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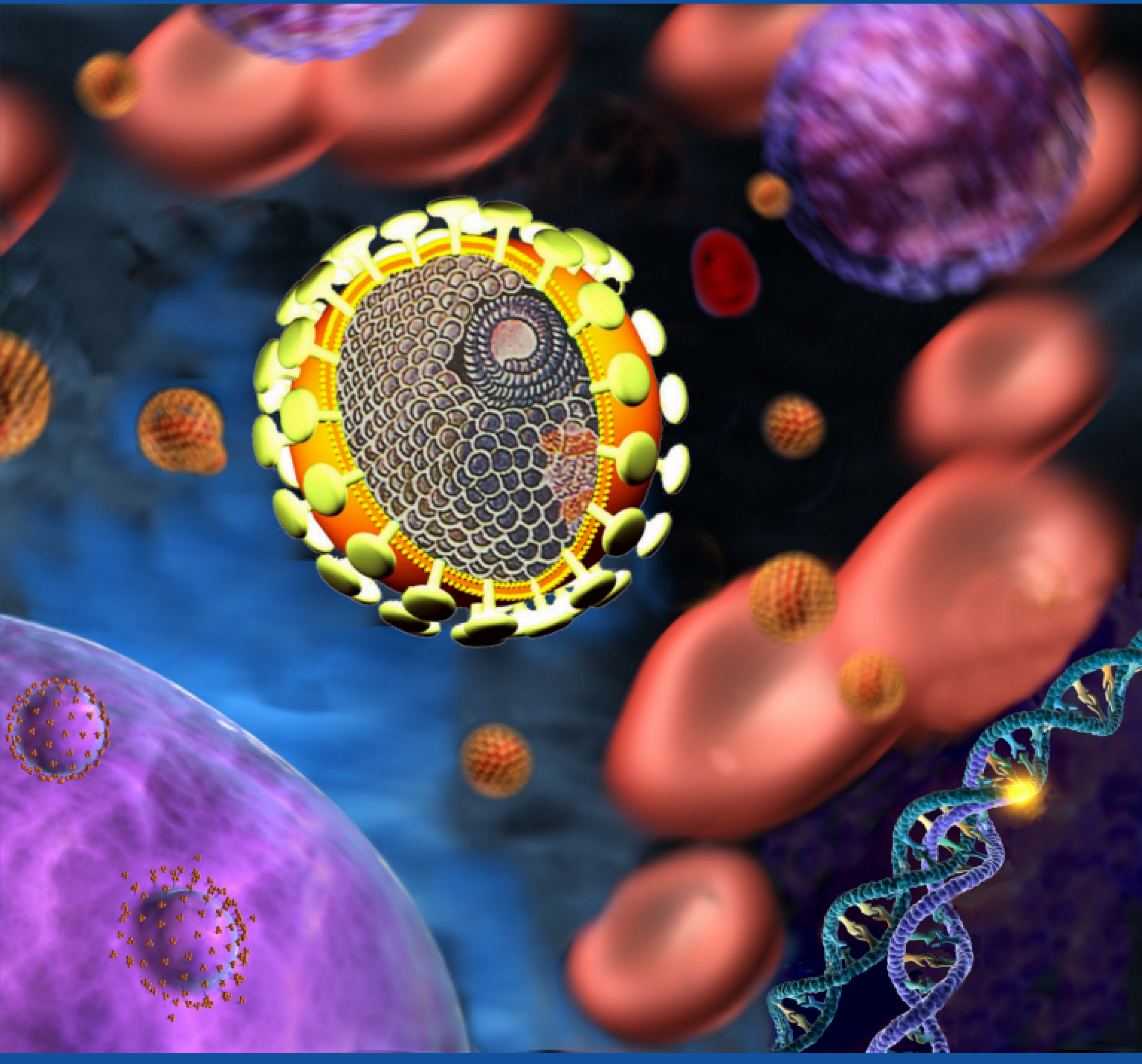

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CNCSIS - Din anul 2008, RRML este inclusă în categoria A de publicaţii a CNCSIS, cu codul CNCSIS 739.
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Asociația de Medicină de Laborator din România

VOLUME OF ABSTRACTS

THE 32nd MEETING OF THE BALKAN CLINICAL LABORATORY FEDERATION

THE 16th CONFERENCE OF THE ROMANIAN ASSOCIATION OF LABORATORY MEDICINE

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Presentation duration: Plenary Report (R) – 20 min, Oral Communication (C) – 10 min, Short Communication / Poster (P) – 5 min.

R1. NAVIGATING CURRENT AND FUTURE ADVANCES, INNOVATIONS, AND CHALLENGES IN LABORATORY MEDICINE. OVERVIEW OF CURRENT TRENDS AND OBSTACLES

Tomris Ozben

IFCC, President & EFLM, Past-President (current)

Laboratory Medicine (LabMed) plays a critical role in enhancing the quality of healthcare by delivering accurate, precise, and timely laboratory test results. These results support evidence-based clinical decisions, contributing to more effective and targeted therapies, reduced morbidity, risk prediction and reduction, improve treatment compliance, and better monitoring of recovery and therapeutic outcomes. LabMed ultimately shortens hospital stays, reduces the risk of hospital-acquired infections, and improves patients' quality of life.

Laboratory Medicine and In Vitro Diagnostics (IVD) represent a sound and strategic investment in healthcare, encompassing a broad spectrum of technologies—from cutting-edge technologies performed in advanced clinical laboratories to user-friendly point of care and self-testing. The global IVD market is expected to double over the next decade, driven by an aging population and the rising burden of non-communicable and chronic diseases across both developed and emerging economies. This growth is occurring despite increasing pressures to demonstrate medical value, navigate complex regulatory frameworks, and manage economic constraints. Next-generation Point-of-Care Testing (POCT) platforms are expected to grow slightly faster than central laboratory markets. The implementation of the In Vitro Diagnostic Regulation (IVDR) is transforming the landscape for IVD companies, redefining product development, lifecycle management, and commercialization strategies. Clinical evidence must demonstrate scientific validity, analytical and clinical performance, and their interconnected roles in performance evaluation.

Key Challenges in Laboratory Medicine are Data Security and Privacy: Ensuring patient data protection and regulatory compliance; Quality Control: Maintaining accuracy, precision, and reliability of test results; Cost Management: Balancing innovations with budgetary constraints and Regulatory Compliance: Adapting to evolving standards and stringent regulations.

Key Advances in Laboratory Medicine: Automation and Robotics; Molecular Diagnostics; Precision Medicine; Genomics, and Multi-omics; Point-of-Care Testing; Digitalization of Healthcare; Artificial Intelligence (AI) and Machine Learning; Integrated Diagnostics; Lab-on-a-Chip Technologies and Microfluidics.

The emergence of "Industry 4.0" and the big data revolution are reshaping Laboratory Medicine. Smart technologies and cyber-physical systems are enhancing the quality and efficiency of diagnostics and patient care. It is essential for clinical laboratory professionals to build digital literacy and gain fluency in these emerging technologies, which will increasingly be integrated into healthcare delivery. Laboratory 4.0 is transforming laboratory operations from sample logistics to data management enabling personalized, efficient, and responsive diagnostic services. Big Data and Cloud computing are pivotal in driving future growth and scalability. Breakthroughs in biotechnology, genetic engineering, and diagnostics, alongside high-throughput and high-performance analytical techniques, are fueling innovation, especially in the realm of personalized medicine. AI-powered laboratories overcome challenges, such as inaccurate and inconsistent results, data overload, labor-intensive processes, limited expertise, cost and resource constraints. AI algorithms are enhancing diagnostic accuracy, automating routine workflows, and unlocking insights from complex datasets leading to faster and more reliable diagnostic outcomes.

Going forward, Laboratory Medicine must emphasize Advanced and Integrative Diagnostics to extend its influence beyond technical health service provision. It is imperative that the discipline positions itself at the core of clinical dialogue. Innovations in digitalization and automation will continue to drive improvements in diagnostic speed, accuracy, and cost-efficiency.

Keywords: artificial intelligence, in vitro diagnostics, laboratory medicine, personalized medicine, point-of-care testing

R2. ACTIVITIES OF EFLM – TRENDS IN LABORATORY MEDICINE / NEW TRENDS IN EDUCATION

Tomáš Zima

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The laboratory medicine is dramatically change during these times. The new trends in laboratory medicine follow the trends in healthcare as arteficial intelligence and machine learning, real time diagnostics, personalised healthcare, precision medicine and genomics. The our main trends including total laboratory automation – TLA, connecting disciplines and technologies, redesign of core labs – with satellite labs and POCT systems, new technologies e.g. LC/MS-MS and its automation, nanotechnology,-omics, telemedicine and integrated data and working on integrated diagnostics (labs and imaging). We need strong IT technologies supporting and integrated data for machine learning and AI expert systems.

Our discipline- laboratory medicine ask for update education and training of our professional and also high educated staff from different disciplines (IT, economy, physicists, etc.). The education and training of laboratory medicine professionals are evolving to meet the demands of advancing technology, changing healthcare environments, and emerging global health challenges. Training programs incorporate new emerging technologies, molecular biology techniques, digital pathology and artificial intelligence (AI) to improve diagnostic accuracy and efficiency and prepare professionals. Information technologies innovate the educational process, to provide new possibilities, including modeling, simulations, telemedicine, virtual reality, artificial intelligence. Online tools enable anyone to access high-quality educational and professional content around the world, Digitization of teaching improves the availability of education, individualization of learning, increases the interactivity and effectiveness of teaching with AI driven learning programmes. Artificial intelligence and robotics will increasingly enter healthcare, and it is necessary to educate professionals in this area.

The education and training of laboratory medicine professionals are undergoing significant changes to keep pace with technological advancements, healthcare demands, and global health challenges. By integrating advanced technologies, emphasizing interdisciplinary collaboration, ensuring regulatory compliance, and promoting lifelong learning, the field is preparing professionals to deliver high-quality, patient-centered care in a dynamic healthcare landscape.

Key words: AI, education, mass spec, new trends

R3. EFI ACCREDITATION IN TRANSPLANT IMMUNOLOGY: ADVANTAGES AND BENEFITS

Ileana Constantinescu[1,2], Ion Maruntelu[2], Adriana Talangescu[1,2], Maria Tizu[1,2], Alexandra-Elena Constantinescu[1]

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2. Centre for Immunogenetics and Virology, Fundeni Clinical Institute, Bucharest, Romania

Introduction: The European Federation of Immunogenetics (EFI) is a European professional association that sets standards in Transplant Immunology. The EFI structure consists of the Accreditation Committee, the Standards Development Committee, the EFI Commissioners of the European Regions (EFI has 8 European Regions- Romania is part of Region 8), inspectors and HLA laboratories accredited or in the process of accreditation. EFI accreditation involves the continuous improvement of standards for histocompatibility and immunogenetics. These standards are continuously changed and improved to allow laboratories working in the field of transplantation immunology to work and communicate in the same language.

Material and methods: https://efiweb.org/fileadmin/Efi_web/Committees/Standards/Standard_v8.1_clean.pdf. For a transplantation immunology laboratory, it is important to qualify the staff and to continuously maintain quality standards. The quality assessment program requires continuous implementation, facilities, results rendered through software that is always updated, reagents must be adequate, there must be a procedures manual. Participation in external quality control schemes is mandatory for all parameters worked on. Personnel competence must be evaluated periodically, and results must be archived both electronically and on paper. Quality control targets the components of the pre-analytical processes, the analytical process and the post-analytical stages, all of which are equally important.

Results: The performance indicators for the transplant immunology laboratory are reflected in the success of all types of transplants it serves.

Conclusions: Accreditation with EFI ensures a high-performance activity, corresponding to the standards so that all results have a special accuracy so necessary for all transplant procedures.

Keywords: European Federation of Immunogenetics (EFI), histocompatibility and immunogenetics standards, laboratory accreditation, transplant immunology, quality control

R4. ISO ACCREDITATION – PRACTICAL ASPECTS

Radu Ilinca, Ionuț Adrian Chiriac

Faculty of Dentistry, ”Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

Introduction: The concept of “accreditation” is a broad one and has very different meanings and implications. Sometimes, “accreditation” is confused with “certification”, especially since some certification schemes use referentials from the ISO family of standards. In order to benefit from the advantages offered by an accreditation from the ISO family of standards, it is necessary to clarify the benefits and value offered by such accreditation. The presentation of the practical aspects of ISO accreditation is also made from the international perspective on such an outcome.

Methods: Aspects related to ISO accreditation, both at a conceptual level as resulting from the hierarchy of international documents (International Laboratory Accreditation Cooperation – ILAC, European Cooperation for Accreditation – EA) and national, but also at a practical level with a view to implementation, are examined.

Results: Successful implementation of an ISO accreditation standard generates real and measurable benefits for a laboratory. These benefits go far beyond the scope of the laboratory's internal activity and have a positive impact on patients, consumers, the business environment, and society in general.

Conclusions: The decision to work under an accredited regime is an individual decision of each laboratory and should be motivated beyond short-term net benefits. These are highlighted on multiple dimensions (technical, economic, legal).

Keywords: accredication, ISO 15189, medical laboratory, standardization, quality assurance culture

C5. ANMCS ACCREDITATION – THE VALUE FOR CLINICAL LABORATORIES

Monica Dugăeșescu[1], Ion Maruntelu[1], Andreia-Ioana Constantinescu[1], Alexandra-Elena Constantinescu[2], Ileana Constantinescu[1,2]

1. Centre for Immunogenetics and Virology, Fundeni Clinical Institute, Bucharest, Romania
2. Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Introduction: The accreditation provided by the National Authority for Quality Management in Healthcare (ANMCS) is based on an integrated approach to the quality and safety of the medical act, in which the clinical laboratory occupies a central position. By ensuring accuracy, speed, and traceability, the clinical laboratory supports clinical decisions and facilitates efficient patient management.

Material and method: The information publicly available on the website https://anmcs.gov.ro/web/ was accessed and synthesized for the current paper, selecting those aspects that are applicable in the field of laboratory medicine.

Results: The second edition of the accreditation standards and the accreditation procedure for healthcare units were included in order no. 446/2017 of the Ministry of Health. The applicability of the standards refers to all areas of activity of a healthcare unit, including the clinical laboratory. The aspects of interest for the activity of the clinical laboratory covered by the ANMCS accreditation include the flow of samples and information between the attending physicians and the clinical laboratory, quality control, waste management resulting from the activity of the clinical laboratory, control of healthcare-associated infections, and more. In addition, for clinical laboratories operating on an outpatient basis, ANMCS approved separate accreditation standards, by order no. 353/2019 of the President of ANMCS, according to which the emphasis is on the assessment of the quality management system, organizational management, and the activity of the medical analysis laboratory staff, in relation to the complexity of the activity carried out.

Conclusions: The medical analysis laboratory represents a fundamental pillar in healthcare services, representing for these reasons the object of ANMCS accreditation, an approach that aims to ensure and continuously improve integrated medical care for patients.

Keywords: accreditation standards, clinical laboratory, National Authority for Quality Management in Healthcare (ANMCS), patient safety, quality management

C6. QUALITY MANAGEMENT SYSTEM IN LEGAL MEDICINE INSTITUTIONS

Mihai Marinescu, Sorin Hostiuc

National Institute of Legal Medicine ”Mina Minovici”, Bucharest, Romania

Introduction: The implementation of the quality management system within forensic medicine institutions has proven to be a strategic decision, both in terms of improving its overall performance and providing a solid foundation for sustainable development initiatives. The main benefits of implementing the quality management system are the ability to consistently provide products and services that meet customer requirements and applicable legal and regulatory requirements, facilitating the opportunity to increase customer satisfaction in relation to identified risks and opportunities, as well as compliance with requirements and reproducibility of actions and decisions.

Methods: We have chosen a process-based approach for our quality management system. The reference standard SR EN ISO 9001: 2015 promotes the process-based approach when developing, implementing and improving the effectiveness of a quality management system, in order to increase customer satisfaction by meeting their requirements. Understanding and managing interrelated processes as a system contributes to the efficiency and effectiveness of the organization in achieving the intended results. The management of processes and the system as a whole can be achieved using the PDCA cycle with a general focus on risk-based thinking aimed at obtaining advantages and opportunities, as well as preventing unwanted results. The strength lies in improving processes, so that in this way performance can be improved.

Results: Since the implementation of the quality management system at the National Institute of Legal Medicine "Mina Minovici" Bucharest, we have observed a continuous and significant improvement in the quality and performance of processes, a streamlining of the processes involved in the development of forensic documents, as well as an increase in the degree of customer satisfaction. Also, risks and non-conformities are much more easily identified, making it possible to implement effective measures to remedy them.

Conclusions: In an environment with an ever-increasing dynamic complexity, consistently complying with requirements and taking into account future needs and expectations is a challenge for any medical institution, which is why we consider, based on our experience so far, that implementing a quality management system represents an optimal decision.

Keywords: ISO 9001:2015, PDCA cycle, process-based approach, quality management system

R7. THE COSTS OF A THOROUGH INTERNAL AUDIT: IS IT WORTH IT?

Chris Gunning

Director of Operational Excellence, American Association of Laboratory Accreditation (A2LA), United States of America

Introduction: This ISO 15189 auditor presentation will introduce participants to ISO 19011, the guideline for auditing management systems as applied to ISO 15189. The participant will learn about auditing principles and develop skills for performing higher-value internal audits.

Methods: The presentation includes audit planning, establishing, implementing, and maintaining an audit program, and also focuses on developing auditing methods, questioning techniques, and record-sampling.

Results: The audience will be introduced to the guidance in ISO 19011 to construct an effective audit program and plan. Discussions will include various types of audit plans and methods, along with the benefits and drawbacks of each. Finally, we will demonstrate the interpersonal skills needed to effectively gather information.

Conclusions: Performing a thorough internal audit is essential for any laboratory to determine compliance with both the requirements of the international standards and also the laboratories own management system requirements. The effect of this thoroughness is to “find your own problems before the rest of the world does”. Development of an effective internal audit program is not an easy task, but will lead to immeasurable benefits.

Keywords: accreditation, internal audit, interpersonal skills, ISO15189, ISO 19011, quality assurance

C8. IMPLEMENTATION AND MANAGEMENT OF POINT-OF-CARE TESTING

Neda Milinković

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Standard laboratory tests are part of large healthcare systems and are under the control of experienced laboratory professionals. However, different disease patterns, patient location and specific treatment methods often require rapid laboratory testing to ensure timely and appropriate health care.

Over time, portable testing devices/instruments with smaller dimensions have been developed that can provide a laboratory result in a very short turnaround time of the analysis. Such tests in close proximity to the patient, i.e. at the point of care (POCT), are increasingly accepted as equivalent to classical laboratory diagnostics. However, despite the number of tests that are routinely determined by POCT testing and on the basis of which a clinically meaningful and relevant decision can be made, there are several challenges that need to be overcome.

POCT refers to all tests that are performed outside of a traditional core or central laboratory. POCT is usually performed by non-laboratory personnel and the results are used to make clinical decisions, so it is very important to establish clear criteria for who performs POCT. This aspect is very important from a regulatory perspective, so it is important that the test itself has a minimal level of complexity and a low risk of false results, that a non-invasive test is used that involves a sample such as capillary blood, saliva or urine.

The laboratory director should evaluate the justification for this type of testing based on technical and economic requirements as well as institutional needs. The participation of medical biochemists, medical specialists and pharmacy students in POCT programs and ongoing training in this area can contribute to the continuous quality assurance of POCT.

Keywords: clinical decision-making, point-of-care testing (POCT), quality assurance, regulatory standards, turnaround time

C9. RISK MANAGEMENT IN PRIMARY HEALTHCARE LABORATORIES: IDENTIFYING AND MITIGATING SOURCES OF ERROR

Danijela Ristovski Kornic

Health Centre Pancevo, Pancevo, Serbia

The clinical laboratory is an integral part of patient care, diagnosis, therapy monitoring, and clinical outcome prediction. Errors can occur at any stage of the total testing process, potentially compromising patient safety. Therefore, identifying sources of error and implementing preventive strategies is essential in laboratory testing.

Risk management starts with identifying potential error sources, assessing their effects and frequency. Strategies to mitigate risks are implemented, with continuous monitoring to maintain risks at clinically acceptable levels. Healthcare professionals must understand different types of medical errors to prevent adverse events. Primary healthcare faces challenges in balancing preventive medicine and chronic disease management. Patients have greater autonomy compared to hospital settings, influencing therapy adherence and test preparation, which increases risks outside healthcare institutions.

Adoption of new technologies, digitalization, improved communication, and error-reporting protocols is transforming laboratory culture. Institutions that foster a patient safety culture and apply risk management significantly enhance safety for both patients and healthcare workers.

Keywords: error prevention, medical laboratory, patient safety, primary healthcare, risk management

C10. A NEW QC RULE FOR IMMEDIATE ERROR DETECTION, MORE EFFICIENT THAN WESTGARD RULES

Atilla Barna Vandra

Brașov, Romania

Introduction: The QC in the clinical laboratory aims to detect errors immediately. Four different dynamics can be identified to reach a critical bias value: (1) after human intervention, (2) after an unexpected shift in bias, (3) a gradual increase in bias, and (4) a constant bias. (Missed immediate error detection). Westgard does not discriminate between them. Makes efforts to be efficient in case 2, but in calculations uses case 4 (assuming erroneously a constant bias in the case of cross-run rules: R4-1S și R10X). After a human intervention, there are no data to apply cross-run rules (R4-1S și R10X).

