficient sample volume.

Results: The literature reports relatively high rejection rates in public laboratories. In contrast, data obtained from Praxis Health Laboratory, where the sample collection process is strictly controlled by the laboratory staff, demonstrated significantly lower non-compliance rates. Out of a total of 92,638 CBC samples, only 9 samples (0.009%) were coagulated, and 1 sample (0.001%) was incorrectly collected. For coagulation testing, 23 samples (0.13%) out of 16,478 were coagulated. Regarding ESR determination, 43 samples (0.11%) out of 36,737 showed coagulation. Additionally, among the 122,873 biochemistry samples analyzed, only 20 samples (0.016%) presented hemolyzed plasma.

Conclusions: Rigorous control of the sample collection process at Praxis Health Laboratory results in significantly lower rates of non-compliance compared with public laboratories, highlighting the importance of integrating preanalytical processes, particularly sample collection, into the overall laboratory quality management system.

Keywords: coagulated samples, hemolysis, insufficient volume, preanalytical non-conformities

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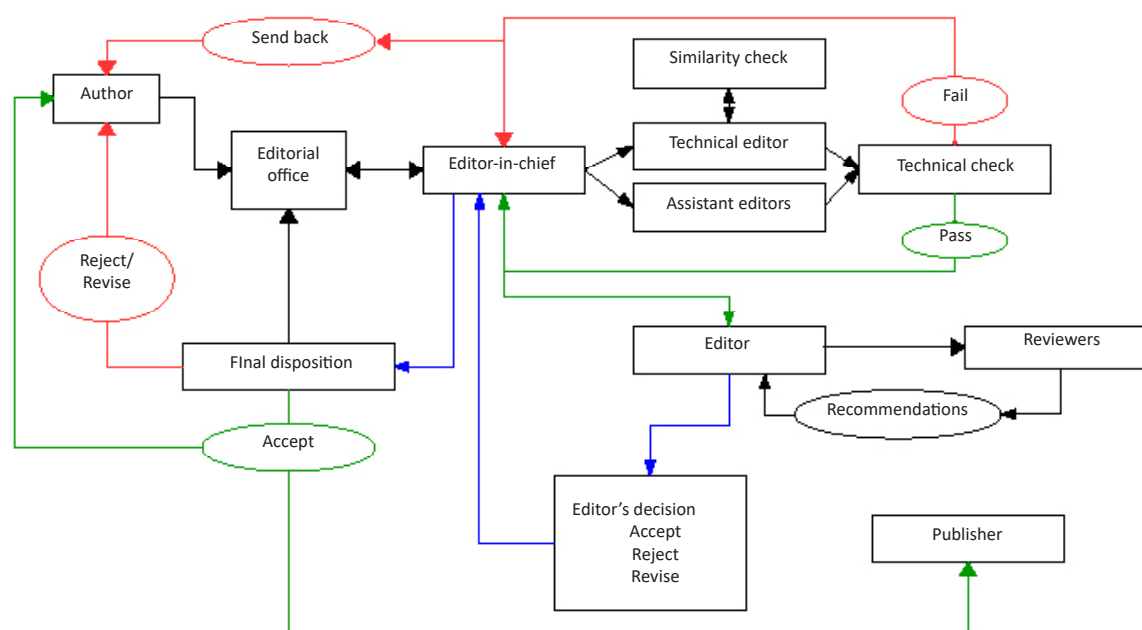
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