Methods: It is a theoretical study based on accurate calculations based on the laws of the normal distribution made in EXCEL. Results were compared with JO Westgard's computer simulations. The Rra-2S (run average over 2SD) is applied to values expressed as a percent, and it is calculated the average deviation from the target value (100%)

Results: According to the power function graphs, the Rra-2S rule is more efficient than the within-run rules (R1-3S și R2-2S). Because it can be applied more times from the same data set from which the cross-run rules (R4-1S și R10X) are calculated, it substitutes efficiently for the multi-rules, (all Westgard rules). The QC rules, as calculated by Westgard, would give hundreds of unnecessary alarms. To avoid them (as he acknowledged), Westgard increased the decision limits using sRW instead of sr the correct estimator of s, increasing proportionally the decision limits. An improved and more accurate solution is proposed to increase the decision limits with a constant: the incorrigible bias. (Using the Rra-3S rule in follow-ups)

Conclusions: The proposed rules are simpler to apply and more efficient in all four situations, in which the bias reaches the critical value.

Keywords: bias, decision limits, incorrigible bias, quality control, westgard rules

R11. SUSTAINABLE REFERENCE INTERVALS AND CLINICAL DECISION LIMITS: TOWARDS STANDARDIZATION & HARMONIZATION

Khosrow Adeli

Past President, IFCC.
Head and Professor, Clinical Biochemistry
The Hospital for Sick Children, University of Toronto, Ontario, Canada

Establishing sustainable reference intervals (RIs) and clinical decision limits (CDLs) is essential for ensuring accurate interpretation of laboratory results and supporting evidence-based clinical decision-making. However, substantial variability persists across laboratories, regions, and populations, due to differences in methodologies, instrumentation, and population characteristics. This inconsistency poses a significant challenge to the global standardization and harmonization of laboratory medicine.

Sustainable RIs and CDLs must be scientifically robust, inclusive of diverse populations, and adaptable to evolving clinical practices and analytical technologies. Harmonization efforts, such as the IFCC's global initiatives and the CALIPER project, have demonstrated the feasibility of developing age-, sex-, and ethnicity-specific RIs using standardized protocols. Similarly, efforts to establish universally applicable CDLs for common biomarkers—particularly in areas like cardiovascular disease, diabetes, and infectious diseases—are helping align clinical practice with international best standards.

To ensure long-term sustainability, reference intervals must be periodically re-evaluated to reflect demographic changes, technological advancements, and emerging biomarkers. Integrating big data analytics, real-world evidence, and multicenter collaborations will be critical in refining both RIs and CDLs. Additionally, standardizing pre-analytical and analytical processes, and adopting common measurement procedures traceable to reference systems, are crucial steps toward global harmonization.

This presentation will explore current efforts, challenges, and future directions in achieving sustainable and harmonized reference intervals and clinical decision limits. It will highlight collaborative models that promote equitable access to accurate laboratory interpretation, particularly in under-resourced regions. Ultimately, advancing standardization in this area supports global health equity and improves diagnostic accuracy and patient outcomes across healthcare systems.

Keywords: clinical decision limits, harmonization, reference intervals, standardization, sustainability

C13. ORGANIZATION OF EXTERNAL QUALITY ASSESSMENT SCHEMES: THE CRUCIAL POINT OF EDUCATION AND TRAINING OF SCIENTISTS IN THEIR OPERATION AND MANAGEMENT

Serafeim Karathanos, Alexander Haliassos

Eseap, Athens, Greece

The retirement of older and experienced scientists highlights the urgent need for new staff members to maintain and expand the operation of External Quality Assurance (EQA) Proficiency Testing (PT) providers. ESEAP addresses this by recruiting and training young laboratory scientists on all aspects of EQA schemes.

New colleagues first undergo training on the statistical analysis (consensus mean, CV%, SD, SDI, Δ%) used to evaluate the results and the graphs for displaying the statistics (histograms, Levey-Jennings diagrams, and Youden Plots). A lot of important information can be extracted from these. Additionally, new staff are introduced to the implementation and application of ISO 17043.

The statistical evaluation of the results is crucial, as the possible causes of erroneous results should be detected at this step. Although control sample shipments are always accompanied by instructions for their handling, preparation, and reconstitution, sometimes these instructions may be lost or ignored, resulting in improper dilution of the lyophilized control samples and consequently wrong results (pre-analytical errors). Moreover, some of the most common errors are the incorrect entry of results due to typing errors, inappropriate reporting units of measurement, or exchanging the results of the first control sample with the second and vice versa (post-analytical errors).

Another point of interest for someone new to EQA is the commutability of samples and the need for grouping specific methods or analytical systems. Some analyzers consistently measure higher or lower analyte concentrations than others in the EQA samples, so a separate statistical analysis needs to be done and used within the group of these analyzers.

Finally, the younger staff have to understand that EQA schemes are dynamic and continuously improved by developing existing schemes or designing new ones that cover new needs and enhance participants' performance, which positively impacts patients.

Keywords: EQA, ISO 17043, quality management, training

C14. ON SELECTING AN APPROPRIATE PROFICIENCY TESTING PROVIDER: THEORY

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Introduction: Participation in proficiency testing schemes is both a regulatory and accreditation requirement. The results of participation in proficiency testing schemes are an important but they are not the only component of a much broader concept: ensuring the quality of results. In a globalized market and with the consequent elimination of trade barriers, laboratories have access to a multitude of proficiency testing services offered by a wide range of providers. However, the laboratory is responsible for selecting the proficiency testing schemes in which it participates in order to achieve its ultimate goal: ensuring the quality of results. The main objective of the paper is to present the fundamental criteria that should be taken into account when selecting proficiency testing providers for an informed decision by the laboratory.

Methods: To identify these fundamental criteria for the selection of proficiency testing providers, the most important reference documents in the field issued by the International Laboratory Accreditation Cooperation (ILAC), European cooperation for Accreditation (EA) and International Organization for Standardization (ISO) were studied, as well as relevant scientific articles in the field.

Results: Beyond the commercial offer, a suitable provider should offer the service on an accredited basis or be organized by a respected organization in the industry. The test item should be commutable, the results of participation should be available within a reasonable timeframe for the laboratory and the reports should be accompanied by technical comments on the laboratory's performance.

Conclusions: Selecting a proficiency testing provider is an individual decision for each laboratory. Not all high-quality services are automatically appropriate for the laboratory. Therefore, it is essential for the laboratory to make an informed selection of the provider to ensure that the service meets real needs and is not just a formality.

Keywords: accreditation, commutability, ISO 17043, proficiency testing provider, quality assurance

C15. COMMUTABILITY AND HOMOGENEITY OF PROFICIENCY TESTING SAMPLES

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Introduction: The lack of commutability and homogeneity in external quality control (EQC) samples may lead to the misinterpretation of EQC results, suggesting poor analytical performance when in fact the performance is acceptable. The aim of this study was to evaluate the commutability and homogeneity of human-derived samples used in the UnivQual external quality assessment program.

Methods: Human serum-based surrogate samples prepared within the UnivQual program were assessed for commutability and homogeneity. For commutability testing, 20 patient samples and 3 surrogate samples intended for distribution were analyzed in triplicate within the same analytical run for hormones and infectious disease markers. Deming regression was applied, and the resulting equations were interpreted. For homogeneity testing, two surrogate samples were randomly selected and analyzed in 10 replicates each for biochemical tests, hormones, and infectious disease markers. The resulting data were subjected to ANOVA, and differences were compared to allowable limits based on biological variation.

Results: Deming regression equations for hormones (TSH, free T4, and prolactin) yielded slope values close to 1 and intercepts around 0.001. Similar results were obtained for infectious disease markers. In homogeneity testing, differences observed in biochemical and immunoassay parameters did not reach statistical significance ($p \geq 0.05$), and all differences remained within acceptable limits.

Conclusions: The testing demonstrated that the surrogate samples are commutable, showing analytical behavior similar to that of patient samples. Moreover, the results confirm that the prepared materials are homogeneous and suitable for use in external quality assessment schemes.

Keywords: commutability, homogeneity, proficiency testing

C16. STABILITY OF SERUM LIPOPROTEIN(A) DURING SHORT-TERM REFRIGERATED STORAGE: ANALYTICAL AND QUANTITATIVE ASSESSMENT

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Introduction: Serum lipoprotein(a) [Lp(a)] is a well-established, independent cardiovascular risk factor. However, its analytical stability under short-term refrigerated storage conditions remains insufficiently studied, and recent data are lacking. This study aimed to evaluate the stability of serum Lp(a) concentrations after 3 and 8 days of storage at 2–8 °C, compared to baseline levels.

Methods: A total of 43 serum samples were analyzed for Lp(a) concentration at baseline (Day 0), Day 3, and Day 8 using the Roche Cobas Integra immunoturbidimetric assay. Results were expressed in nmol/L. Statistical analyses included Wilcoxon signed-rank tests, Spearman correlation, and Bland–Altman plots. Changes were calculated both in absolute values (nmol/L) and as individual percentage differences.

Results: No statistically significant changes were observed after 3 days (mean change: +0.52 nmol/L +3.28%; $p = 0.271$) or 8 days (+0.07 nmol/L; +2.39%; $p = 0.876$). All values remained within the 95% limits of agreement in Bland–Altman analysis. Correlation across timepoints was strong (Spearman $\rho \geq 0.996$). Slightly greater variability was noted in samples with Lp(a) <50 nmol/L, though without statistical significance.

Conclusion: Serum Lp(a) remains analytically stable during refrigerated storage at 2–8 °C for up to 8 days. Minor fluctuations, particularly in samples with low baseline concentrations, do not compromise the reliability of Lp(a) testing for clinical or research purposes.

Keywords: immunoturbidimetric assay, lipoprotein (a), preanalytical variability, refrigerated serum stability

C17. COMPARABILITY OF A1C HEMOGLOBIN BETWEEN ALINITY ci AND THE REFERENCE METHOD

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Introduction: Hemoglobin A1c (HbA1c) is used for both diagnosis and monitoring of diabetes mellitus, with clinical decision thresholds established using the reference method (high-performance liquid chromatography, HPLC). However, lack of comparability between routine methods like immunoturbidimetry and the reference method can affect diagnosis and treatment decisions. This study aimed to evaluate the comparability of HbA1c testing between the immunoturbidimetric method on the Alinity ci platform, HPLC using two analyzers, and capillary electrophoresis.

Methods: Samples were collected in EDTA tubes from non-diabetic individuals and patients with diabetes mellitus under treatment. These samples were first analyzed by capillary electrophoresis, followed by the Alinity ci analyzer. Additionally, two sets of samples were analyzed using HPLC: one with the Bio-Rad Variant II analyzer and another with the Tosoh analyzer, followed by measurement with the Alinity ci. Comparability was assessed using Bland-Altman analysis, Passing-Bablok regression, and kappa agreement based on clinical decision thresholds.

Results: For the comparison between Alinity ci and capillary electrophoresis, a mean difference of 0.16% was obtained, with a kappa coefficient of 0.76 (95% CI: 0.66–0.85) across 98 samples. When comparing the Alinity ci and HPLC performed with the Bio-Rad Variant II, 83 samples were tested, yielding a mean difference of 0.05% and a kappa coefficient of 0.89 (95% CI: 0.81–0.97). For HPLC performed with the Tosoh analyzer, 71 samples were analyzed, resulting in a mean difference of 0.22% and a kappa coefficient of 0.80 (95% CI: 0.69–0.91).

Conclusions: The differences observed between Alinity ci and the three methods were lower than the minimum performance criteria based on biological variation recommendations (Bias <2.7%). The kappa coefficient indicated excellent agreement between Alinity ci and the two HPLC methods, and very good agreement between Alinity ci and capillary electrophoresis.

Keywords: comparability, HbA1c, reference method

P1. METHOD FOR CALCULATING STANDARD DEVIATION MEASURED IN REPEATABILITY CONDITIONS FROM INTERNAL QUALITY CONTROL DATA WITHOUT EXTRA MEASUREMENTS

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Introduction: Determining the standard deviation in repeatability conditions (sr) is compulsory but needs several extra measurements. This study presents a method to calculate it from internal QC data without extra measurements.

Methods: The method of calculating sr from duplicate measurement dates back to 1940. The original contribution is to express the results as a percentage of the mean, which permits the inclusion of the results for different levels in the same data set. Such calculations in absolute values would be incorrect. Data obtained in the precision testing according to EP15-3A was used in calculations. The results were compared using three methods (including EP-15-3A), and real-life data were compared with the values measured in the previous precision testing.

Results: The mean coefficient of variation values obtained with the proposed method did not differ more from those obtained with three comparison methods or in the precision testing than the results obtained with the comparison methods from each other. Differences are only due to the usual uncertainties of the statistical methods.

Conclusions: The proposed method assumes: (1) sr has a linear variation with concentration with negligible intercept, and (2) sr is constant. The results confirmed the second assumption (present in the comparison methods, too). The most significant advantage is that no extra measurements are necessary. The amount of data is unlimited, and accuracy can be increased. As with all methods, rounding errors must be minimized. The interference of the reconstitution errors can be avoided. In conclusion, the method is simple, accurate, and economical.

Keywords: quality control, repeatability conditions, reproducibility within laboratory conditions, standard deviation

P2. CREATINE KINASE-MB HIGHER THAN TOTAL CREATINE KINASE, A PARADOXICAL RESULT THAT MAY BE ASSOCIATED WITH TUMOR PATHOLOGY

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Introduction: Creatine kinase (CK) is an enzyme involved in energy metabolism. Both CK and its isoenzyme CK-MB are biomarkers used for the diagnosis of acute myocardial infarction. However, in our current activity we often encounter increased values of these parameters, without association with cardiac pathology. Moreover, the CK-MB activity can be greater than the total CK activity. Observing that this paradoxical result is associated with different malignancies, we set out to investigate the association of different diagnoses of neoplasia with values of the total CK-MB/CK ratio >1.

Methods: We conducted a retrospective study that evaluated the values of CK and CK-MB activity in patients admitted to the Regional Institute of Gastroenterology and Hepatology "O. Fodor" in Cluj-Napoca between June 2023 and March 2024. The association between clinical characteristics (presence of primary tumors or metastases, types of cancer) and laboratory test results on the enzymatic activity of CK-MB and total CK was studied.

Results: Between June 2023 and March 2024, 5233 determinations of CK activity were performed. Of these, in 198 cases it was found that the total CK-MB>CK activity. After excluding duplicates, there were 163 patients with total CK-MB>CK activity values, of which 108 patients (66%) were associated with various forms of neoplasia, primary or secondary. More commonly, these results were observed in patients with colorectal (33.7%), pancreatic (15.95%) and liver (15.33%) tumors. Also, of the total number of patients with CK-MB >total CK, 38% (62 patients) had a poor prognosis, demonstrated by the rapid evolution towards death.

Conclusions: In this study, the total CK-MB/CK ratio >1 showed a significant association with the presence of different forms of neoplasia. A significant percentage of these patients had an unfavorable outcome. The results obtained support the need to continue these investigations, in order to elucidate the pathogenetic mechanisms involved.

Keywords: creatine kinase (CK), creatine kinase-MB (CK MB), tumor pathology

P3. SERUM BETA-GLUCURONIDASE AS A POTENTIAL BIOMARKER IN RENAL LITHIASIS

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Introduction: Renal lithiasis is a common urological condition influenced by metabolic, infectious, and inflammatory factors. The identification of serum biomarkers capable of reflecting pathological activity could significantly enhance disease monitoring and the prevention of complications. Beta-glucuronidase (β-GUS), a lysosomal enzyme involved in the hydrolysis of glucuronides, has been investigated as a potential biomarker in various inflammatory processes, including renal lithiasis.

Methods: The study included 239 patients diagnosed with renal lithiasis, in whom serum β-GUS activity was measured. The values were categorized into three groups: <20 U/L, 20.06–30.44 U/L, and >30.44 U/L (up to 58.87 U/L). The distribution of these values was analyzed to assess a possible association with lithiasis activity.

Results: Of the patients included, 77 (32.2%) had values <20 U/L, 94 (39.3%) fell within the 20.06–30.44 U/L range, and 68 (28.5%) had values >30.44 U/L. The majority (67.8%) showed elevated serum levels, suggesting an active inflammatory response or the presence of a urinary tract infection. These findings support the potential role of β-GUS as a biomarker of lithiasis activity.

Conclusions: Elevated serum β-GUS levels in patients with renal lithiasis suggest the enzyme's potential role as a biomarker of inflammation and lithiasis activity. Its measurement may aid in monitoring disease progression and assessing the risk of recurrence. Further studies are necessary to validate these findings and to establish a clinically relevant reference range. Serum β-GUS may become a valuable tool for the early detection of active lithiasis forms, especially in infectious or recurrent cases.

Keywords: beta-glucuronidase, recurrence, renal lithiasis

P4. TRANSCUTANEOUS BILIRUBIN MEASUREMENT: A NONINVASIVE ALTERNATIVE FOR NEONATAL JAUNDICE SCREENING

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Introduction: Severe neonatal hyperbilirubinemia can be prevented by screening for neonatal jaundice. The preferred test for bilirubin in neonates remains the serum bilirubin measurement. Unfortunately, this is invasive, painful, and costly. Transcutaneous bilirubin (TcB) measurement is a noninvasive method for screening in neonates. The aim of this study is to determine the correlation between TcB and total serum bilirubin (TSB) measurement in term neonates.

Methods: A prospective study was conducted involving 50 healthy term neonates with a gestational age of ≥36 weeks. In all patients the measurements of TcB and TSB were performed. TcB readings were obtained from the infant's sternum using a transcutaneous bilirubinometer, while TSB levels were determined through standard photometric analysis of serum samples.

Results: The mean and standard deviation (SD) were calculated for TcB and TSB across all patients. TSB level was 13.2 ± 3.6 mg/dL, and for TCB the level was 16.6 ± 4.1 mg/d. Statistical analysis of the data shows a significant correlation between TSB and TcB measurements ($p < 0.001$), but the correlation loses its importance at high levels of bilirubin.

Conclusions: In neonates, transcutaneous bilirubin (TcB) and serum bilirubin are equally reliable screening tests for hyperbilirubinemia in the term neonatal population. The study demonstrates clearly that there is a good correlation between the TCB and TSB estimation when the bilirubin values are low. TcB monitoring is a useful, noninvasive, painless, and cheaper, clinical screening test to evaluate for the risk of significant jaundice in neonates. However, is suggested that at higher bilirubin levels, the values of TcB must be confirmed by serum bilirubin test.

Keywords: newborns, serum bilirubin (TSB), transcutaneous bilirubin

P5. ROLE OF URIC ACID IN MULTIPLE SCLEROSIS SEVERITY

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Introduction: Multiple Sclerosis (MS) is characterized by inflammation and chronic neurodegeneration due to demyelination of the central nervous system. Oxidative stress plays an important role in its pathophysiology. Uric acid (UA) is characterized by its antioxidant capacity, acting as a natural scavenger of peroxynitrite. The aim of this study was to evaluate UA levels in MS patients and its correlation with sex and the disease severity.

Methods: We included 125 patients. For each participant, a blood sample was taken to measure UA levels. The degree of neurological disability for each patient was evaluated using the Expanded Disability Status Scale (EDSS) whose score varies from 0-10 depending on the disease severity.

Results: The mean age of patients was 36.9 years (15 - 67). The female-to-male sex ratio was 2:1. We divided patients in two groups according to their EDSS score: 1-4.5 and 5-9.5 with predominance of group with score 1-4.5 (70.4% and 29.6% respectively). The UA level was lower in 27.2% of all patients and 18.4% of them were score 5-9.5. Based on sex patient, the females resulted with UA level more lower than males 21.6% and 5.6% respectively.

Conclusions: MS affected women patients about two times more often than men. Female patients with MS showed lower serum UA levels compared with male patients. The UA concentrations decreased with high MS severity.

Keywords: Expanded Disability Status Scale (EDSS), multiple sclerosis, uric acid

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P9. FROM ROUTINE TO RELEVANT: LABORATORY-BASED INDICES FOR OPTIMIZING CARE IN PREDIABETIC AND DIABETIC PATIENTS

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Introduction: The global rise in type 2 diabetes mellitus (T2DM) highlights the need for early detection and intervention during the prediabetic (preDM) phase. This study aims to evaluate and compare metabolic, inflammatory, and lipid profiles between preDM and T2DM groups to identify key biomarkers for better patient stratification and treatment strategies.

Methods: A total of 150 adult patients were enrolled, including 50 individuals with preDM and 100 with T2DM. Demographic, clinical, and laboratory parameters were collected and analyzed. Standard tests such as fasting plasma glucose (FPG), 2-hour postprandial glucose (2hPG), glycated hemoglobin (HbA1c), lipid profile, liver enzymes, inflammatory markers (CRP, ESR), and various derived indices (metabolic score for insulin resistance (METS-IR); TyG/HDL-c; Glu/Hb) were evaluated. Statistical comparisons between groups were performed using Pearson's chi-squared and Student's t-test, with a significance threshold of $p < 0.05$.

Results: Patients with T2DM demonstrated markedly elevated levels of FPG, 2hPG, and HbA1c compared to those in the preDM group. Additionally, they exhibited significantly higher indices of metabolic insulin resistance, specifically METS-IR, as well as elevated TyG/HDL-c and Glu/Hb ratios, with p-values less than 0.0001, indicating strong statistical significance. Significant differences were also observed in total cholesterol, LDL-C, HDL-C, AST, ALT, WBC, and CRP levels. However, no statistical significance was noted in ESR, creatinine, or lipid accumulation product (LAP). Interestingly, CRP levels were higher in the preDM group, potentially indicating early inflammatory activity.

Conclusions: Distinct laboratory markers and composite indices, particularly METS-IR, TyG/HDL-c, and Glu/Hb, show potential as valuable tools for differentiating between preDM and T2DM stages. Routine use of these indices could enhance early detection, stratification, and management of metabolic risk in clinical settings.

Keywords: laboratory indices, metabolic risk, prediabetes, type 2 diabetes mellitus

P10. DIAGNOSTIC SIGNIFICANCE OF LYMPHOCYTE-TO-MONOCYTE RATIO IN YOUTH WITH TYPE 1 DIABETES

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Introduction: The Lymphocyte-to-Monocyte Ratio (LMR) is a hematologic index that reflects the balance between immune activation and inflammation. Its significance in patients with Type 1 Diabetes Mellitus (T1DM) lies in its potential to serve as a marker of immune dysregulation and inflammatory status, which are central to the pathogenesis of T1DM. We aimed to analyze LMR, an inexpensive and easily obtainable marker, in children with T1DM and compare it to healthy peers.

Methods: This study was conducted at the Clinical Center of the University of Sarajevo, including 90 children with T1DM and 40 healthy controls, aged 12-18 years, with no other underlying conditions. Blood samples were analyzed to determine HbA1c and LMR using standard laboratory procedures. Nonparametric statistical analyses were performed, with $p<0.05$ considered significant. The T1DM group was subdivided into three categories based on glycemic control: good (HbA1c <7%), intermediate (HbA1c 7.1–8.4%), and poor (HbA1c >8.5%).

Results: The groups were matched for age and gender. The T1DM group consisted of 50 males and 40 females, while controls included 20 males and 20 females. Chi-square analysis showed no significant gender distribution difference ($p=0.757$). The median (IQR) age was 14.0 (13.0–16.0) years in the T1DM group and 15.0 (13.0–17.0) years in controls ($p=0.104$). Median (IQR) HbA1c was significantly higher in children with T1DM 8.0% (7.2–9.2%) compared to controls 5.1% (4.9–5.25%); $p<0.001$. The median (IQR) LMR was significantly lower in children with T1DM 3.25 (2.50–3.95) versus controls 4.52 (4.01–5.35); $p<0.001$. HbA1c showed a significant negative correlation with LMR (rho =-0.548, $p<0.001$). Additionally, Kruskal-Wallis analysis revealed significant differences in median (IQR) LMR across the three T1DM control groups: good 3.7 (2.88–4.49), intermediate 3.87 (3.05–4.39), and poor 2.54 (2.20–2.91); $p<0.001$.

Conclusions: Although not yet a standard clinical marker, LMR shows promise as an accessible, cost-effective indicator of immune and inflammatory status in T1DM. It may provide insights into disease severity, progression, and immune involvement, potentially aiding personalized management strategies in the future. Furthermore, LMR correlates with glycemic control, suggesting its utility in monitoring disease activity.

Keywords: glycemic control, immune dysregulation, inflammation, lymphocyte-to-monocyte Ratio, type 1 diabetes mellitus

P12. SCREENING FOR THE METABOLIC PROFILE OF HIRSUTE WOMEN

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Introduction: Hirsutism affects about 5% to 10% of women. In most cases, hirsutism must be the result of pathologies such as PCOS, androgen-secreting tumors, or insulin resistance. The exception may be those patients with "idiopathic hirsutism" (IH), where hirsutism is present in women with normal serum androgen levels.

Methods: In the study were included 140 cases with idiopathic hirsutism, the diagnosis of which was established according to the criteria of the Ferriman Gallwey system, which evaluates by scoring in terms of pilosity. The study included cases with a score greater than 10. In all these cases a clinical, biochemical and hormonal evaluation of the patients was performed.

Result: On the group of 140 patients,71 % were diagnosed with PCOS and 29 % with HI. From the evaluation of the results for glycemia, triglyceride, cholesterol, HDL-cholesterol, LDL-cholesterol, insulin and HOMA between patients with IH and the control group, a positive correlation for insulin and triglyceride ($p < 0.001$) and HOMA ($p < 0.048$) was observed. Between IH and PCOS group, a positive correlation with insulin and HOMA ($P< 0.001$) and triglyceride ($p =0.031$) was observed. In the IH group, a significant correlation was observed between the TT/DHT ratio and glycemia and triglyceridemia.

Conclusions: In hirsutism patients we observed the presence of insulin resistance due to high levels of androgens, which interfere with glucose and lipid metabolism. The results showed a statistically significant association of IH with high values of insulin and HOMA-IR compared to the control group, while insulin and HOMA-IR were significantly lower in IH than in PCOS patients. A statistically significant association of IH was also observed with the levels of triglyceride.

Keywords: cholesterol, HOMA-IR, idiopathic hirsutism, triglycerides

P14. CASE PRESENTATION: NONALCOHOLIC FATTY LIVER DISEASE AND METABOLIC SYNDROME IN AN 11-YEAR-OLD BOY

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Introduction: Fatty liver disease is a group of disorders that often overlap with inherited metabolic disorders (IMD), which require prompt diagnosis and specific management. Nonalcoholic fatty liver disease (NAFLD) is increasingly prevalent in the pediatric population, closely associated with obesity, insulin resistance, and dyslipidemia.

Case report: This case report discusses an 11-year-old boy diagnosed with nonalcoholic fatty liver disease (NAFLD) and metabolic syndrome. It presents the clinical, imaging, and laboratory findings of this patient. Based on the clinical presentation, laboratory, and ultrasound findings, the patient was diagnosed with NAFLD and metabolic syndrome; Insulin Resistance, Dyslipidemia, Obesity, Elevated liver enzymes. At 1.5-year follow-up, the patient showed modest weight loss and improved liver function tests. Subsequent ultrasound showed a mild decrease in liver echogenicity. Continued lifestyle modifications and regular follow-up were advised.

Conclusions: This case highlights the association between insulin resistance, dyslipidemia, obesity, and NAFLD in the pediatric population. Early recognition and intervention are essential in managing these conditions and preventing progression to more severe liver disease.

Keywords: dyslipidemia, insulin resistance, metabolic syndrome, non-alcoholic fatty liver disease, obesity

R18. COMPREHENSIVE LIPID ANALYSIS IN PATIENTS WITH GRAVES' ORBITOPATHY: INSIGHTS INTO LIPID METABOLISM IN RELATION TO THE CLINICAL PHENOTYPE OF DISEASE

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Graves' orbitopathy (GO) is an inflammatory orbital condition and the most frequent extrathyroidal manifestation of Graves' disease (GD). It is a debilitating disease that can be sight-threatening in its severe form. Its clinical symptoms range from functional impairments to aesthetic issues, with severe cases potentially leading to corneal ulceration or dysthyroid optic neuropathy. Due to GO's chronic nature and the absence of targeted treatments, it often results in permanent vision loss and a diminished quality of life. On a histological level, GO is marked by increased production of glycosaminoglycans and adipogenesis, which causes expansion of the orbital fat and muscle tissue. GO is a multifactorial disease, caused by specific autoimmune processes. It is considered to develop as a result of joint interaction of genetic predisposition, endogenous, and environmental factors. However, the exact etiopathology of GO is still unknown.

Hypercholesterolemia has been identified as one of the risk factors for developing GO. Although statins are considered a potential adjuvant treatment for GO, the mechanisms linking dyslipidemia and GO are still not well understood. Hypercholesterolemia and GO share some metabolic traits, and their association may stem from a systemic lipid metabolism disruption causing local lipid buildup in the orbit, or from the pro-inflammatory effects of hypercholesterolemia.

This lecture addresses the perplexing relationship between GO and lipid metabolism and the clinical potential of a comprehensive lipid analysis in patients with GO. It offers several novel findings pertaining to the clinical relevance of lipid biomarkers, both basic lipid profile and a variety of specific markers, including fatty acid content, non-cholesterol sterols, sphingolipids, etc. The aim of this lecture is to gain a closer insight into the lipidome of patients with GO, its association with the underlying mechanism of disease and its potential as novel therapeutic targets.

Keywords: Graves' orbitopathy, hypercholesterolemia, lipid biomarkers

R19. CHOLESTEROL METABOLISM AND INTIMATE LINK WITH FAMILIAL HYPERCHOLESTEROLEMIA – NEW INSIGHTS

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Introduction: Particular focus is put on cholesterol's ability to link Familial hypercholesterolemia (FH), a genetic disorder associated with elevated low-density lipoprotein LDL-C, often underdiagnosed and undertreated. For an effective cardiovascular (CV) disease prevention in FH, early detection of the condition through cascade screening of family members of known FH patients, and balance toward normal of LDL-C levels are crucial pillars. Considering that patients with HF in Romania do not always benefit from an accurate diagnosis due to the lack of a holistic approach, the study aimed identification of HF subjects in the NE area of the country and new CV events risk assessment, correlated with lipid-lowering medication.

Methods: We carried an observational, prospective study over a period of 2 years, in three NE Romanian medical centers, where 980 patients were evaluated. Following the inclusion/exclusion criteria, 61 patients with clinically diagnosed HF were enrolled.

Results: The subjects with a clinical diagnosis of HF included in the study were predominantly young patients, especially female, whose lipid profile did not record different values according to gender. Hypertension was the main CV risk factor, followed by a sedentary lifestyle associated with obesity in female patients and active smoking status in male patients. It was found that lipid-lowering drugs decreased the plasma levels of LDL-C, hsCRP and cIMT- carotid intima-media thickness and increased the values of ankle-brachial index and HDL-C, but without reaching the targets set by the European dyslipidemia guidelines.

Conclusions: The most common new CV event was coronary artery disease, followed by stroke and peripheral arterial disease. The onset of new CV events was delayed by all lipid-lowering medications, with no discernible variation among treatments. Grasping the advantages and risks of cholesterol in a clinical context will enhance the clinician's capability to manage conditions linked to this distinctive molecule.

Keywords: cardiovascular risk, cholesterol, familial hypercholesterolemia

C20. PARAOXONASE 1 AND HDL SUBCLASS DISTRIBUTION AS PROSPECTIVE BIOMARKERS OF ST-SEGMENT ELEVATION ACUTE MYOCARDIAL INFARCTION

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Introduction: ST-segment elevation acute myocardial infarction (STEMI) is characterized by myocardial ischemia, initiating inflammatory and oxidative processes that lead to myocardial injury or necrosis. These changes disrupt the structure and composition of high-density lipoprotein (HDL), diminishing its antiatherogenic properties. Such alterations also affect HDL-associated enzymes, including paraoxonase 1 (PON1), which provides antioxidative protection by hydrolyzing lipid peroxides. This study aimed to: (1) analyze HDL subclass distribution and functionality in STEMI patients and healthy controls; (2) evaluate PON1 activity distribution across HDL subclasses; and (3) assess the impact of sdLDL proportion on HDL subclass distribution, antioxidative properties, and PON1 activity.

Methods: The study included 69 STEMI patients and 67 healthy controls. HDL and LDL subclasses were separated using polyacrylamide gradient (3–31%) gel electrophoresis. The relative proportion of sdLDL and each HDL subclass was determined by measuring the areas under the peaks of densitometric scans. PON1 activity distribution across HDL subclasses (pPON1 within HDL) was assessed using the zymogram method.

Results: Compared to controls, STEMI patients showed significantly lower proportions of HDL2a and HDL3a subclasses and reduced pPON1 within HDL3b, but higher proportions of HDL3b and HDL3c. A positive correlation between sdLDL and pPON1 within HDL3a was identified in the STEMI group.

Conclusions: The reduced antioxidant capacity and impaired functionality of HDL3 subclasses, accompanied by an increased proportion of sdLDL and diminished antioxidative function of small HDL3 particles, along with altered pPON1 activity in STEMI patients, suggest that HDL subclass distribution and PON1 activity may serve as valuable prospective biomarkers for STEMI.

Keywords: HDL subclasses, paraoxonase 1, ST elevation myocardial infacrtion (STEMI)

R21. CEREBROSPINAL FLUID EXAMINATION: PRACTICAL APPROACHES AND CLINICAL SIGNIFICANCE

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Introduction: Cerebrospinal fluid (CSF) analysis remains a vital diagnostic tool in neurology. It is most often performed in patients with suspected meningitis or encephalitis, especially when presenting with fever, headache, altered consciousness, or meningeal signs. In immunocompromised individuals, CSF examination is essential due to the elevated risk of atypical central nervous system infections. It also plays a key role in diagnosing subarachnoid hemorrhage and demyelinating diseases. Guidelines from major societies such as the European Academy of Neurology (EAN), American Society for Microbiology (ASM), Infectious Diseases Society of America (IDSA), and American Academy of Pediatrics (AAP) provide clinical direction. Proper pre-analytical handling and timely processing are essential to ensure diagnostic accuracy. Here we aimed to present findings from our laboratory's experience in CSF analysis, with a focus on the occurrence and significance of CSF eosinophilia.

Methods: Over 11 years, 2840 CSF samples were analyzed at the Clinical Laboratory of UH St. Ivan Rilski. Tests included macroscopic evaluation, biochemical profiling (total protein, albumin, glucose, and electrolytes), cell count and morphology (Romanowski-Giemsa), and electrophoretic assessment, including isofocusing.

Results: Eosinophils (≥0.01) were detected in 5.28% of cases. Marked CSF eosinophilia (≥0.10) was identified in only 0.39% (n=11).

Conclusions: CSF analysis is a specialized investigation with significant diagnostic value. Our findings align with existing literature, confirming that while eosinophils are occasionally present in CSF (about 5%), true CSF eosinophilia is rare. It may point to parasitic infections, shunt-related complications, or certain fungal and viral causes.

Keywords: CSF, eosinophilia, shunt-related complications

C22. EPIDEMIOLOGY OF CYSTIC FIBROSIS: A RETROSPECTIVE 10-YEAR SINGLE CENTRE EXPERIENCE

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Introduction: Cystic fibrosis (CF) is an autosomal recessive disorder, and most carriers of the gene are asymptomatic. It is a disease of exocrine gland function that involves multiple organ systems but chiefly results in chronic respiratory tract infections, pancreatic enzyme insufficiency, and associated complications in untreated patients. The diagnosis of CF is based on typical pulmonary manifestations, gastro-intestinal tract manifestations, family history, and positive sweat chloride test results.

Methods: We performed an epidemiologic retrospective study including 567 patients that had performed the sweat chloride test in our laboratory from May 2015 to May 2025. We used Sweat-Chek Analyzer Model 3120 Macro duct by Eli Tech Group. The statistical analysis was performed using Jamovi Statistical Software version 2.3.28.

Results: We had 265 females (47%) and 302 males (53%), mean age 36.3 months (1-468 months). Respiratory tract manifestations predominated with 57%, followed by gastrointestinal tract manifestations with 14%, 12.4 % were healthy individuals, 6% of children had failure to thrive, 2.5% had family history, 2% had positive immunoreactive trypsinogen (IRT), 1.6% had confirmed mutations in the CFTR gene, and 4.5 % had atypical manifestations. We got normal results from 85.4% of patients, borderline results from 3.1% of patients, and positive results from 11.5% of patients. In 2.3 % of cases, we had a “quantity not sufficient” (QNS) result.

Conclusions: CF is a multi-systemic disease with a lot of complications and with a high prevalence in the Albanian population, this is the reason Cystic Fibrosis neonatal screening and sweat test will be of great benefit, since outcomes can be improved through early diagnosis.

Keywords: cystic fibrosis, IRT, QNS, sweat

R23. SWEAT CHLORIDE TESTING FOR CYSTIC FIBROSIS IN MONTENEGRO: ACHIEVEMENTS AND CHALLENGES

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Cystic fibrosis (CF) is a genetic disorder with multisystem involvement, especially the respiratory and digestive systems. The defective or absent CF transmembrane regulator function results in elevated sweat chloride concentration. Detection of elevated values of sweat chloride by the quantitative pilocarpine iontophoresis test performed via chloridometer is accepted as the gold standard in CF diagnosis. The Cystic Fibrosis Foundation recommends CF genotyping in patients with positive sweat test results. The sweat chloride test has been performed in the Department of Laboratory Diagnostics of the Institute for Children's Disease for more than 40 years. Each year, approximately 300 individuals are tested; the majority of them are children. Our laboratory utilizes the FDA-cleared chloridometer for sweat testing. Until recently, the sweat chloride test was the only diagnostic option for CF in Montenegro, but now efforts to implement a national NBS program have been ongoing in our country.

The Montenegrin Association for Aid and Support to People with CF is a national NGO founded in 2017 and a part of the Cystic Fibrosis Europe federation. Montenegro is one of the countries that has provided every patient with CF who meets the criteria with the latest innovative therapy elexacaftor/tezacaftor/ivacaftor, which profoundly modifies the natural history of CF. In 2023, 27 CF patients, out of a total of 40 in Montenegro, got a chance for a new life. The criteria for therapy administration were: age above 6 years old and the presence of at least one delta F508 mutation. The state provides on an annual basis over 5 million euros for the aforementioned therapy. In 2024, it was announced that children aged 2–5 with CF should also be eligible for the medicine.

Despite our extensive experience with sweat chloride testing, it should not remain a primary option for diagnosing CF. An NBS program for CF should be incorporated into national legislation, along with the development of standardized clinical and laboratory algorithms to guide follow-up based on screening results.

Keywords: cystic fibrosis, Montenegro, sweat chloride test

R24. ARTIFICIAL INTELLIGENCE (AI) AS A MEDICAL DEVICE

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Artificial intelligence (AI) is rapidly transforming healthcare by enabling automated interpretation, prediction, and decision support from complex clinical data. When embedded in tools intended for diagnosis, treatment, or health management, AI systems function as medical devices and therefore must satisfy clinical, technical, and regulatory requirements distinct from conventional software.

This abstract synthesizes current understanding of AI as a medical device, highlighting core considerations across lifecycle development: data curation and representativeness, algorithm design and explainability, validation and clinical performance, real-world monitoring, and regulatory compliance. It draws on recent regulatory frameworks and best-practice guidance to outline necessary safeguards for safety, efficacy, and equity.

Key challenges include dataset bias and limited generalizability, opaque model behavior that complicates clinician trust and liability, evolving regulatory pathways for adaptive algorithms, and operational risks such as cybersecurity and interoperability failures. Robust prospective clinical validation, transparent reporting of performance across subgroups, human-centered design promoting appropriate clinician oversight, and continuous post-market surveillance are critical mitigations. Regulatory convergence is accelerating requirements for documented evidence, risk classification, and lifecycle governance.

AI-based medical devices hold substantial promise to improve diagnostic accuracy, personalize therapy, and optimize workflows. Realizing this promise requires multidisciplinary development, rigorous validation, regulatory alignment, and ongoing monitoring to ensure safe, effective, equitable deployment in clinical practice.

Keywords: AI, clinical practice, cybersecurity challenges, health management, medical device

C25. ALGORITHMS AND BIOMARKERS: HOW ARTIFICIAL INTELLIGENCE (AI) IS TRANSFORMING THE APPROACH TO METABOLIC SYNDROME IN THE LABORATORY

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Metabolic syndrome (MetS) affects over a quarter of the global adult population, generating substantial economic costs due to associated complications (cardiovascular and metabolic diseases), loss of individual productivity, and intense use of medical resources. It remains a major public health concern, characterized by metabolic dysfunctions such as central obesity, insulin resistance, dyslipidemia, and hypertension.

Laboratory medicine plays a key role in identifying and monitoring MetS through the analysis of key biomarkers. In recent years, artificial intelligence (AI) has opened new avenues in interpreting these biological data, enabling the integration of large-scale information and the identification of complex predictive patterns that would otherwise be difficult to achieve through conventional analysis. Machine learning algorithms have been employed to predict MetS risk, classify metabolic subtypes, and personalize therapeutic interventions. Recent studies highlight the potential of Random Forest, XGBoost, and neural network algorithms in the integrative analysis of biological data.

Among the most accurate predictors of MetS are the triglyceride-glucose index (TyG), the TyG-BMI score, and C-reactive protein. Furthermore, by integrating machine learning algorithms with nuclear magnetic resonance (NMR) spectroscopy, differential metabolomic profiles have been identified, revealing alterations in the metabolic pathways of key metabolites such as arginine and glutathione. These findings suggest their involvement in the pathophysiological mechanisms associated with MetS.

The application of AI in laboratory medicine has the potential to enhance the management and prevention of metabolic syndrome by: early identification of at-risk individuals, integrating traditional and emerging biomarkers into robust predictive models, supporting clinical decision-making through automated risk scores and algorithmic interpretations.

Keywords: artificial intelligence, biomarkers, machine learning algorithms, metabolic syndrome, obesity

C26. DIGITAL TOOL APPLICATION IN CLINICAL LABORATORY ENVIRONMENT: FOCUS ON DIAGNOSIS OF HEPATOCELLULAR CARCINOMA

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Liver cancer is the sixth most common cancer worldwide. Hepatocellular carcinoma (HCC) is the most prevalent primary liver malignancy, and the third leading cause of cancer death. It is estimated that liver cancer cases and deaths will rise by over 50% by 2040.

The main risk factors for HCC development include cirrhosis, hepatitis B and C virus infection, Metabolic dysfunction-associated steatotic liver disease and alcoholic-related liver disease. Current guidelines recommend routine surveillance programs of high-risk patients every six months using ultrasonography with or without biomarkers, but the effectiveness for early-stage HCC detection is limited. The most commonly used biomarker for HCC is serum alpha-fetoprotein (AFP). Protein-induced by vitamin K absence-II (PIVKA-II), also known as des-gamma carboxyprothrombin (DCP) is another significant serum biomarker for HCC diagnosis, especially in patients with normal AFP level. These biomarkers have been inconsistently incorporated into guidelines worldwide.

To further improve the diagnosis of early-stage HCC, the digital tool Elecsys® GAAD, medical algorithm score that combine gender (biological sex), age, AFP and PIVKA-II levels, has been developed. Elecsys® GAAD reveals a risk factor score from 0-10, which is the likelihood of patient developing HCC. A score above 2.57 indicates an increased risk of HCC. During the lecture series of cases from tertiary medical center will be presented, together with data extracted from clinical records presenting features, diagnostic workups, GAAD medical algorithm scores and therapeutic decisions.

GAAD integration into routine practice underscores the importance of combining biomarker-based assessments with clinical judgment. This series confirms the potential of GAAD to refine clinical decisions and enhance outcomes in diverse patient populations.

Keywords: algorithm, biomarker, GAAD, hepatocellular carcinoma.

C27. ARTIFICIAL INTELLIGENCE PREDICTIVE MODEL FOR PROSTATE CANCER USING MIR-222-3P EXPRESSION, GLEASON SCORE, TNM, AND PROSTATE SPECIFIC ANTIGEN

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Introduction: A few studies have evaluated the efficacy of artificial intelligence (AI) in predicting the prognostic and follow-up of patients with prostate cancer (PCa). In men with recently diagnosed PCa, this research aimed to assess the efficacy of AI usage as a fast and accurate helper to conventional treatment.

Methods: This study included patients diagnosed with PCa (n=89), aged 40–85 years, who were classified based on the severity of their conditions, tumor-node-metastasis stage (TNM) stage. The outcome consisted of predicting the survival rate (survival period in months). Prostate-specific antigen (PSA), Gleason score, TNM stage, diagnosis, mir-222-3p expression, and survival period were the main variables.

Results: Most patients were aged 55-80 years (mean 63 years, standard deviation 11.83). In terms of miR-222-3p, the patient's frequency for miR-222-3p was 0=15 patients (16.85%); 1=74 patients (83.15%). An advanced analysis of this study sought to employ artificial intelligence to forecast the Survival rate (months) based on miR-222-3p, PSA (ng/ml), and Gleason score. Applying rigorous AI algorithms (Cox PH with Lasso model C-index (0.260), Random Survival Forest – C-index (0.410), Gradient Boosting Survival Model C-index (0.335)), they fitted them to the analyzed data. With a SHAP value of around 1.06 in the Gradient Boosting model and a noticeably higher value of roughly 2.43 in the RSF model, mir-222-3p stands out as the most significant predictor across both models.

Conclusions: In all diagnosed men with PCa, the mir-222-3p expression demonstrated its value as an early predictive biomarker for most patients.

Keywords: artificial intelligence (AI), miR-222-3p, prostate cancer (PCa), prostate-specific antigen (PSA), tumor-node-metastasis stage (TNM)

R28. EXPOUNDING MYTHS WITH MEDICAL BIOCHEMISTRY

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Medical biochemistry is a useful way to clear up common health myths by linking everyday beliefs to scientific facts. This lecture will enlighten some popular misconceptions, like the idea that everyone needs multivitamins, that drinking lemon water alkalizes the body, or that drinking water can detox the system.

By checking these claims against how metabolism, enzyme functions, nutrient absorption, and the body's natural systems work, we can get a clearer picture of what's true and what's not. For instance, the claim that diet can quickly change blood pH is discussed in light of how the body keeps pH levels stable.

The lecture will also question the one-size-fits-all approach to supplements by pointing out that people have different nutritional needs. This approach aims to identify what's real and show how medical biochemistry helps us make smarter health choices. This myth-busting method supports scientific understanding and encourages a more careful, fact-driven view of wellness by simplifying complex ideas. Ultimately, knowing the science behind these myths helps us appreciate how complex our bodies are.

Keywords: health myths, medical biochemistry, myth-busting

C29. POLYPHARMACY ANALYSES IN CLINICAL LABORATORY

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Introduction: Elderly patients with multimorbidity are the typical polypharmacy population and are exposed to multidrug interactions. Antihypertensives, cholesterol lowering drugs such statins, antidiabetics, antidepressants, anticonvulsants, proton pump inhibitors, analgesics, antipyretics are commonly used in polypharmacy. It is extremely difficult to predict the clinical effects or side effects of combined drug use since their agonistic or antagonistic behaviour.

Methods: We set up a single run method to analyse drug levels in polypharmacy patients. In order to develop multidrug analysis we used an LC-MS/MS system. Eighteen commonly used drugs (enalapril, ramipril, losartan, valsartan, metoprolol, paracetamol, quetiapine, aripiprazole, hydroxyzine, levocetirizine, atorvastatin, metformin, pioglitazone, gliclazide, carbamazepine, escitalopram, sertraline and amlodipine) were analysed. The drugs were quantified on an ABSCIEX API 3200 tandem mass spectrometer in positive electrospray ionisation mode using d9-Trimethylamin-N-oxide as an internal standard. CLSI guidelines (EP5A, EP15-A3, EP07-A3 and EP14-A3) and FDA bioanalytical method validation protocols were used during method development.

Results: We developed a method which is capable of analysing 18 commonly used drugs simultaneously. Although there were some different values for each drug, the linearity changed between 0.15-12000 ng/ml and R^2=0.989-999. Accuracy was between 98-102% and imprecision <8%. The run time was 12 minutes. The minimum interference rate was 87.8% and the maximum interference rate was 114.6% for hemolysis, lipemia and icteric samples. A minimum of 12.8% and a maximum of 14.6% were observed as matrix effect. Interference in freeze-thaw cycles was <4%.

Conclusions: In routine laboratory practice digoxin, valproic acid, lithium and phenobarbital, phenytoin, cyclosporine and tacrolimus analysis are commonly used as therapeutic drug monitoring. These drugs are not in the therapeutic drug monitoring. However, since the population getting older and morbidity rate is increasing it may be important to monitor multiple drug use in terms of side effects and treatment efficacy. This method allows the measurement of multiple drugs with a minimal sample volume using a single analytical method and device.

Keywords: drug analysis, mass spectrometry, polypharmacy, toxicology

C30. A NOVEL ELECTROCHEMICAL BIOSENSOR-BASED MEDICAL DEVICE FOR IBUPROFEN DETECTION WITH APPLICATIONS IN CLINICAL LABORATORIES AND „ORGAN-ON-CHIP" PLATFORMS

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Introduction: Ibuprofen (IBP) is the third most widely used first-generation non-steroidal anti-inflammatory drug (NSAID), listed among "essential medicines". The primary objective of this study is the development of an electrochemical biosensor for the specific quantification of IBP.

Methods: Electrochemical measurements were performed using an Interface 1010E potentiostat (Gamry Instruments). A sensor with a gold working electrode (WE), provided by HUN-REN-Microsystems-Lab, was used. The WE were functionalized with a self-assembled monolayer (SAM) of L-cysteine (Cys), followed by covalent immobilization of the Anti-Ibuprofen (Anti-IBP) antibody. Electrochemical techniques such as Electrochemical Impedance Spectroscopy (EIS) were used for the detection of the IBP analyte.

Results: IBP quantification was achieved through EIS measurements and analysis of changes in charge transfer resistance (Rct). The obtained results demonstrated a strong correlation between impedance variation and IBP concentration in the range of 78 ng/mL to 1 mg/mL, with $R^2 = 0.97$. The surface of the WE were characterized using Scanning Electron Microscopy (SEM).

Conclusions: The quantification of small molecules (NSAIDs) remains a significant challenge. Considering high analytical performance in IBP detection, the developed biosensor qualifies as a promising medical device for clinical laboratory applications or potential integration into an "organ-on-chip" platform. The next step involves validation through testing with biological samples.

Keywords: EIS, electrochemical biosensors, ibuprofen

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C31. IMPACT OF CREATININE MEASUREMENT METHODS ON eGFR AND GFR CATEGORY ASSIGNMENT

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Introduction: Accurate measurement of serum creatinine (SCr) is critical in estimating glomerular filtration rate (eGFR) and classifying kidney dysfunction. This study evaluated the analytical differences between the enzymatic and Jaffe methods for SCr measurement and their impact on eGFR estimation using two widely applied equations: CKD-EPI and EKFC.

Methods: The study included 427 patients over 40 years old. SCr was measured using both enzymatic and Jaffe methods on the AbbottAlinity c platform. eGFR was calculated with the CKD-EPI 2009 and EKFC equations. Agreement between methods was assessed using Bland-Altman and Passing-Bablok regression. eGFR differences were analyzed using the Wilcoxon signed-rank test and multiple linear regression. Agreement in GFR category classification was evaluated using weighted kappa and Kendall’s tau.

Results: While the mean difference between methods was small, both systematic and proportional biases were statistically significant. eGFR values differed significantly between methods in both sexes ($p < 0.01$), regardless of the equation used. ΔeGFR was significantly associated with SCr values, but not with age. Although overall agreement in GFR categories was high (kappa > 0.91), method-dependent reclassification of patients was observed, which may influence CKD diagnosis and clinical decision-making.

Conclusions: Even minor analytical differences between enzymatic and Jaffe SCr measurements can lead to clinically relevant discrepancies in eGFR values and GFR categorization. These findings highlight the need for harmonization in laboratory methods to ensure consistent reporting and patient management.

Keywords: eGFR, enzymatic method, GFR categories, Jaffe method, kidney function, serum creatinine

C32. THE RACE-FREE FORMULA IN PRACTICE: EVALUATING EUROPE'S ADAPTATION TO CKD-EPI 2021 AND ITS CLINICAL RELEVANCE COMPARED TO OTHER GFR EQUATIONS

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Chronic kidney disease (CKD) is a significant health issue worldwide, leading to both cardiovascular diseases and the development of end-stage chronic kidney failure. Guidelines recommend the use of serum creatinine and glomerular filtration rate (GFR) calculations as the first step in the assessment of renal function.

While various estimation methods have existed since the 1970s, the 1999 Modification of Diet in Renal Disease (MDRD) and 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI 2009) equations gained widespread clinical acceptance. In 2021, a new CKD-EPI 2021 equation was introduced, omitting race as a variable recognizing that it is a social rather than a biological construct.

While this "race-free" formula represents a crucial step towards equity, its clinical implementation has sparked debate. Studies highlight concerns, including the risk of missed CKD diagnosis (misclassification) and underestimation of CKD stage (GFR overestimation) in Black populations, alongside the potential for delayed diagnosis in non-Black populations Despite these concerns, the CKD-EPI equation has gained widespread adoption in clinical laboratories due to its overall performance, particularly in populations with near-normal renal function and is recommended by Kidney Disease: Improving Global Outcomes (KDIGO) guidelines.

Keywords: chronic kidney disease, creatinine, estimated glomerular filtration rate, kidney function

C33. DEVELOPMENT OF NEW THERAPEUTIC BIOMARKERS FOR INFLAMMATORY PAIN

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Introduction: According to the International Association for the Study of Pain (IASP), pain is determined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. However, pain is of critical importance since it protects the individual from harmful stimuli. Tissue injury or infection results in inflammatory pain, a situation characterized by pain hypersensitivity followed by activation of the immune system. Dehydroepiandrosterone (DHEA) is an adrenal hormone with strong neuroprotective and immunomodulatory properties, which has been shown to exert positive effects on pain. In addition, Corticotropin-releasing hormone (CRH), the main regulator of the Hypothalamic-Pituitary-Adrenal (HPA) stress axis, plays an important role in the relief of pain by releasing analgesia-associated molecules in several inflammatory states. Based on the above, our present study aimed to evaluate the anti-nociceptive properties of synthetic neurosteroids and stress neuropeptides during inflammatory pain.

Methods: For our study, we used adult male wild-type and Crh-deficient (Crh-/-) mice, in the CFA (Complete Freund's Adjuvant)-induced inflammatory pain model. CFA (20μL) was injected in the right hind paw while control animals were injected with saline. We had two groups from each genotype: Saline and CFA injected mice. At least 4 mice were used/treatment/genotype/experiment, and each experiment was performed at least twice. Pain thresholds and edema were evaluated with the Hargreaves apparatus and the Plethysmometer, respectively.

Results: Our results indicate that both synthetic neurosteroids and CRH reversed hyperalgesia induced by CFA at all time points examined. The analgesic effects of both molecules were likely mediated by the μ-opioid receptor (MOR), since the mRNA levels of MOR were elevated in inflamed tissues. Proopiomelacortin (POMC) and Proenkephalin (PENK) mRNA levels were also found elevated in the inflamed paw. All tissues for the evaluation of the mRNA levels were obtained at the end of each experiment.

Conclusions: Our data demonstrate, for the first time, considerable analgesic and anti-inflammatory properties of the DHEA synthetic analogues and stress neuropeptides. Their possible mechanism as well as the identification of therapeutic biomarkers for their analgesic and anti-inflammatory action is under investigation and they are likely to involve proinflammatory cytokines and the nerve growth factor (NGF) pathway.

Keywords: analgesia, biomarker, corticotropin-releasing hormone (CRH), inflammatory pain, μ-opioid receptor (MOR)

C34. THE CENTRAL ROLE OF LABORATORY MEDICINE IN THE DIAGNOSTICS OF SEPSIS

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Globally the disease burden of sepsis is immense. Although the incidence and prevalence of sepsis is already very high in developed countries, the burden of disease is even higher in low- and middle-income countries. This creates a major challenge for hospitals and ICUs.

Recently, the diagnostic criteria have been updated internationally, and the SOFA score is now well established. The majority of criteria rely on laboratory testing. In terms of immunopathogenesis, patient suffering from sepsis are challenged by two extreme immune situations: on the one hand, overactivation of the immune system and, on the other hand, immunosuppression. The activation of the innate and adaptive immune responses is strongly associated to and accompanied by the activation of the clotting system. Although we have quite a panel of parameters that allow us to assess hyperactivation, we still lack reliable routine parameters for the immediate assessment of immunosuppression. This caveat needs to be resolved as quickly as possible. Frequent longitudinal assessments of patients are of utmost importance in order to assess the status of our patients with regard to the above-mentioned hemostatic situations, as well as their response to treatment.

Only the future development of new tests, combined with frequent and repeated analysis of these patients and early diagnostics, particularly in susceptible individuals such as neonates and the elderly, will help to reduce disease, burden and mortality. In conclusion, sepsis is a very good used case that illustrates the pivotal role of laboratory medicine in the routine work flow for the benefit of patients. However, this depends on the global availability of these tests.

Keywords: biomarker, clinical laboratory, criteria, diagnostics, sepsis

C35. SERUM MARKERS FOR INFLAMMATION AND INFECTION IN NEWBORNS: CURRENT RESEARCH AND PERSPECTIVES

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The early detection of infection and inflammation in neonates is crucial, as their immature immune systems leave them particularly vulnerable to such conditions. Timely diagnosis can significantly reduce both morbidity and mortality, especially in preterm or critically ill infants.

C-reactive protein (CRP) and procalcitonin (PCT) are well-established acute-phase proteins commonly used to assess systemic inflammation and bacterial infections in neonates. However, these markers have limitations in terms of specificity, particularly for differentiating bacterial infections from other inflammatory conditions. As a result, additional biomarkers, including cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), have been explored due to their significant roles in immune responses and their potential to reflect the intensity of inflammation.

One of the most promising new biomarkers in neonatal sepsis is Presepsin, a soluble fragment of CD14. Presepsin has gained attention due to its high sensitivity and specificity for diagnosing sepsis, particularly when compared to CRP and PCT. It shows potential for earlier detection of infection in critically ill neonates, which is essential for guiding timely treatment decisions in neonatal intensive care units (NICUs). Moreover, emerging biomarkers such as microRNAs and extracellular vesicles are being studied for their ability to provide a more sensitive, specific, and non-invasive means of diagnosing neonatal infections.

In addition to infection and inflammation, ongoing research is also examining the long-term effects of these inflammatory responses on neonatal development. There is growing concern that early-life infections and inflammatory conditions may have lasting impacts on development, making accurate and timely diagnosis even more critical. Technological advancements in point-of-care diagnostics and multiplex assays are enabling faster and more precise detection of infection in NICU settings. However, challenges persist in standardizing biomarker thresholds and integrating these markers into routine clinical practice, particularly across different patient populations and healthcare systems.

Keywords: C-reactive protein, infection, inflammation, presepsin, procalcitonin

C36. USE OF BIOMARKERS IN A NEW CHARACTERISATION OF ACUTE TRAUMATIC BRAIN INJURY

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Traumatic brain injury (TBI) stands as a leading cause of death and disability across the globe. Currently, TBI is typically classified using the Glasgow Coma Scale (GCS) sum score: mild TBI (GCS 13–15), moderate (GCS 9–12) and severe TBI (GCS 3–8). However, this approach has several limitations, prompting the US National Institutes of Health’s National Institute of Neurological Disorders and Stroke (NIH-NINDS) to propose a new, more comprehensive framework for TBI classification in 2025. This framework comprises four key pillars—the clinical, biomarker, imaging, and modifier pillars—that collectively form the CBI-M framework. Each pillar includes both, core components (for use in all patients) and additional elements, modifiers for particular subpopulations, care settings, or for further characterization.

The biomarker pillar includes assessment of one or more of the following: glial fibrillary acidic protein, ubiquitin C-terminal hydrolase L1 or S100 calcium-binding protein B (S100B) within 24 hours post-injury. These biomarkers are currently recommended by Scandinavian and French guidelines to aid in identifying patients with GCS scores of 13–15 who may safely avoid CT scanning, and their use has been shown to reduce the need for imaging by approximately 30%. The principal aim of these markers is to enable a reliable rule-out of significant abnormalities in patients with mild TBI. Modifiers for these biomarker measurements include factors that can affect their concentrations, such as the time of sampling after injury, patient age, and the presence of extracranial injuries in the case of S100B. Furthermore, additional biomarkers, such as neurofilament light, may be incorporated into the CBI-M framework in the future.

A large, multicenter European study we recently conducted further supports the clinical utility of these biomarkers in safely excluding intracranial abnormalities in cases of mild TBI. Detailed results from this study will be shared and discussed in depth.

Keywords: acute, biomarker, Glasgow Coma Scale, traumatic brain injury (TBI)

C37. THE INVOLVEMENT OF NON-B*27 HLA-B ALLELES IN THE PHENOTYPES OF SPONDYLOARTHRITIS

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Introduction: Spondyloarthritis (SpA) represents a heterogeneous group of inflammatory rheumatic diseases closely associated with major histocompatibility complex antigens, particularly HLA-B27. However, a significant proportion of patients are HLA-B27-negative, suggesting the involvement of other HLA-B alleles in disease susceptibility and phenotypic expression. Based on this hypothesis, the present study aimed to investigate the distribution and clinical relevance of non-HLA-B*27 HLA-B alleles among patients with various forms of SpA.

Methods: We analyzed 263 HLA-B27-negative patients from Northeastern Romania who met the ASAS (Assessment of SpondyloArthritis international Society) criteria for SpA. HLA-B genotyping was performed at low resolution, and allele distributions were compared with two HLA-B27-negative control groups (n = 335 with low-resolution genotyping and n = 1,705 with high-resolution genotyping), using chi-square tests and logistic regression.

Results: Compared to control groups, significantly higher frequencies of HLA-B47 (p = 0.0007) and HLA-B54 (p = 0.0013) alleles were observed among SpA patients, while HLA-B40 was underrepresented (p = 0.0287). Notably, HLA-B54 was identified exclusively in patients with axial SpA. Within the cohort, HLA-B13 and HLA-B57 were associated with psoriasis, and HLA-B37 and HLA-B41 clustered in reactive arthritis. HLA-B35 and HLA-B18 were the most frequently observed alleles across most clinical forms.

Conclusions: These findings highlight the role of non-B27 HLA-B alleles in SpA susceptibility and in modulating clinical phenotypes in an Eastern European population. The data emphasize the importance of population-specific immunogenetic profiling and support the need for expanded genetic characterization in HLA-B27-negative patients.

Keywords: clinical forms, cross-reactivity, HLA-B27 negative, spondyloarthritis

C38. SEROLOGY TRAPS: HOW MEDICAL INTERVENTIONS CAN MISLEAD DIAGNOSTIC TESTS

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Introduction: Immunoglobulin administration is a common practice in managing patients with various immunodeficiencies or severe infections. However, the administration of blood products before serological testing can negatively affect the results. The study aims to evaluate how medical interventions such as immunoglobulins or other blood products infusion before testing influence the results of viral serology.

Methodology: Revision of some cases where serological results were inconsistent with the patient's medical personal history or clinical findings following the administration of blood products prior to blood collection. The study also includes an analysis of the serological biomarkers profile in a batch of immunoglobulin (Ig) products intended for intravenous administration (IVIg). Additionally, examples are provided to illustrate cases where results were influenced by the administration of blood products.

Results: Testing of IVIg products has revealed the presence of a wide range of antibodies, some of them effective in managing patients with various medical conditions. However, administering these products before serological tests can induce an altered serological response, making the interpretation and diagnosis more challenging. To address these discordant results, it is recommended to analyze the patient's history, to consider alternative diagnostic methods (PCR for Nucleic Acids), and to ensure communication between clinicians and laboratory staff.

Conclusions: Serological test results should be carefully evaluated and interpreted in the clinical context, particularly for patients who have received immunoglobulins or other blood products.

Keywords: false positive results, IVIg therapy, serology

C39. DISTINCT PROFILES OF SOLUBLE CHECKPOINTS ARE ASSOCIATED WITH DISEASE SEVERITY, MORTALITY OR SARS-COV-2 VARIANTS IN COVID-19

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Introduction: Over the past four years, the COVID-19 pandemic has posed a major global public health challenge. Severe forms of the disease and death are closely linked to the failure of immune regulatory mechanisms, reflected by a dual “storm” of pro-inflammatory cytokines and soluble immune checkpoints (sICPs). Identifying individual factors involved in disease severity and progression, as well as exploring their interconnections, remains a key scientific interest.

Methods: This study included 153 hospitalized patients with confirmed SARS-CoV-2 infection. Upon admission, serum levels of an innovative panel of ten soluble immune checkpoints (sICPs) were measured using the Luminex technique. The objective was to assess their predictive value regarding disease severity, mortality, and differentiation between Delta and Omicron variant infections, in relation to inflammatory biomarkers. Molecular association patterns were analyzed using artificial neural networks, and patients were stratified into mild, moderate, and severe forms of COVID-19.

Results: Distinct sICP profiles were associated with disease stages and Delta variant infections. The molecule sCD40 played a central role across all disease forms, but significant differences were driven by the distribution of four recently described molecules: sCD30, s4-1BB, sTIM-1, and sB7-H3. Serum levels of sTIM-1 and Galectin-9 at admission emerged as strong predictors of mortality. Anti-interleukin therapy (Tocilizumab, Anakinra) was associated with improved survival in patients with high sTIM-1 levels. In Omicron infections, sCD40 and Galectin-9 were the main markers, while the sCD40–sTREM-1 combination characterized Delta infections.

Conclusions: This study provides an integrative analysis of circulating immune factors involved in COVID-19 pathology and highlights the significance of sCD40, sTIM-1, and Galectin-9 as predictive biomarkers of mortality and potential therapeutic guidance tools.

Keywords: COVID-19, Galectin-9, mortality, soluble immune checkpoints, sTIM-1

R40. THYROID HORMONE CHANGES DURING PREGNANCY AFTER THE COVID-19 PANDEMIC. WHAT HAVE WE LEARNED?

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Pregnancy induces significant physiological changes, including alterations in the endocrine and immune systems, which can influence susceptibility to infections and the progression of comorbid conditions. The global COVID-19 pandemic, caused by SARS-CoV-2, has prompted growing interest in understanding its implications for maternal health, particularly concerning thyroid gland function.

The thyroid gland plays a crucial role during pregnancy by supporting metabolic demands and fetal neurodevelopment through the production of thyroid hormones. Disruption in thyroid function during pregnancy—whether due to autoimmune, infectious, or inflammatory causes—can increase the risk of adverse outcomes such as preterm birth, preeclampsia, and neurodevelopmental impairments in the fetus.

Emerging evidence suggests that COVID-19 may affect thyroid homeostasis through direct viral invasion or indirectly via cytokine-mediated immune responses. Some studies have reported cases of subacute thyroiditis and non-thyroidal illness syndrome (NTIS) in patients with COVID-19, indicating possible viral-induced thyroid dysfunction. In pregnant women, these alterations could be exacerbated by the immunomodulatory effects of pregnancy, creating a complex clinical picture.

Furthermore, thyroid dysfunction may also influence the severity of COVID-19 due to its involvement in immune regulation and systemic metabolism. Thus, monitoring thyroid function in pregnant women with COVID-19 is critical to optimize both maternal and fetal outcomes.

Thyroid dysfunction, whether triggered or exacerbated by SARS-CoV-2 infection, may contribute to adverse maternal and fetal outcomes. Timely recognition, diagnosis, and management of thyroid abnormalities in pregnant women with COVID-19 are essential to mitigate these risks.

Here we will present our research for the prevalence of thyroid dysfunction among pregnant women in R. N. Macedonia.

Keywords: COVID-19, dysfunction, Macedonia, pregnancy, SARS-CoV-2, thyroid

C41. DECODING MACRO TSH: SOLVING THE LABORATORY PUZZLE FOR CLINICIANS

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Immunochemical methods are widely used for in vitro diagnostic techniques in laboratory practice. Despite their excellent performance, immunoassays are sensitive to numerous interferences that can lead to incorrect clinical decisions. The incidence of interferences in immunoassays ranges from 0.4% to 4.0%.

One possible interference during the analysis of thyroid hormones is macro-TSH. This refers to a large circulating form of the TSH molecule, which is a complex of monomeric TSH and anti-TSH autoantibodies. The macro form of TSH is biologically inactive, as the bound autoantibodies, due to the altered conformational structure of the molecule, prevent activation of TSH receptors in target tissues. The prevalence of macro-TSH among patients with subclinical hypothyroidism is 0.6–1.6%, and hormone replacement therapy is not required.

The first step when there is suspicion of the presence of interference is to measure TSH on another platform using a different assay method. The next step involves serial dilutions of the patient's serum, which typically evolve in a nonlinear manner. A polyethylene glycol precipitation procedure follows this. The gold standard for confirming macro-TSH is gel filtration chromatography.

In everyday practice, it is essential to consider both predictable and always possible unpredictable and unrecognized interferences. These represent a potential health risk for patients, as they can lead to inaccurate and unreliable results.

Keywords: immunoassays, interference, macro, TSH

C42. SERUM CONCENTRATION OF ANTI-MULLERIAN HORMONE (AMH), FOLLICLE STIMULATING HORMONE (FSH), LUTEINIZING HORMONE (LH), AND LH/FSH RATIO AND THEIR CORRELATIONS WITH AGE IN WOMEN

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Introduction: Anti-Müllerian hormone (AMH) has been proposed as a clinical predictor of improvements in reproductive aging function in women. Gonadotropin-releasing hormone (GnRH) controls the production of gonadotropins from the pituitary gland, namely FSH (Follicle-stimulating hormone) and LH (Luteinizing hormone), which are responsible for the growth of the gonads and their reproductive activity. The study aimed to investigate the concentration of AMH, FSH, LH, and the LH/FSH ratio in women 25-50 (n=115) years and 51-55 (n=35) years and then to compare results.

Methods: AMH concentration was determined on the AFIAS-1 immunochemical analyzer, Boditech Med. Inc., using the fluorescence immunoassay (FIA) analysis method. The concentration of FSH and LH was determined on Cobas e 411, Roche Diagnostics, using the electrochemiluminescence immunoassay (ECLIA) method. In 150 healthy females ranging from infancy until the end of the reproductive period, serum AMH, FSH, and LH levels were determined. The inclusion criteria were regular menses (duration of cycle: 25–35 days, with 5 days or less inter-cycle difference) and presence of both ovaries. In our study, exclusion criteria were participants on hormone therapy in the past 6 months, history of confirmed infertility, PCOS, overt autoimmune disease, along with chronic, metabolic, and endocrine disease (including hyperandrogenism).

Results: The mean concentrations of AMH were 0.59-5.54 ng/mL, FSH were 0.20-116 mIU/mL, and LH were 0.10-46.61 mIU/mL in the 25-50 years group. In subjects 51-55 years old, the mean concentration of AMH was 0.25-0.67 ng/mL, FSH was 1.90-143.41 mIU/mL, and LH was 2.17-60.12 mIU/mL. The percentage representation of elevated AMH values in the studied categories, according to the results of the statistical analysis, shows that they are more prevalent in the category of participants younger than 51 years of age (52.4%). As many as 40.1% of participants over the age of 51 have reduced AMH values. The percentage of low FSH values in the examined sample was 27.6%, and for LH, 31.5% in participants under 51 years of age. In participants older than 51 years, the percentage representation of lower values for FSH was 14.7%, and for LH, 21.9%. . AMH showed a strong negative correlation with age ($r = -0.724$, $p < 0.001$). LH/FSH ratios have shown age-dependent changes.

Conclusions: Statistically significant differences were found in the levels of AMH, FSH, and LH in relation to the age groups of participants older than 51 years and 25-50 years. As females age, rice, the number of eggs decreases, which causes AMH levels to decrease.

Keywords: anti-Müller hormone, follicle-stimulating hormone (FSH), luteinizing hormone (LH)

R43. PROTEIN C PATHWAY – CLINICAL IMPLICATIONS AND THERAPEUTIC PERSPECTIVES

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Protein C pathway, consisting of protein C (PC), its cofactor protein S, endothelial protein C receptor (EPCR) and thrombomodulin (TM), has an anticoagulant and profibrinolytic effect, an anti-apoptotic and anti-inflammatory activity resulting in a cytoprotective effect, and is involved in angiogenesis and tissue repair. These findings opened perspectives towards therapeutic applications of protein C pathway components.

Patients suffering from acute sepsis having severe alterations in coagulation and life threatening organ dysfunction benefit from activated protein C (APC) administration. APC has a neuroprotective effect in patients with stroke, and cardio-protective effects on cardiomyocytes by inhibition of apoptosis and the expression of inflammatory cytokines after myocardial ischemia. APC was shown to reduce inflammation and joint pain in rheumatoid arthritis. APC has beneficial effects in asthma, on renal cell damage in diabetic patients and in reducing tumor cells adhesion and metastasis in cancer.

EPCR plays a pivotal role in anti-coagulation pathways and inflammation, being considered a potential effector/mediator of inflammatory diseases, mostly in systemic lupus erythematosus and rheumatoid artrithis.

Due to the anticoagulant properties of TM, which functions as a cofactor for thrombin activation of protein C, the recombinant human soluble TM has been used for the treatment of disseminated intravascular coagulation (DIC). Studies have shown that TM can also exert anti-inflammatory and anti-tumor effects.

The multifunctionality of PC pathway provides a complex approach to understanding and addressing various pathological conditions.

Keywords: anti-inflammatory effect, cytoprotective effect, endothelial protein C receptor, protein C, thrombomodulin

C45. ASSOCIATIONS OF PLATELET INDICES WITH MICRO- AND MACROVASCULAR COMPLICATIONS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Introduction: The aim of the study was to evaluate the prognostic value of platelet indices (PI) in relation to micro- and macrovascular complications in patients with type 2 diabetes (T2D).

Methods: A total of 178 T2D patients (45% men, age 62 ± 11.87 years, diabetes duration 10.20 ± 8.53 years), hospitalized at UMBAL "St. Marina", Varna (2023–2024), were included. A control group of 59 age- and gender-matched healthy individuals (55.9% men, age 45.1 ± 9.1 years) was used. PI (MPV, PDW, P-LCR, PLT) were derived from complete blood count (Sysmex XN1000). Data on diabetic retinopathy (DRP), nephropathy (DNP), polyneuropathy (DPNP), acute myocardial infarction (AMI), coronary artery disease (CAD), and stroke were retrospectively reviewed.

Results: PI values were significantly higher in T2D patients compared to controls ($p < 0.05$). DRP correlated with MPV (r = 0.229), PDW (r = 0.208), and P-LCR (r = 0.389). DNP showed associations with PLT (r = 0.271) and PCT (r = 0.353). AMI correlated with MPV (r = 0.166), PDW (r = 0.187), and P-LCR (r = 0.209) ($p < 0.05$ for all). No associations were found for DPNP, CAD, or stroke. Each 1 fL increase in MPV was linked to a 1.917-fold higher DRP risk and 1.675-fold AMI risk; 1 fL in PDW to 1.233-fold DRP and 1.237-fold AMI risk; 1% P-LCR to 1.114-fold DRP and 1.08-fold AMI risk. Cut-off values for DRP were derived: males – MPV >10.90 fL, PDW >13.15 fL, P-LCR >33.2%; females – MPV >11.05 fL, PDW >13.25 fL, P-LCR >33.1%. For DNP in women: PLT >291×10^9/L, PCT >0.315%. For AMI in men: MPV >10.90 fL, PDW >14.30 fL, P-LCR >34.45%.

Conclusions: Elevated PI are promising biomarkers for predicting micro- and macrovascular complications in T2D. The derived cut-off values highlight the potential of PI as clinically relevant biomarkers for identifying patients at risk of DRP, DNP and AMI.

Keywords: acute myocardial infarction, diabetic retinopathy, nephropathy, platelet indices

C46. OSTEOPOROSIS TREATMENT VIA Wnt SIGNALING PATHWAY

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Bone metabolism is a dynamic process related to the alteration of specific circulating metabolites that can be associated with bone mineral density. In 2024, a guideline called "Recommendations for the optimal use of bone-forming agents in osteoporosis" was published, and commented on anabolic therapies as first-line therapies due to their ability to stimulate new bone formation and improve bone microarchitecture, offering significant benefits in rapid fracture reduction over antiresorptive therapies.

Nowadays, the Wnt/beta-catenin pathway, which plays an important role in regulating bone homeostasis and its inhibitors in bone-related disease, is a challenging topic as a new approach to bone physiology. The extracellular Wnt antagonists (sclerostin and dickkopf-1) regulate bone formation by binding directly to Wnt ligands or by competing with Wnt ligands for binding to the co-receptors' lipoprotein-related proteins 5 and 6 expressed on the surface of bone cells. These inhibitors are expressed and secreted within the bone microenvironment and regulate bone formation and resorption.

In order to quantify the serum levels of sclerostin, ELISA, EIA, and automated chemiluminescent assays have been used in different studies. However, accurate measurement of sclerostin from serum and plasma sources remains a significant impediment and needs more detailed structural definitions for the preanalytical phase. Besides, to determine the serum levels of dickkopf-1, limited ELISA kits are available for scientific purposes.

The talk will address the potential pathophysiological role of sclerostin and dickkopf-1, mainly in bone disease, and their potential and future use as a biochemical marker of health and disease.

Keywords: osteoporosis treatment, sclerostin, Wnt ligands

R47. METABOLOMICS BY ^{1}H-NMR SPECTROSCOPY IN CLINICAL CHEMISTRY

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Metabolites play many roles in human health including metabolism, regulation and signalling, biological structures and by acting as precursors for the synthesis of other biomolecules. Metabolomics, the study of metabolites, is emerging as a promising tool in clinical chemistry in screening disease-related biomarkers, discovering novel biomarkers as early predictors of disease outcome, and diagnosing and monitoring various diseases to ensure effective management.

Nuclear magnetic resonance (NMR) spectroscopy combined with advanced data modelling is one of the key analytical platforms used for metabolomics analysis. The unique metabolic 'signatures' it reveals allow clinical chemists to better understand the complex underlying factors causing disease and develop personalized, tailored therapies to prevent and treat disease. On a population scale, this information will help predict disease risk factors in communities and aid in the development of preventive measures. Despite its modest sensitivity, NMR is an advantageous technique for metabolomic research and clinical application, providing high reproducibility, simple sample preparation and the ability to measure different metabolites simultaneously.

Clinical applications of NMR- based metabolomics have been reported for the discovery and monitoring of disease biomarkers, precision medicine and the monitoring of treatment responses. The use of metabolomics analysis in everyday clinical practice is limited by the high cost and large size of conventional high-resolution NMR spectrometers. The new, compact and low-cost alternative, benchtop NMR, offers the potential to overcome these limitations and to facilitate the broader use of NMR-based metabolomics in clinical settings. Benchtop NMR has been used to identify metabolic biomarkers in a range of biofluids, including urine, plasma, fecal water and saliva. Further research is needed to optimize the use of benchtop NMR for clinical applications and explore its potential to impact diagnosis and monitoring of "point-of-care" clinical chemistry.

Keywords: biofluids, biomarkers, clinical chemistry, metabolomics, NMR

C48. FODMAP INDEX AS A MARKER OF DIETARY FERMENTATION POTENTIAL AND DYSBIOSIS: AN NGS-BASED CLINICAL STUDY

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Introduction: The intestinal microbiota (IM) is a key regulator of gastrointestinal function, immune modulation, and host metabolism. Diet, particularly the intake of fermentable oligo-, di-, monosaccharides and polyols (FODMAPs), significantly influences microbiota composition and activity. These substrates are poorly absorbed and readily fermented by gut bacteria, contributing to gas production and gastrointestinal (GI) symptoms in susceptible individuals. The FODMAP index, derived from bacterial composition, estimates microbiota's fermentation potential and may inform targeted nutritional interventions. Here, we aimed to investigate the relationship between the FODMAP index, intestinal dysbiosis, and bacterial phyla distribution in Albanian patients with functional gastrointestinal symptoms.

Methods: Fecal samples from 29 symptomatic patients (presenting with bloating, abdominal pain, nausea, heartburn, diarrhea, and/or constipation) were analyzed using Next-Generation Sequencing (NGS). Parameters assessed included pH, microbial diversity, *Firmicutes*/*Bacteroides* (F/B) ratio, bacterial metabolites (acetate, propionate, butyrate, lactate, histamine, sulfide, methane), mucin degradation, LPS-producing bacteria, FODMAP index, bacterial phyla composition, and enterotype.

Results: Low microbial diversity (<2.7) was detected in 53.3% of patients, while elevated fecal pH (>6.5) was present in 46.7%, consistent with dysbiosis. All participants exhibited a FODMAP index >1.0, indicative of increased microbial fermentation capacity. Altered metabolite profiles were frequent: butyrate (80%), acetate/propionate (40%), lactate (53.3%), histamine (46.7%). Sulfide elevation (16.7%) was significantly associated with butyrate reduction ($p = 0.0025$); methane elevation (31%). A significant association was found between FODMAP index >2 and elevated lactate production ($p = 0.0106$), indicating that higher microbial fermentation potential corresponds with increased lactate levels, likely reflecting enhanced carbohydrate fermentation. Dominant phyla included *Firmicutes*, *Bacteroides*, *Actinobacteria*, and *Proteobacteria*, with *Eurybarchaeota* and *Tenericutes* significantly higher in patients with elevated FODMAP index.

Conclusions: The data indicates widespread intestinal dysbiosis and enhanced fermentation potential, reinforcing the microbiota's role in symptom generation. The findings suggest that low-FODMAP nutritional interventions may confer clinical benefit. NGS-based microbiota profiling offers a valuable tool for personalized management of GI disorders. Recommendations: Future research should aim to validate the clinical utility of the FODMAP index as a predictive tool for dietary response and symptom control. Additionally, studies assessing the long-term impact of dietary modulation on microbial diversity and metabolite balance are warranted.

Keywords: bacterial metabolites, dysbiosis, fermentation, FODMAP, intestinal microbiota

C49. CASE REPORT: GUT MICROBIOME DYSBIOSIS, LOW CITRATE, AND FREE FATTY ACID LEVELS AS EARLY INDICATORS OF IMMUNOMETABOLIC DISTURBANCE IN A PATIENT WITH MILD METABOLIC DYSFUNCTION

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Introduction: Emerging evidence suggests that gut microbiome composition and metabolic intermediates such as citrate and free fatty acids (FFAs) are tightly linked to host immunometabolism. Dysbiosis and altered metabolite profiles may serve as early indicators of metabolic dysfunction, even in the absence of overt clinical disease.

Case presentation: We report the case of a 55-year-old patient who presented mild insulin resistance and low-grade systemic inflammation, without overt diabetes, obesity, or known liver or kidney disease. The patient reported abdominal discomfort but had no significant weight fluctuations. Physical examination was unremarkable.

Laboratory investigations revealed: low urinary citrate levels (hypocitraturia) with normal serum bicarbonate and no evidence of renal tubular acidosis; significantly decreased total free fatty acid (FFA) levels in blood; and normal serum concentrations of vitamins (A, D, E, K, B-complex) and minerals (magnesium, zinc, calcium). Stool microbiota analysis showed: reduced alpha diversity, increased pro-inflammatory bacterial taxa, and decreased beneficial commensals. These findings suggested impaired mitochondrial metabolism, subclinical inflammation, and gut-derived dysregulation.

This case highlights how subclinical metabolic disturbances may be mediated by gut microbiome alterations and bioenergetic deficits. Low urinary citrate levels may reflect impaired TCA cycle activity or mitochondrial stress, while low FFAs may indicate altered lipid mobilization or absorption. The preserved vitamin and mineral status suggests that the observed abnormalities were not due to malnutrition but rather an early-stage immunometabolic imbalance.

This case supports the hypothesis that microbiome-derived metabolites and systemic metabolic markers can serve as sensitive tools for the early detection of immunometabolic risk. It also suggests that targeting the gut microbiota through dietary modulation or microbial therapies may provide a therapeutic pathway even in mildly symptomatic patients.

Conclusions: Gut microbiome dysbiosis, combined with low urinary citrate and reduced blood free fatty acid levels, may serve as early, non-invasive indicators of immunometabolic dysfunction. This case underscores the importance of comprehensive metabolic and microbiome profiling in patients with subtle or atypical presentations of metabolic disorders.

Keywords: free fatty acids, gut, immunometabolism, microbiome dysbiosis

C50. PRECISION NUTRITION AND GENETIC POLYMORPHISMS IN METABOLIC DISEASE MANAGEMENT

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Introduction: Recent studies have demonstrated a significant link between genetic polymorphisms and metabolic risks, particularly in the context of type 2 diabetes and cardiovascular diseases, which highlights the importance of nutrigenetic diets in optimizing preventive and therapeutic strategies. This study aims to examine the impact of genetic variations on metabolism and disease-related metabolic risks by evaluating specific genetic variants involved in the regulation of glycemia, lipid metabolism, and inflammation.

Methods: Between November 2022 and January 2025, 73 participants with a mean age of 41 (±5) years were divided into three groups: control group – standard diet; genetic diet group – subjects with genetic polymorphisms receiving a nutrigenetic diet; non-intervention group – participants with genetic polymorphisms without nutrigenetic intervention. Analyzed genes: IRS1 (rs2943641), TCF7L2 (rs7903146), ADIPOQ (rs17300539), APOC3 (rs5128), LPL (rs328), FABP2 (rs1799883), APOE (rs429358), IL6 (rs1800795), TNF (rs1800629), FADS1 (rs174546), FADS2 (rs174574).

Results: In the genetic diet group, significant improvements were observed. Fasting glucose decreased from 98.2 mg/dL to 90.1 mg/dL ($p < 0.01$); hemoglobin A1c from 6.1% to 5.4% ($p < 0.01$). Insulin levels dropped from 14.3 µU/mL to 8.9 µU/mL ($p < 0.001$); triglycerides decreased from 180 mg/dL to 150 mg/dL ($p < 0.05$). Total cholesterol decreased from 220 mg/dL to 200 mg/dL ($p < 0.01$). HDL cholesterol increased from 47.25 mg/dL to 59.12 mg/dL in Group 2 ($p < 0.001$). LDL cholesterol decreased from 150.34 mg/dL to 120.11 mg/dL in Group 2 ($p < 0.001$). Homocysteine significantly decreased from 11.4 µmol/L to 8.22 µmol/L ($p < 0.01$) in the genetic diet group, compared to a slight increase in the non-intervention group, from 15.1 µmol/L to 16.15 µmol/L ($p > 0.05$).

Conclusions: These results suggest that personalized nutritional intervention based on the genetic profile of the participants led to significant improvements in metabolic parameters, emphasizing the essential role of genetic factors in modulating the dietary response. The study highlights the importance of adapting diets to individual genetic profiles to optimize preventive and therapeutic strategies, thus offering a promising direction for the development of personalized interventions in the treatment and prevention of metabolic diseases.

Keywords: genetic polymorphisms, lipid metabolism, metabolic syndrome, nutrigenetic diet, Omega-6/Omega-3 ratio

C51. SONICATION – A VALUABLE TOOL IN THE DIAGNOSIS OF IMPLANT-ASSOCIATED INFECTIONS

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Introduction: Implant-related infections represent a significant complication contributing to increased morbidity and mortality, in addition to becoming a major problem of public health, largely due to the ability of bacteria to form biofilms on the surface of medical devices. The structure of biofilms protects microorganisms of immune system actions and of antimicrobial treatments, thus decreasing the sensitivity of conventional microbiological methods. Sonication, by disrupting the biofilm structure, helps release bacteria into suspension and significantly improves the likelihood of identifying the causative pathogen.

Methods: A critical review of studies published over the past ten years on the use of sonication in the diagnosis of implant-associated infections, using PubMed and Web of Science as databases was conducted. The sources included in the analysis were 112 original articles and international guidelines, being selected according to clinical and methodological relevance. Only sources available in English were included.

Results: Included papers suggest the most frequently isolated pathogens are Coagulase-negative Staphylococci, *S. aureus*, gram-negative bacilli, anaerobic bacteria (e.g. *Cutibacterium acnes*) and fungi. In the case of sonication usage for prosthetic joint Infections (PJIs), studies reveal sensitivity levels up to 77% and maximal specificity of 96%. All studies place sonication above periprosthetic tissue cultures in terms of pathogen isolation, especially amongst patients previously undergoing antimicrobial treatment, who are at increased risk for false negative culture results.

Conclusions: Sonication is a valuable tool in the microbiological workup of implant-associated infections. Current literature strongly supports its integration into routine laboratory practice, as it significantly enhances diagnostic accuracy.

Keywords: diagnosis, implant-associated infection, sonication

C52. APPLICATIONS OF LIQUID BIOPSY IN THE EARLY DETECTION OF COLORECTAL CANCER

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Introduction: Liquid biopsy is a procedure through which various cancer-associated components are extracted from peripheral blood or other body fluids and analyzed: circulating tumor cells, circulating tumor DNA, microRNAs, long non-coding RNAs, and proteins. These can be used for early detection of colorectal cancer (CRC), monitoring, and treatment. The 5-year survival rate for colorectal cancer ranges from 91% (localized disease) to 15% (metastatic disease).

Methods: The data used in this study were collected through a comprehensive review of the relevant literature available on the PubMed platform (118 articles). Only articles written in English and published between 2019 and 2025 were included.

Results: Circulating tumor cells are difficult to detect in early stages, but one study demonstrated an accuracy of 88% for all stages, including precancerous lesions. Circulating endothelial cell clusters showed high efficiency in distinguishing between healthy individuals and patients with early-stage CRC. Circulating tumor DNA, especially when combined with carcinoembryonic antigen, showed 84% sensitivity and 88% specificity. DNA integrity indexes and ctDNA methylation (especially mSEPT9 – methylated Septin 9) demonstrated higher specificity than traditional tests (such as fecal occult blood test and others), although their efficiency in detecting precancerous lesions remains limited. MicroRNAs (miRNA) from blood, feces, or saliva may serve as useful biomarkers; salivary miR-21 showed a sensitivity of 97% and specificity of 91%, with other examples including fecal miR-106a, which may be especially useful when combined with other tests.

Conclusions: Liquid biopsy offers promising methods for early detection of colorectal cancer, with high accuracy through ctDNA, circulating endothelial cell clusters, and salivary miRNA. Although some biomarkers remain limited in identifying precancerous lesions, combining tests significantly increases diagnostic sensitivity and specificity.

Keywords: circulating tumor cells, circulating tumor DNA, colorectal cancer, liquid biopsy, microRNA, miR-21, mSEPT9

C53. COMPLIANCE WITH ROUTINE LABORATORY TESTING RECOMMENDATIONS: INSIGHTS FROM A SURVEY

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Introduction: Routine laboratory testing is commonly perceived by patients as a tool to validate their health status. However, excessive or unnecessary testing can lead to unintended consequences and increased healthcare costs. In the context of a direct-to-consumer laboratory services being widely available in Romania, this study aims to highlight potential trends among Romanians without medical educational and professional background.

Method: Data were collected through an online survey as part of a broader study on laboratory medicine conducted under the Medical Research education project. The survey gathered general responses regarding personal experiences and attitudes towards routine laboratory testing.

Results: A total of 145 respondents without medical or biomedical educational and professional background completed the survey. Most participants (77.2%) reported always following their physician's recommendations regarding routine testing. However, a notable portion (80%) also accessed laboratory services independently, without prior medical advice. Among those who did not adhere to testing recommendations, the primary reasons cited included the perception of being healthy (31%), financial constraints (17.9%), and lack of time (16.5%). The majority of respondents (79.3%) identified themselves as generally health-conscious, a factor that may contribute to increased engagement with routine testing.

Conclusions: While medical recommendations are generally followed, the widespread availability of laboratory services and a prevailing concern for personal health may contribute to a pattern of self-initiated routine testing. These findings underscore the need for better public education on the appropriate use of laboratory investigations.

Keywords: compliance with the physicians' recommendations, direct-to-consumer testing, routine testing

C54. ADVANCES IN CRISPR DIAGNOSTICS: A PROMISING TOOL IN DIAGNOSING ANTIMICROBIAL RESISTANCE

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Introduction: In the context of the global threat of antimicrobial resistance, especially of bacteria from the critical "ESKAPE" group, there is an urgent need to develop new, high-throughput diagnostic methods for resistance genes. Conventional methods such as PCR and enzyme immunoassays require specialized equipment and underperform in the early stages of infections, when the amount of biomarker is quite low.

Methods: A literature review on the subject was performed using the PubMed and HINARI databases, targeting articles on the applicability of CRISPR-Cas systems in detection of antibiotic resistance (87 articles). The filters used were "Last 10 years" and "Full text".

Results: CRISPR-based methods are simple, fast, more sensitive and specific and allow multiple detection. CRISPR-Cas9, 12, 13, 14 identify and cleave DNA/RNA sequences associated with antimicrobial resistance. CRISPR-Cas9 combined with an optical DNA mapping process identified the blaCTX-M, blaNDM, and blaKPC genes in plasmid molecules. The FLASH technique allows multiplex detection of resistance sequences in *S. aureus* and vancomycin-resistant *E. faecalis*. The E-Si-CRISPR biosensor detected MRSA without using amplification, with a detection limit of 3.5 fM and high selectivity in human serum. A fast colorimetric assay based on CRISPR-Cas12a and the Au-Fe3O4 nanoenzyme detects genes that provide resistance to kanamycin, ampicillin, and chloramphenicol.

Conclusions: Identification of antimicrobial resistance genes using CRISPR-Cas systems is a growing field of interest, prompting development solutions with high sensitivity and specificity and increasingly rapid detection. Moreover, the portability, low cost, and simultaneous detection of multiple resistance genes that characterize many platforms make them effective options for point-of-care testing.

Keywords: antimicrobial resistance, CRISPR, point-of-care testing

C55. ARTIFICIAL INTELLIGENCE FOR THE INTERPRETATION OF NGS DATA IN SOLID TUMOR DIAGNOSTICS

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Introduction: Molecular diagnostic technologies are advanced tools that have substantially contributed to the progress in diagnosis, prognosis, and clinical management of patients. Their rapid evolution and wide applicability have resulted in the generation of large volumes of complex data, requiring the implementation of specialized analytical systems. Consequently, numerous platforms for data processing and interpretation have been developed to enhance analytical efficiency and improve clinical outcomes.

Methods: In this study, biological samples obtained from patients diagnosed with one of the four types of malignancies — non-small cell lung cancer (NSCLC), breast cancer, ovarian cancer, and colorectal cancer — were analysed using molecular diagnostic methods integrated with artificial intelligence (AI)-based technologies. For NSCLC patients, molecular profiling was performed using Next-Generation Sequencing (NGS) and Real-Time Polymerase Chain Reaction (Real-Time PCR). Samples from patients with breast or ovarian cancer were analysed for reportable mutations in the BRCA1 and BRCA2 genes using NGS. In the case of colorectal cancer, mutational analysis focused on the KRAS and NRAS genes using Real-Time PCR. All specimens were formalin-fixed paraffin-embedded (FFPE); NGS was performed using the Illumina platform, while Real-Time PCR was conducted using the EasyPGX® system.

Results: AI-assisted molecular analysis revealed recurrent mutations in patients with non-small cell lung cancer (NSCLC), particularly in the EGFR, KRAS, BRAF, ALK and MET genes. In patients with breast or ovarian cancer, the analysis focused exclusively on the detection of pathogenic variants in BRCA1 and BRCA2. The identified variants were classified into five categories based on their clinical significance: (1) oncogenic, (2) likely oncogenic, (3) variants of uncertain significance (VUS), (4) likely benign, and (5) benign. Additionally, these variants were stratified according to the AMP/ASCO/CAP guidelines into Tier I (variants of strong clinical significance), Tier II (potential clinical significance), Tier III (uncertain significance), and Tier IV (likely benign or benign). In the colorectal cancer cohort, targeted analysis of clinically relevant mutations revealed that approximately 40% of patients harbored KRAS mutations, with 68% of those located at codon 12. Furthermore, NRAS mutations were identified in 6% of the patients.

Conclusions: The integration of molecular diagnostics with AI-assisted data analysis enables precise identification and classification of clinically relevant genetic variants across multiple cancer types. Variant interpretation according to current guidelines ensures standardized clinical reporting and supports informed therapeutic decisions. Overall, these findings emphasize the clinical utility of integrated molecular profiling in personalizing cancer care and optimizing patient outcomes.

Keywords: artificial intelligence, NGS, cancer

C56. EXPLORING THE GUT MICROBIOME’S ROLE IN COLORECTAL CANCER

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Introduction: Colorectal cancer (CRC) is a major public health concern worldwide and ranks among the leading causes of cancer-related mortality globally. During the development of CRC, a multitude of heterogeneous genomic, epigenomic and transcriptomic transformations occur, undergoing complex processes. There is growing evidence suggesting that the gut microbiome plays a crucial role in the initiation, progression, and metastasis of CRC. Metagenomic studies have demonstrated notable alterations in the gut microbiome composition in both fecal and mucosal samples from patients with CRC compared to healthy individuals.

Methods: A comprehensive literature search was conducted using PubMed to investigate the gut microbiome’s role in CRC development, targeting articles published within the past year. After filtering by title, abstract and content, 78 articles were selected based on their focus on the identification of bacterial species involved in colorectal oncogenesis.

Results: The major protumorigenic bacteria identified in the studies are *F. nucleatum*, polyketide synthase-positive *E. coli*, enterotoxigenic *B. fragilis*, and *S. gallolyticus*. Increased levels of *F. nucleatum* in CRC have been associated with an elevated cytokine production, including IL-17A and TNF-α, that promotes tumor growth by sensitization of the nuclear factor kappa B (NF-κB) signaling pathway. *E. coli* has also been found to promote CRC metastasis by disrupting the intestinal vascular barrier.

Conclusions: Evidence such as increased levels of *F. nucleatum*, *E. coli*, or *B. fragilis* in CRC supports the potential use of these microorganisms as biomarkers to complement conventional diagnostic methods. Further studies are needed to help fully determine the pathogenic role of the gut microbiome in carcinogenesis and its response to treatment. By developing interest in this topic, the gut microbiome could become a crucial part of future cancer diagnosis, prevention, and treatment methods.

Keywords: biomarker, colorectal cancer, gut microbiome

C57. STEP INSIDE EFLM: YOUR GATEWAY TO GROWTH IN LABORATORY MEDICINE

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Curious about how to shape your career beyond the lab bench? In this engaging and interactive session, Daniel Rajdl — Chair of the EFLM Communication Division — will introduce you to the world of EFLM: who we are, what we do, and how you can get involved.

From the EFLM Academy and EuSpLM Register to webinars, publications, and functional units, you'll gain insights into the many opportunities EFLM offers to young scientists. We’ll also explore the practical digital tools — like Canva, ChatGPT, and social media aggregators — that we use to promote EFLM’s activities and that can help you build communication skills essential for laboratory professionals in the digital era.

Whether you're looking to network, grow professionally, or contribute to the future of laboratory medicine, this is your gateway to making it happen.

Keywords: EFLM, laboratory medicine, opportunities, young scientists

C58. UNLOCKING YOUR FUTURE: EFLM-IFCC-ADLM FUNDING, NETWORKS & OPPORTUNITIES FOR YOUNG SCIENTISTS

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Young scientists in laboratory medicine face both exciting opportunities and unique challenges in building their careers. This session provides a practical, comprehensive overview of key resources available through leading professional organizations—the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM), the Association for Diagnostics and Laboratory Medicine (ADLM), and the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC).

Attendees will learn about bursaries, travel grants, fellowships, and educational programs designed to support early-career researchers and clinicians. The presentation also highlights vibrant scientific networks, mentoring programs, publishing avenues, and valuable volunteer roles that foster professional development and expand career horizons.

This interactive session aims to empower young laboratory medicine professionals to effectively leverage these opportunities, with practical guidance on applications and active engagement. Join us to discover how to unlock funding, build scientific networks, contribute your voice through publications, and develop new skills—fueling your path toward a successful and impactful career.

Keywords: career development, EFLM, laboratory medicine, opportunities, young scientists

C59. SHARE KNOWLEDGE WITH EFLM LabX, SHOWCASE THE PROFESSION WITH EULabDay

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The EFLM LabX programme is designed to foster knowledge exchange among laboratory medicine professionals across the EU. This session will present the benefits of the programme for both applicants and offerers, including how to offer practice and training free of charge and how to apply using the LabX platform.

Sharing knowledge is our professional duty, and the LabX network offers valuable enrichment for both applicants and host laboratories. Information on who can apply for an EFLM bursary, how to apply, and experiences from previous applicants and hosts will also be shared. As laboratory medicine professionals, we are aware that our field is often underrecognized and hidden within the healthcare system. To raise awareness and appreciation, EFLM launched EuLabDay, celebrated annually on November 5th. On this day, laboratories across the EU are encouraged to open their doors to the public and healthcare professionals, organize educational events, and run social media campaigns to improve the visibility of our profession.

This session will also highlight how to organize EuLabDay events and share experiences from past celebrations. Together, LabX and EuLabDay promote the visibility, mobility, and professional development of laboratory medicine professionals. The important contributions of young scientists in both initiatives demonstrate meaningful opportunities for international collaboration and growth.

Keywords: EULabDay, laboratory medicine, LabX

P15. THE ROLE OF FECAL CALPROTECTIN IN DETECTING INTESTINAL INFLAMMATION

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Introduction: Calprotectin is a protein present in human neutrophils and released into feces during active intestinal inflammation. It serves as a noninvasive clinical screening tool for inflammatory bowel disease (IBD), primarily Crohn's disease and ulcerative colitis. Fecal calprotectin demonstrates high sensitivity and specificity for detecting and diagnosing mucosal and histological inflammation. However, elevated fecal calprotectin levels can also occur in other conditions, such as infections (bacterial, parasitic, viral) and gastrointestinal bleeding. The aim of this study was to evaluate the diagnostic performance of fecal calprotectin in detecting IBD.

Methods: This retrospective study analyzed one year of data collected from the Clinical Center of the University of Sarajevo. Laboratory results of fecal calprotectin were obtained from adult patients (≥18 years) with suspected IBD presenting gastrointestinal symptoms such as abdominal pain, diarrhea, and rectal bleeding. IBD diagnosis was confirmed via endoscopy, which served as the gold standard. Fecal calprotectin levels (µg/ml) were measured using enzyme-linked immunosorbent assay (ELISA) (DRG Diagnostics GmbH). Calprotectin levels >100 µg/ml were considered positive.

Results: The study included fecal calprotectin results from 652 adult patients, of whom 261 (40%) were male and 391 (60%) female. The median age was 47.0 years (IQR: 32.0–63.0). Forty-four patients (6.75%) had colonoscopy-confirmed IBD. Additionally, 103 patients (15.8%) exhibited fecal calprotectin levels >100 µg/ml, with a median (IQR) of 276.3 (168.5–471.5). The sensitivity of fecal calprotectin for detecting IBD was 0.909 (95% CI: 0.788–0.964), and specificity was 0.898 (95% CI: 0.871–0.920).

Conclusions: Fecal calprotectin is a valuable diagnostic tool with good performance in detecting intestinal inflammation. It has significant clinical applications in the diagnosis and monitoring of IBD, assessing treatment response, and guiding the need for further invasive procedures such as endoscopy.

Keywords: calprotectin, inflammatory bowel disease (IBD), sensitivity, specificity

P16. SERUM ADIPONECTIN LEVELS IN SEVERE BURNS

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Introduction: Severe burns are life-threatening injuries that often result in significant morbidity, emotional distress, and a decreased quality of life. A key factor contributing to poor outcomes following a severe burn injury is the hypermetabolic response, which triggers substantial changes in glucose, lipid, and amino acid metabolism. The primary objective of our study was to evaluate serum levels of adiponectin in severely burned children with 25% total body surface area (TBSA) at two different time points: 48 hours and 21 days post-burn.

Methods: Our study included 32 children with burns primarily caused by flames and hot liquids, along with 21 healthy subjects. Serum adiponectin levels were measured using the multiplex technique.

Results: Serum levels of adiponectin decreased 48 hours after the burn; however, after 21 days, this hormone showed increased levels compared with the healthy group (p=0.048). We identified a negative, statistically significant correlation between adiponectin levels after 48 hours and TBSA, as well as a statistically significant positive correlation with the hot liquid burn mechanism (p<0.05).

Conclusions: The decreased serum adiponectin level at 48 hours may indicate the severity of trauma, while the elevated level at 21 days is associated with a favorable prognosis. Adipose tissue is one of the primary organs involved in the systemic response to significant trauma. Therefore, , in this context, adiponectin acts as a marker for the severity of the systemic inflammatory response in severe burns.

Keywords: adiponectin, burn, children, correlation, hormone, severity

P17. ANTINUCLEAR ANTIBODIES IN PATIENTS WITH POSITIVE THYROID ANTIBODIES

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Introduction: Antinuclear antibodies (ANA) are important biomarkers of autoimmunity and are highly prevalent in systemic or organ-specific autoimmune diseases, as well as in autoimmune thyroiditis. Autoimmune thyroid disease occurs when the body's immune system attacks the thyroid gland and can be identified by the presence of Thyroglobulin antibodies (Anti-TG) or Thyroid Peroxidase antibodies (Anti-TPO) in serum. The aim is to identify the relationship between thyroid antibodies and Antinuclear Antibodies.

Methods: This observational study involved 140 patients of Genius Laboratory Clinic from January 2024 to December 2024. The patients were between 20 to 80 years old, 100 were females and 40 were males. Patients with positive results for Anti-TPO and/or Anti-TG were tested for ANA screening IgG. Thyroid antibodies (Anti-TG, Anti-TPO) and thyroid function tests as thyroid-stimulating hormone (TSH), free tri-iodothyronine (FT3), and free thyroxine (FT4), were measured using Chemiluminescence immunoassay (CLIA). ANA IgG was measured with immunofluorescence using Hep-2 cells.

Results: In our study was seen that of 80 (58%) patients who were positive for Anti-TPO with a mean value of 1250 IU/ml, 24 patients (30%), of which 20 females and 4 males had positive ANA titers from 1:160- 1:1280, with a mean of 1:320. Of 40 (28%) patients with positive Anti-TPO and Anti-TG simultaneously, with a mean of Anti-TPO 1360 IU/ml and Anti-TG 980 IU/ml, 16 patients (40%) were positive for ANA with a mean of 1:320 titer. Of 20 (14%) patients who were positive for Anti-TG with a mean value of 1030 IU/ml, 5 patients (25%) were positive with a mean ANA of 1:160. The patients with the highest Anti-TPO, Anti-TG, highest TSH, and lowest FT4 values had the highest titer of ANA with a mean of 1:640.

Conclusions: Positive antinuclear antibodies were associated with positive thyroid antibodies. The highest values of anti-TPO, anti-TG were associated with the highest ANA titer.

Keywords: antinuclear antibodies, thyroid peroxidase antibodies (TPO), thyroglobulin antibodies (TG)

P18. EVALUATION OF THE PARACLINICAL PROFILE OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Introduction: In rheumatoid arthritis (RA), both clinical manifestations and laboratory markers are key elements in establishing the pathology in relation to the disease stage at diagnosis. The relationship between the paraclinical profile of RA patients and the stages of the disease was investigated. Autoimmune markers—anti-cyclic citrullinated peptide antibodies (Anti-CCP) and rheumatoid factor (RF)—as well as inflammatory markers—erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)—were evaluated.

Methods: This retrospective study included a total of 85 patients with RA who presented at the Emergency County Clinical Hospital of Targu Mures between August and December 2024. Rheumatoid Factor and Anti-CCP were measured using the CLIA (chemiluminescence) technique. Demographic, clinical, and laboratory data were collected from the hospital's information system. Statistical analysis was performed using MedCalc® Version 23.2.1 and Microsoft Excel 2021.

Results: A percentage of 80% of patients with RA were female, and 86% were over 50 years old. The disease was classified in four stages, with the following patient distribution: 13% in stage I, 44% in stage II, 23% in stage III, and 20% in stage IV. Of the patients, 11% had systemic autoimmune diseases, 6% had organ-specific autoimmune conditions, while 67% of patients were tested positive for Anti-CCP. Rheumatoid Factor was positive in 67% of patients, and 68% of the patients showed elevated inflammatory status, which did not correlate with the disease stage. Double positivity for RF and Anti-CCP was found in 55% of the patients. Among the double-positive patients, 4% were in stage I, 43% in stage II, 23% in stage III, and 30% in stage IV.

Conclusions: Early-stage RA diagnosis requires testing for Anti-CCP and RF biomarkers. Only Anti-CCP serum levels and acute-phase reactants were correlated with disease stage. Once RA is diagnosed, repeated RF testing becomes unnecessary.

Keywords: anti-CCP, rheumatoid arthritis, rheumatoid factor

P19. CORRELATION OF LABORATORY PARAMETERS WITH CLINICAL CHARACTERISTICS AND LUNG X-RAY IN COVID-19 PATIENTS

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Introduction: At the end of 2019, a new strain of coronavirus was discovered in China, which was not known in humans until now. The World Health Organization (WHO) named this new strain SARS-CoV-2 (SARScoronavirus-2), and the disease caused by COVID-19 ("coronavirus disease"). The SARS-CoV-2 virus is distinct and therefore it is necessary to monitor its manifestations on certain hematological, biochemical and coagulation parameters, on pneumonia (pneumonia) caused by the SARS-CoV-2 virus. The aims of this study were to observe the correlation between inflammatory parameters (C-reactive protein - CRP and erythrocyte sedimentation), D-dimer and the clinical status of a COVID-19 patient, as well as the correlation of X-ray images of the lungs with the mentioned parameters.

Methods: This research included 76 patients positive for SARS-CoV-2 infection, who were divided into three groups based on oxygen saturation (>93% mild, 85-93% moderately severe and <83% severe clinical status). Laboratory analyzes are determined on an automatic analyzer, while SaO2 is determined by pulse oximetry and X-ray image of the lungs is obtained by X-ray imaging.

Results: In this study, CRP, erythrocyte sedimentation and D-dimer were significantly elevated in the group of patients with severe clinical status compared to mild status. When a significant association of D-dimer with the degree of severity of the infection and its manifestations was observed, D-dimer represented the basic analysis that, together with the X-ray of the lungs, determined the further treatment of the COVID-19 disease. Patients who were older and had certain comorbidities were followed with a more severe clinical picture accompanied by bilateral pneumonia described as bilateral hazy shadows.

Conclusions: All laboratory findings including hematological, biochemical and coagulation were elevated in all subjects infected with SARS-CoV-2 virus. D-dimer represented the basic analysis which, together with CRP and erythrocyte sedimentation, determined the severity of the clinical status as well as the death outcome of hospitalized patients.

Keywords: COVID-19, C-reactive protein, D-dimer, lung X-ray

P20. IMPACT OF IRON, VITAMIN D, AND B12 DEFICIENCIES ON ANEMIA AND SYSTEMIC INFLAMMATION: A RETROSPECTIVE COMPARATIVE STUDY

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Introduction: Micronutrient deficiencies, especially iron, vitamin D, and B12, are common and may contribute to anemia and systemic inflammation, impacting patients' overall health.

Methods: A retrospective comparative study was performed on laboratory data from 599 patients: 367 outpatients from Bistrița Hospital and 232 inpatients from Câmpia Turzii Hospital. The prevalence of iron, vitamin D, and B12 deficiencies and their correlations with anemia markers (hemoglobin, mean corpuscular volume) and inflammation marker (C-reactive protein) were analyzed. Associations were assessed using the Phi coefficient.

Results: Vitamin D deficiency was present in over 70% of patients in both groups. Iron deficiency showed a moderate correlation with anemia ($\phi=0.34$) and a weak correlation with inflammation ($\phi=0.21$). The prevalence of anemia was significantly higher in patients with combined iron and vitamin D deficiencies (75%) compared to those without deficiencies (4.17%) or with isolated vitamin D deficiency (16.10%).

Conclusions: Nutritional deficiencies, particularly vitamin D and iron, are frequent and associated with anemia and systemic inflammation. Extended laboratory screening is essential for comprehensive evaluation and personalized therapeutic interventions.

Keywords: anemia, iron, nutritional deficiencies, systemic inflammation, vitamin D

P21. DISORDERS OF SEX DEVELOPMENT DUE TO 5-α REDUCTASE DEFICIENCY

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Introduction: Disorders of sex development (DSD) refer to a diverse group of conditions in which chromosomal, gonadal, or anatomic sex development is atypical. DSDs can also be classified into disorders of gonadal development or defects in hormone synthesis or action. 5-alpha-reductase deficiency is a rare disorder characterized by incomplete differentiation of male genitalia in 46, XY patients. The 5α-Reductase is mostly known for converting testosterone, the male sex hormone, into the more potent hormone, dihydrotestosterone (DHT). Because DHT is required for the normal masculinisation of the external genitalia in utero, genetic males with 5-alpha-reductase deficiency are born with ambiguous genitalia (46, XY DSD).

Methods: Testosterone total (TT), dihydrotestosterone (DHT), and TT/DHT ratio were evaluated in the serum of 6 cases of ambiguous genitalia with 46 XY karyotype, before and after HCG stimulation. Four patients were neonates, and 2 cases were in puberty. The TT/DHT ratio was calculated to reflect 5-alpha-reductase activity.

Results: In two neonate patients, we observed a high level of TT and DHT, with a normal TT /DHT ratio. In two other neonate cases, the levels of TT, DHT, and the TT /DHT ratio were normal. After the HCG stimulation, we observed an increase in the level of TT in all cases, and in 2 of them, we found a TT/DHT ratio >27. In two pubertal patients, we observed a high level of TT and DHT with a normal TT/DHT ratio, before and after HCG stimulation.

Conclusions: In conclusion, the TT/DHT ratio can help in the investigation of 46, XY patients with ambiguous genitalia and normal testosterone synthesis. TT/DHT ratio can be used to select newborns affected by 5alpha-reductase deficiency. 5α-reductase deficiency should be included in the differential diagnosis of all newborns with 46 XY DSD with normal testosterone production.

Keywords: DHT, TT, TT/DHT ratio, 5α-reductases activity

P22. EFFECTS OF Wnt PATHWAY IN GASTRIC CANCER

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Introduction: The prognosis of certain cancer types, such as gastric cancer, is poor, and significant progress in its treatment has not been achieved. Reactive oxygen species (ROS), apoptosis, angiogenesis, and the Wnt signaling pathway play crucial roles in tumor growth, spread, differentiation, and metastasis. One of the main signaling pathways involved in various physiological and pathological processes, including embryonic development, tissue regeneration, cell proliferation and differentiation, cancer, neurodegenerative diseases, and bone metabolism disorders, is the Wingless/β-catenin (Wnt/β-catenin) pathway. In the absence of β-catenin, the Wnt signaling pathway is regulated by oxidative stress following ionizing radiation (IR) treatment, as ROS levels increase and the level of catalase, which eliminates hydrogen peroxide, decreases. By balancing the predominantly proliferative Wnt-TCF signaling pathway and the forkhead box O (FOXO) signaling pathway, β-catenin can protect against oxidative stress (mainly stress response). This study aims to investigate the relationship between pre- and post-operative activation of the Wnt signaling pathway and serum levels of Dickkopf1 (DKK1), Wnt, β-catenin, ROS, and FOXO in patients diagnosed with operable gastric cancer.

Methods: Our study group consists of 20 cases (preoperative and postoperative) and 20 control subjects (selected from healthcare personnel in the same age range as the case group) who have no chronic diseases and voluntarily participated in the study. The levels of Dickkopf1 (DKK1), Wnt, β-catenin, ROS, and FOXO in blood samples collected from the study participants were determined using ELISA and Western blot analysis.

Results: In patients with gastric cancer, we observed an increase in Wnt, ROS, and β-catenin levels before and after surgery, while DKK1 levels decreased.

Conclusions: Based on these findings, we consider using these markers for diagnostic purposes. Early diagnosis of patients may reduce treatment costs and improve patient outcomes.

Key words: Dickkopf1 (DKK1), FOXO, gastric cancer, ROS, Wnt, β-catenin

P23. PROTEIN BIOMARKERS FOR CERVICAL CANCER SCREENING

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Introduction: Cervical cancer (CC) is the fourth most common cancer in women, with around 660000 new cases in 2022. Cervical cancer remains a significant global health burden, necessitating innovative approaches for improved diagnostics and personalized treatment strategies. While traditional screening methods such as Pap smears and HPV testing have been effective in reducing cervical cancer incidence and mortality, there is ongoing research to identify and validate novel biomarkers that can enhance early detection and risk stratification.

Methods: A systematic literature review in PubMed and HINARI was performed for original articles based on a search strategy related to the objectives.

Results: HIF 1 and VEGF: The predictive value of HIF 1α, HIF 2α, and VEGF is mainly associated with their increased levels in CC and their correlation with poor response to treatment. Reduction in VEGF and HIF 1α levels were significantly associated with improved clinical responses. P16INK4a: P16INK4a, a tumor suppressor protein, controls the cell cycle by blocking cyclin-dependent kinases (CDKs). Elevated levels of p16INK4a are frequently detected in cervical intraepithelial neoplasia and cervical cancer. HPV E6/E7 oncoproteins: The E6 and E7 oncoproteins encoded by high-risk HPV types such as HPV16 and HPV18 play crucial roles in cervical carcinogenesis. Cytokeratin 7 (CK7) and cytokeratin 17 (CK17) are commonly upregulated in cervical squamous cell carcinoma and adenocarcinoma, respectively.

Conclusions: Protein biomarkers offer considerable potential for enhancing early identification, diagnosis, and treatment of cervical cancer. Furthermore, the integration of protein biomarkers with other diagnostic methods, such as HPV testing and imaging technologies, could augment the precision of cervical cancer detection and ultimately enhance patient outcomes.

Keywords: cervical cancer, protein biomarkers, screening

P24. THE ROLE OF PROSTATE-SPECIFIC ANTIGEN IN MONITORING AND THERAPEUTIC FOLLOW-UP IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA

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Introduction: Prostatic disorders, including benign prostatic hyperplasia (BPH) and prostate cancer, are common in men over 50. While prostate cancer contributes to significant morbidity, BPH is the most prevalent non-malignant condition. Prostate-Specific Antigen (PSA) is used not only for early cancer detection but also for monitoring BPH progression and response to therapy. Clinical biochemistry laboratories play a key role in interpreting PSA values within the clinical context to support treatment decisions.

Methods: This retrospective study included 50 male patients (mean age 66.5 years) undergoing routine PSA testing at the Biochemical Laboratory of the Clinical Hospital in Tetovo. All patients had previously been diagnosed with BPH and were treated with Tamsulosin 0.4 mg and/or Dutasteride 0.5 mg. PSA levels before and after a 6 to 12-month treatment period were compared to assess therapeutic response.

Results: Baseline PSA values ranged from 0.5 to 18 ng/ml (mean 4.2 ng/ml). After treatment, 70% of patients showed reduced or stable PSA levels, while 30% had increases that, in some cases, prompted clinical re-evaluation and imaging. PSA monitoring supported therapeutic adjustment where necessary.

Conclusions: Biochemical monitoring of PSA provides valuable insight into BPH treatment response and disease progression. Laboratory-clinician collaboration is essential for individualizing patient care and guiding long-term management strategies.

Keywords: benign prostatic hyperplasia (BPH), laboratory medicine, monitoring, prostate-specific antigen (PSA), treatment response

P25. MMP-9: A PROMISING EARLY BIOMARKER IN PARKINSON'S DISEASE

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Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the loss of dopaminergic neurons and is typically diagnosed at an advanced clinical stage. There is a growing need for reliable biomarkers that can detect early pathological changes before the onset of motor symptoms. In this context, matrix metalloproteinases (MMPs), particularly MMP-2 and MMP-9, have emerged as potential candidates due to their involvement in neuroinflammatory and neurodegenerative processes.

Methods: This study aimed to investigate the role of MMP-2 and MMP-9 in the pathogenesis of Parkinson's disease using an established mouse model (with a 100% survival rate) based on systemic administration of MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine). This neurotoxin selectively targets dopaminergic neurons. The experiment was conducted on CD21 mice randomly divided (n=10) into MPTP and Control groups (25 mg/kg b.w., i.p., every two days for two weeks). Mice were sacrificed following treatment, and blood samples were collected for biochemical analysis. The expression and enzymatic activity of MMP-2 and MMP-9 were assessed using zymography and Western blot techniques. The ethical statement was authorized by National Authority for Veterinary Health and Food Safety with No. 356/14.03.2023 in accordance with Government decision no. 42/2004 and Law No. 215/2004.

Results: Our results revealed a significant increase in MMP-9 activity and expression in the brains of MPTP-treated mice, while MMP-2 levels remained relatively unchanged compared to controls. The elevated levels of MMP-9 suggest its active involvement in the neurodegenerative process characteristic of early PD, likely contributing to blood-brain barrier disruption and neuronal matrix remodeling. These findings support the hypothesis that MMP-9 could serve as an early, non-invasive biomarker, particularly if detected in accessible biological fluids such as blood or cerebrospinal fluid (CSF).

Conclusions: MMP-9 represents a promising molecular target for the early detection and monitoring of Parkinson's disease. Further studies are needed to validate its diagnostic potential in clinical settings and to explore the mechanistic role of metalloproteinases in PD pathology.

Keywords: biomarker, early diagnosis, MMP-9, Parkinson's disease, zymography

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P26. RUBELLA IMMUNITY AMONG PREGNANT WOMEN: A CROSS-SECTIONAL STUDY AND ITS IMPLICATIONS

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Introduction: Despite the availability of the measles-mumps-rubella (MMR) and single-antigen rubella (RCV) vaccines, congenital rubella syndrome remains a preventable cause of fetal loss and birth defects wherever immunity gaps persist. We assessed the current immune status to rubella among pregnant women enrolled in a TORCH (*Toxoplasma*, Others, Rubella, CMV, HSV) screening programme.

Methods: This cross-sectional study included all women who presented for antenatal care between January 2023 and January 2025 in a tertiary maternity centre (N = 4,473). Serum IgG and IgM antibodies against rubella virus were determined by ELISA; demographic data and vaccination-eligibility status were extracted from electronic records. Associations were analysed with logistic and multinomial regression.

Results: Valid Rubella serology was available for 4,185 pregnancies (93.6%). Protective IgG antibodies were detected in 3,755 women, yielding an overall seroprevalence of 89.7% (95% CI 88.5–90.9), while acute/recent infection, reflected by IgM reactivity, was rare (0.38%, 16/4,185). Only 0.56% (26/4,613) of women were simultaneously IgG- and IgM-positive, suggesting very recent infection or secondary immune response. Age distribution did not differ between immune and susceptible groups. In multivariable analysis, women who had missed routine childhood vaccination were significantly more likely to lack protective IgG (adjusted OR 0.43, 95% CI 0.30–0.61, $p < 0.001$), whereas eligibility for the adolescent RCV booster or the two-dose MMR schedule doubled the odds of immunity, significant only for the MMR group ($p < 0.001$). No significant predictors were identified for IgM positivity because of its low frequency.

Conclusions: Nearly one in ten pregnant women remained susceptible to rubella, and sub-optimal vaccine coverage explained most cases of non-immunity. Strengthening pre-conception screening and catch-up MMR/RCV vaccination—especially for cohorts missed during earlier campaigns—is essential to close the immunity gap and to progress toward elimination of congenital Rubella syndrome.

Keywords: immunity, Rubella, screening, seroprevalence, vaccination

P27. CHALLENGES OF LABORATORY DIAGNOSIS IN *T. PALLIDUM* INFECTION

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Introduction: *T. pallidum* infection continues to show an increasing incidence worldwide, despite effective antimicrobial therapies that once seemed to offer the chance to eradicate this disease. Among the causes of this recrudescence are the lack of an effective vaccine, the culturing characteristics of the pathogen, variable clinical forms of the disease, and the limitations of serological tests. In this presentation, we attempted to review the main limitations faced by clinicians and laboratory specialists in diagnosing syphilis.

Methods: We presented the screening algorithms (the traditional algorithm and the reverse screening algorithm), treponemal tests (FTA-ABS—Fluorescent Treponemal Antibody Absorption test, TPPA—*T. pallidum* Particle Agglutination assay) and non-treponemal tests (VDRL—Venereal Disease Research Laboratory test, RPR—Rapid Plasma Reagin test), as well as confirmatory tests: dark-field microscopy, immunohistochemical techniques, enzyme immunoassays (EIA), silver stains, and molecular techniques.

Results: Clinical diagnosis can be challenging in many situations, especially during the latent/asymptomatic stages, in paucisymptomatic forms, or when it is associated with other infections (e.g., HIV). Serological tests also have certain limitations: false-positive results in autoimmune diseases or viral infections, false-negative results in the initial or advanced stages of the disease; additionally, serological tests do not allow for disease staging.

Conclusions: The laboratory diagnosis of *T. pallidum* infection remains a significant challenge due to both technical and biological limitations. An integrated and multidisciplinary approach is essential to improve the detection, treatment, and control of syphilis on a global scale.

Keywords: nontreponemal tests, *T. pallidum*, treponemal tests

P28. ASSOCIATION BETWEEN TOBACCO SMOKE AND IMMUNOGLOBULIN E-MEDIATED SENSITIZATION IN PATIENTS WITH ALLERGIC DISORDERS

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Introduction: Allergic sensitization is common in the European population and is a predisposing factor for multiple respiratory conditions. Those conditions, including asthma and allergic rhinitis, can greatly affect an individual's quality of life and incur a substantial economic burden. Cigarette smoke has a diverse range of effects on the immune system, including enhancement of suppressor T-cell function and decreases in TH cells. These immune-suppressant effects might be expected to influence allergic sensitization. However, currently available evidence on the effect of smoking on allergic sensitization is conflicting. Despite this uncertainty, avoiding exposure to cigarette smoke is frequently recommended to reduce the risk of allergic sensitization. Tobacco exposure has been linked with sinonasal pathology and may be associated with allergic sensitization. This study evaluates the association between exposure to active smoking and the prevalence of rhinitis and allergic sensitization.

Methods: In this study, 133 adult patients aged 20–65 years were included, examined in City General Hospital "8th September"- Skopje, from January to December 2024. Parameters were established as follows: never smoking was defined as reported lifetime smoking less than 100 cigarettes (65 patients), while active smoking was defined as self-reported smoking (68 patients). Self-reported rhinitis was based on symptoms during the past 12 months. Allergen sensitization was defined as a positive response to any of the 24 IgE-specific antigens tested, including Grass pollen (Orchard grass, Meadow fescue, Perennial rye grass, Timothy grass, June grass), Weed pollen (Common ragweed, Mugwort, English plantain, Lambs quarters, Russian thistle), Dust mites (D. pteronyssinus, D. farinae), Molds (Aspergillus, Cladosporium, Alternaria, Penicillium notatum, Candida albicans) and Tree pollen (Oak, Linden, Alder, Hazelnut pollens, Poplar, Walnut trees, Olive).

Results: Half of the patients (53%) had increased levels of IgE specific to at least one inhaled allergen, and 33% of the patients reported a history of rhinitis. A positive association between smoking and specific IgE levels to only one specific allergen- House dust mite was found. The association between active smoking and rhinitis was stronger in individuals without allergic sensitization.

Conclusions: Tobacco smoke exposure was associated with increased prevalence of rhinitis symptoms, but not with allergic sensitization, except for house dust mite. The results indicate that the relationship between tobacco smoke exposure and sinonasal pathology in adults may be independent of allergic sensitization.

Keywords: allergic sensitization, specific IgE, tobacco smoke

C60. INVASIVE FUNGAL INFECTIONS IN THE HEMATO-ONCOLOGICAL PATIENT

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Introduction: Candidemia is the most common invasive fungal infection. Mucormycosis is an emerging invasive fungal infection with high morbidity and mortality in the immunocompromised patient in general and in the haemato-oncological patient in particular. After aspergillosis, mucormycosis is the second most common invasive fungal infection caused by filamentous fungi, with a risk of systemic dissemination of more than 40%. It occurs more frequently in patients with acute leukemia and lymphomas.

Methods: *Candida* spp. strains isolated from blood culture in 2024, within the IRO hospital, were analyzed. Identification was performed by MALDI-TOF, antifungigrams were performed in the MICRONAUT automated system (minimum inhibitory concentration). Filamentous fungi were isolated from rhino-sinus and pulmonary infections. The strains were identified microscopically.

Results: In this paper, we present the clinico-biological aspects of candidemia and mucormycosis in haemato-oncological patients hospitalized in the Regional Institute of Oncology Iași, as well as data on the latest international recommendations regarding the diagnosis and therapeutic options of mucormycosis.

Conclusions: Candidemia and mucormycosis developed against the background of immunosuppression determined by hemato-oncological pathology requires a multidisciplinary approach, the prognosis being conditioned by the early diagnosis and the initiation of specific therapy from the stage of clinical diagnosis, in order to reduce mortality.

Keywords: antifungal, fungal infection, hematologic malignancy, mucormycosis

C61. LUNG CANCER-RELATED HEMATOLOGICAL PARANEOPLASTIC SYNDROMES

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The term paraneoplastic syndromes is an umbrella concept including various tumor-associated clinical and praclinical phenomena not explained by direct neoplastic invasion or disemination. The physiological basis is incompletely understood being frequently related to uncontrolled release of mediator and mediator-like molecules or to immunological phenomena.

Lung cancer paraneoplastic features prevalence is estimated at 10%. The most frequent paraneoplastic syndromes are endocrine in nature – the inappropriate antidiuretic hormone (ADH) secretion and the humoral hypercalcemia of malignancy (HMM). Hematologic features are usually underdiagnosed, associated to late stages of the disease and are considered to have a negative prognostic value. The most frequently reported are neutrophilia, hypereosinophilia, trombocytosis and hypercoagulability. There is no specific pathogenic treatment but controlling the underlying disease usually improves the general medical condition, hematological status and clinical impact.

Keywords: granulocytosis, hypereosinophilia, lung cancer, paraneoplastic syndrome, thrombocytosis

R62. DNA REPAIR IN SENESCENCE AND CANCER THERAPY

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Non-repaired DNA damage is considered to be the main trigger of cellular senescence and cell death. Almost all classic anticancer drugs have genotoxic properties, targeting tumor cell DNA and causing damages, with critical lesions activating signaling pathways that lead to autophagy, cellular senescence, or cell death via apoptosis, necroptosis etc. The key pathways involved are discussed. They include, among others, the ATM/ATR/CHK1/CHK2 axis, the p53-HIPK2 axis, and the p16/p21-CDK axis.

DNA repair is a key defense, protecting normal cells against senescence and cell death and causing drug resistance of cancer cells, which pertains to both the endpoint senescence and cell death. The importance of various repair pathways for protection against genotoxic drugs is discussed, as is the role of DNA repair inhibitors and synthetic lethality in cancer therapy. Furthermore, methods are reviewed measuring the repair capacity of normal and cancer cells as a predictive tool in therapy.

Keywords: cancer, DNA repair, drug resistance, senescence

C63. TELOMERASE-MEDIATED TELOMERE TARGETING THERAPEUTICS IN ONCOLOGY: FROM BENCH TO BEDSIDE

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Introduction: Telomerase and telomeres are crucial in cancer cell immortalization, making them key targets for anticancer therapies. Telomerase elongates telomeres by adding TTAGGG repeats to the chromosomal ends. Hence, it is expressed in 90% of human tumors, but not in most normal cells. Telomere targeting drug, 6-thio-2'-deoxyguanosine (6-thio-dG, Ateganosine), is recognized by telomerase and incorporated into de novo-synthesized telomeres, inducing telomeric DNA damage in telomerase-positive cancer cells.

Methods: MTT assay was used to assess the half-maximal effective concentration (EC50) of 6-thio-dG on several cancer cell lines. TIF (telomere dysfunction-induced foci) assay was conducted to show telomeric DNA damage induced by 6-thio-dG, based on the co-localization of γ-H2AX and telomeric probe by immunostaining. For syngeneic mouse tumor models, murine cancer cells were injected into the flanks of BALB/c mice. Treatment was started when the tumor volume reached 70–100 mm3. In the sequential therapy group, mice received 6-thio-dG (3 mg/kg) twice weekly, coupled with a weekly administration of anti-PD-L1(10 mg/kg). After a 2-week treatment period, the tumors were collected and analyzed via flow cytometry for immunophenotyping.

Results: EC50 value for 6-thio-dG was 0.12–3.036 µM for several cancer cell lines. 6-thio-dG induced telomeric DNA damage and TIF formation following 72-96 hours of treatment, followed by rapid G2/M arrest or cell death. Additionally, cytosolic DNA release increased, which was sensed by dendritic cells via STING/IFN-I signaling pathway, which in turn activated tumor-specific CD8+ T cells. Moreover, 6-thio-dG sequentially followed by anti-PD-L1 therapy eliminated tumor growth in syngeneic mouse tumor models. Based on the clinical trial completed in 2024, Ateganosine dose of 180 mg/cycle was proven to be the most efficacious dose and selected as the optimal dose for further clinical development. Currently, Ateganosine combined with the anti-PD-1 inhibitor-Cemiplimab is under phase II clinical investigation in NSCLC patients resistant to prior immunotherapies.

Conclusions: Ateganosine is telomere targeting agent that selectively kills telomerase positive cancer cells. It has demonstrated promising results in hard-to-treat patient population such as immunotherapy and chemotherapy resistant progressors.

Keywords: cancer, telomerase, telomere, therapeutics

R64. MANAGEMENT OF DIAGNOSIS AND MONITORING OF PATIENTS WITH MULTIPLE MYELOMA IN IRO IASI

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Due to an increased variability of the onset clinical symptoms, early diagnosis of multiple myeloma (MM), the second most prevalent hematological malignancy, is problematic. At present, the confirmation of MM diagnosis needs integration of several clinical signs, imaging technology, and laboratory information, such as bone marrow analysis by cytomorphology, immunophenotyping, and serological tests (serum levels of whole immunoglobulins, electrophoresis, immunofixation, and the kappa lambda FLC ratio). Moreover, evaluation of disease progression and prognosis in patients with MM requires the use of accurate assays. This challenge occurred recently, in the era of targeted immunotherapies with impact on the sensitivity and specificity of several laboratory tests. The aim of the current study is to identify the main interferences affecting the accuracy of laboratory tests essential for providing evidence of monoclonality.

During January 2020 and April 2025 a number of 416 cases were confirmed as having multiple myeloma or other plasma cell dyscrasias (such as monoclonal gammapathy of undetermined significance/ MGUS) in the Regional Institute of Oncology, Iasi. Confirmation of monoclonality was established mainly based on immunofixation and immunophenotyping by flow cytometry, the later using a standard monoclonal antibody panel developed within the EuroFlow multicenter consortium. In the same period of time, a number of 375 cases were evaluated following therapy. Standard therapy approved in Romania since 2018 associates Daratumumab/ Darzalex (Janssen Biotech), an anti-CD38 monoclonal antibody with bortezomib, melfalan and prednison. Since Darzalex masks one of the main target for the identification of plasma cells by flow cytometry, rendering false negative results, we needed to alter the panels used for monitoring in order to re-establish the sensitivity of the assay. For this purpose, a multiepitope CD38 replaced the monoclonal antibody used for diagnosis. On the other hand, Darzalex interferes with protein electrophoresis and immunofixation assays, rendering false-positive immunofixation results. In order to re-establish the specificity of the assay, an alternative technique was implemented (Hydrashift), that was able to distinguish between the true patient's M protein band and Daratumumab band.

In conclusion, evaluation of disease progression and prognosis in patients with MM requires the use of specific and sensitive assays in order to avoid misinterpretation of patient's response to therapy.

Keywords: immunotherapy, monitoring assay interference, multiple myeloma

C65. SERUM PROTEIN ELECTROPHORESIS AS PART OF THE DIAGNOSTIC PLAN IN PATIENTS WITH MULTIPLE MYELOMA

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Introduction: Measurement of monoclonal immunoglobulins in the serum of patients with multiple myeloma (MM) remains the gold standard for monitoring the disease. Since monoclonal immunoglobulins can typically be identified and quantified as an M-peak on serum protein electrophoresis (SPEP), monitoring M-protein concentration is considered one of the most effective methods for assessing a patient's response to treatment. However, this measurement is not applicable in patients with oligosecretory or non-secretory disease, as paraprotein levels are either low or undetectable in the serum in such cases.

Methods: Over a period of three years, we performed 5,261 serum protein electrophoresis tests. The majority were conducted on patients from the Hematology Clinic (3,778), followed by those from the Gastroenterology Clinic (1,216) and other departments (267).

Results: In 336 of the patients studied, the presence of M-protein was detected. Of these, 327 were from the Hematology Clinic, and a diagnosis of multiple myeloma was confirmed in 285 of them. However, in approximately 6% of patients diagnosed with MM, SPEP did not detect M-protein.

Conclusions: Serum protein electrophoresis (SPEP) plays a key role in the diagnosis and monitoring of multiple myeloma. It is used to detect and characterize the presence of monoclonal protein (M-protein), which is a hallmark of the disease. In patients with non-secretory MM, diagnosis is based on bone marrow biopsy and radiological evidence of osteolytic lesions.

Keywords: M-protein, multiple myeloma, serum protein electrophoresis (SPEP)

C66. MULTIPLE MYELOMA WITH EXTRAMEDULARY INVOLVEMENT AND PLEURAL EFFUSION: CASE PRESENTATION

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Introduction: Multiple myeloma is a multifocal proliferation of malignant plasma cells, usually associated with a serum and/or urine monoclonal immunoglobulin, and possible organ damage related to the disease. Generalized or multifocal involvement of bone marrow is present at diagnosis together with lytic bone lesions and focal tumoral masses of plasma cells, most commonly in sites of active hematopoiesis. Extramedullary involvement is usually a manifestation of advanced disease, with higher prevalence among patients with relapsed plasma cell myeloma. A complex case of multiple myeloma with extramedullary involvement and pleural effusion at onset will be presented.

Methods: Pleural fluid was centrifuged at 1000rpm, for 10 minutes. Two smears were made from sediment, fixed and stained with May Grunwald Giemsa and Papanicolaou technique. After microscopic examination, recommendation was flowcytometry from pleural fluid.

Results: Cytologic examination of the smears revealed a large population of atypical single cells of large size that raised suspicion of a haematological malignancy. Flowcytometry showed atipical plasma cells. Microscopic and flowcytometric examination of bone marrow found same atypical cells as in pleural fluid. The diagnosis of multiple myeloma with extramedullary involvement was made.

Conclusions: The Cytology and Flowcytometry of pleural fluid are important tools for diagnosis of the Multiple myeloma with extramedullary involvement and pleural effusion at onset.

Keywords: cytology, extramedullary, immunophenotyping, multiple myeloma, pleural effusion

R68. SOURCES OF VARIABILITY IN CLINICAL FLOW CYTOMETRY: LESSONS FROM THE IBERIAN CYTOMETRY SOCIETY EQA (1999-2024)

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The Iberian Society of Cytometry External Quality Assessment Programme started in 1999 and provides external quality assessment (EQA) to laboratories from Spain, Portugal and Latin America affiliated to the Iberian Society of Cytometry (Sociedad Ibérica de Citometría SIC) and, since 2021, to the Spanish Hematology Society (Sociedad Española de Hematología) in collaboration with the University of Salamanca (USAL) and the Laboratory for External Quality Assessment (LEECH).

In 2024, more than 70 clinical laboratories participated in at least one of the seven EQA programmes: Immunophenotyping of Leukaemia and Lymphoma (1999-), Analysis of Cerebrospinal Fluids (2008-), Paroxysmal Nocturnal Haemoglobinuria screening by flow cytometry (2010-), Minimal Residual Disease (MRD) evaluation in Multiple Myeloma (2017-) and Acute Lymphoblastic Leukaemia (2019) and Multiple Myeloma, and Screening of Mature T-cell neoplasm (2023-).

Because therapeutic interventions depend on accurate laboratory assessment it is extremely important to have in place both internal and external quality systems that can measure the quality and reproducibility of the results generated and facilitate appropriate corrective action. Selection of appropriate monoclonal antibody clones and fluorochromes showed to be critical particularly for the identification of dim markers. Together with the technical factors, the interpretation of the results might be also affected by other issues. For MRD and samples with low infiltration (eg. cerebrospinal fluids) the number of pathogenic events analyzed was the most significant parameter and, when the aberrant clone was below <0.01% of total cells or less than 50 events, more than one-third of participants failed to detect the infiltration. In addition, experience of the operator was also directly correlated with the performance of the participants, and reproducibility of the results was significantly better in those participants that have completed at least one year of participation in the EQA programme.

In summary, participation in EQA is not only a regulatory obligation but an opportunity to identify technical and analytical artifacts that influence results reproducibility, increasing the efficiency and cost-effectiveness of laboratory test and improving the flow cytometry diagnosis at individual laboratories.

Keywords: accreditation, external quality assurance (EQA), flow cytometry, Iberian Cytometry Society

R69. NEW DEVELOPMENTS IN PID SCREENING AND MONITORING BY FLOW CYTOMETRY

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Primary immunodeficiencies (PID) are inherited disorders of the immune system, generally presenting with recurrent, severe and sometimes life-threatening infections. To date, more than 300 genes have been identified that can be mutated in PID patients, that affect the functional abilities and/or numbers of one part of the immune system or one cell type.

Besides “genetics-first” approach using next-generation sequencing has been postulated for PID diagnosis by some investigators, flow cytometry offers considerable advantages for the clinical routine: 1) WES or WGS approaches are too slow and too demanding for routine first-choice diagnostics, 2) different genetic defects might show a different clinical course, 3) even when the genetic alteration has bene fully defined, immunological studies are required to identify the consequences of the defect for the immune system. Because of the central role of immunophenotyping, many PID centers have developed multi-color flow cytometric protocols and antibody panels for diagnosis and classification of PID. However, variability among these single center initiatives in combination with the the low incidence and the clinical-immunological heterogeneity of PID, hamper prospective validation in large patient series and age-matched healthy controls, and limit the exchange of data between PID centers.

Accordingly, we aimed to develop a tool that would be universal for all lymphoid PIDs and offer high sensitivity to disclose a lymphoid defect. This approach takes advantage of the EuroFlow validated procedures and tools, resulting in standardized pre-analytical and analytical, PID-specific ≥8-color antibody panels, and software tools for multidimensional data analysis. This strategy has been validated in >400 PID patients, and immunological alterations have been defined using a group of >200 healthy controls of different age-groups as a reference. Together with this, new lymphoid subpopulations have been identified that might be of interest for diagnosis and monitoring particularly for primary antibody deficiencies.

In summary, this strategy enables sensitive screening, followed by in-depth analysis as cost-effective step-wise strategy that has been validated for a broad applicability for many different PID of the lymphoid system (not targeted on a few types of PID), based on the broad overview of all relevant subsets in a single analysis.

Keywords: diagnostic screening, flow cytometry, primary immunodeficiency

C70. DIAGNOSIS OF RELAPSED ACUTE LEUKEMIA WITH A DIFFERENT CELL LINEAGE

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Introduction: Relapse of acute leukemia after initial treatment to a acute leukemia with different cell lineage is a rare event(1). In this study, is highlighted the essential role of immunophenotyping by flow cytometry and molecular diagnostic tests in relapsed acute leukemia with different cell lineage, namely the case of an adult diagnosed with T-cell acute lymphoblastic leukemia (T-ALL) and relapsed to acute myeloblastic leukemia (AML) after hematopoietic stem cell transplantation.

Methods: Immunophenotyping assays, i.e. labeling, sample acquisition and equipment set-up were performed according to the protocols of the EuroFlow Consortium. Genetic modifications were identified by Multiplex Ligation-dependent Probe Amplification (MLPA) and cytogenetic analysis.

Results: At diagnosis, morphologic analysis of the medullary aspirate showed the presence of more than 85% blasts, and immunophenotypic analysis showed the presence of T lymphoid precursors, with positive(+) expression for intracytoplasmic CD3 (cyCD3), CD34, CD7, CD5 markers, partial expression for nuTdT, CD10, CD2, CD13, CD33 and negative(-) for surface CD3, MPO, CD117, CD19. MLPA tests identified the deletion of both 12p13.2 (ETV6 gene region) and 13q14.2 (RB1 gene region). Cytogenetic analysis did not yield additional information, as no metaphase chromosomes were obtained from marrow aspirate cultures. The patient underwent specialized treatment and at 1 year and 5 months was in complete remission with negative residual measurable disease. After almost 2 years, relapse was noted and the patient received further treatment, followed by hematopoietic stem cell transplantation. 4 months later, the patient relapsed again and immunophenotyping tests showed the presence of blasts with a different phenotype from the diagnosis (cyCD3- CD34+/- CD117+/- HLADR+/- cyMPO- CD13+int/+ CD33+ CD7+) suggesting relapse in AML. Cytogenetic tests showed a complex karyotype (hypotetraploid cell lineage), with preservation of the changes identified by MLPA at diagnosis, but also new genetic alterations (deletion 5q31.2, deletion 7q22q31).

Conclusions: Over 25% of patients with acute leukemia relapse after complete remission. Immunophenotyping tests have an essential role in relapsed acute leukemias, as therapeutic approaches are different if a different cell lineage is identified. Molecular tests can document whether the relapse is from the original clone or is a de novo leukemia. The mechanisms underlying the change in cell lineage are still unknown, leading to the need for in-depth leukemic stem cell research studies.

Keywords: acute myeloblastic leukemia, immunophenotyping, molecular diagnosis, T-cell acute lymphoblastic leukemia

C71. FLOW CYTOMETRIC IMMUNOPHENOTYPING FOR THE DETECTION OF GPI-DEFICIENT CELLS IN THE PERIPHERAL BLOOD : DATA FROM THE HEMATOLOGY LABORATORY OF “PROF. DR. ION CHIRICUTA” INSTITUTE OF ONCOLOGY, CLUJ-NAPOCA, ROMANIA

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Introduction: Paroxysmal nocturnal hemoglobinuria (PNH) is a hematopoietic stem cell disorder caused by a somatic mutation in the PIGA gene. This results in chronic, complement-mediated hemolytic anemia, unexplained thromboses in atypical sites, and muscle dystonia. The disease is frequently underdiagnosed in patients with subtle symptoms or in those with comorbid conditions that mask its presentation. The aim of this work was to evaluate the diagnostic utility of flow cytometric immunophenotyping (FCIPT) in detecting GPI-deficient cell populations in peripheral blood samples, and to characterize the frequency and clinical relevance of identified PNH clones.

Methods: A total of 183 samples were analyzed for the presence of a PNH clone at the Hematology Laboratory of “Prof. Dr. Ion Chiricuță” Institute of Oncology, Cluj-Napoca, Romania, between September 2023 and May 2025. Samples were referred due to bone marrow dysfunction, unexplained hemolysis, or unexplained thrombotic events. PNH clones were identified via FCIPT, performed according to the ICCS/ESCCA guidelines for the detection of GPI-deficient cells in PNH and related disorders.

Results: GPI-deficient cells were identified in 27 (14,75%) samples. The degree of deficiency varied across erythrocytes (<LOD-68%), neutrophils (0.1-100%), and monocytes (<LOD-100%). PNH clones (defined as >1% GPI-deficient cells) were detected in 15 patients; minor PNH populations (0.1-1%) in two patient; and rare GPI-deficient cells (<0.1%) in 10 patients. Patients with major clones (>10% GPI-deficient cells) received specific treatment, while those with smaller clones (<10%) were recommended for surveillance.

Conclusions: FCIPT significantly contributes to the diagnostic work-up of patients with bone marrow failure, hemolytic anemia, and unexplained thromboses by enabling the detection of PNH cell clones. High-sensitivity methods allow for the identification and longitudinal monitoring of rare GPI-deficient cell populations with potential evolution.

Keywords: diagnosis, flow cytometry, GPI-deficient cell, paroxysmal nocturnal hemoglobinuria (PNH)

R72. TECHNICAL CHALLENGES IN MONITORING CAR-T CELL EXPANSION / PERSISTENCE BY FLOW CYTOMETRY IN PATIENTS WITH MALIGNANT HEMOPATHIES POST-IMMUNOTHERAPY

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Recently, Romanian patients with diffuse large B-cell lymphoma or acute lymphoblastic B-cell leukemia may benefit from a novel treatment strategy: autologous T cells genetically engineered to recognize CD19 (CD19-CAR-T - chimeric antigen receptor) and to kill malignant cells (CD19 positive). The aim of this study was to evaluate technical challenges of CAR-T cell detection method by flow cytometry.

During October 2024- May 2025, six patients (2 men, 4 women, 24- and 54-year-old, one case of acute B lymphoblastic leukemia, 5 cases of diffuse large B-cell lymphoma, treated with anti CD19 CAR-T, Kymriah/ Tisagenlecleucel, Novartis) were monitored for the expansion/persistence of the CAR-T product in the peripheral blood (25 tests). Evaluation time points, calculated from the moment of CAR-T administration were: week (W) 1, W2, W3, W4 (6 patients), month (M) 3/ M4 (2 patients). For the detection of the CAR-T product by flow cytometry, the CD19-CAR Detection Reagent (Miltenyi Biotc) conjugated with biotin and secondarily labeled with IgG1 anti-Biotin-PE was used. Sample processing method used was Bulk Lysis.

The sensitivity of the detection method used ranged between 1.00E-04 and 1.18E-05. The method also allowed the measurement of the CD4+/CD8+ ratio and of the distribution of T maturation subsets (naive, memory, transition, effectors), both in the CAR-T lymphoid compartment and in the rest of the T cells, based on the expression of the CD27, CD45RA and CD62L markers. CAR-T cells were measured within the range of 0- 105/uL blood, with the peak of expansion recorded in S1 (3 patients) or in S2 (3 patients).

In conclusion, an accurate and reproductible method for the measurement of the expansion and persistence of CAR-T cells is crucial for evaluating the efficacy and long-term effects of this therapy.

Keywords: CAR-T, flow cytometry, immunotherapy, malignant hemopathies

C73. B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA WITH SWITCH TO MONOCYTIC LINEAGE: REPORT OF TWO CASES AND REVIEW OF THE LITERATURE

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Introduction: B-Acute lymphoblastic leukemia (B-ALL) is a neoplasm of precursor lymphoid cells committed to the B-lineage, involving bone marrow and blood. Immunophenotypically, the B-ALL lymphoblasts are almost always positive for the B-cell markers CD19, cCD79a, and cCD22, variably expressing CD34, CD10, TdT, CD20. The myeloid-associated antigens CD13 and CD33 may be present. Determination of minimal residual disease (MRD) by flow cytometry (FC) relies on B-cell markers. A rare but concerning event in B-ALL is monocytic lineage switch, namely the appearance of monocytoid and intermediate B/monocytoid cells. This is most frequently described in pediatric cases. Recognition of this phenomenon has implications in clinical decisions based on MRD detection.

Methods: We present two pediatric cases of B-ALL with monocytic differentiation, which we characterized immunophenotypically, one already at diagnosis and the second with monocytic switch during induction therapy. We further review previously published data regarding the incidence, genetic profile, possible underlying mechanisms and prognosis in B-ALL with monocytic switch.

Results: Monocytic differentiation at diagnosis or during therapy in B-ALL is a rare phenomenon but has been increasingly reported, especially following the use of immunotherapy. FC has an important role in the detection of this event, as gradual loss of CD19 and CD34 concurrent with upregulated expression of myeloid markers like CD14 and/or CD33 is observed. Higher prevalence of several alterations in genes like DUX4r, PAX5-P80R and ZNF384r have been reported and monocytic differentiation in CRLF2r B-ALL at diagnosis seems to be relatively common, but likely underrecognized. In switched B-ALL, FC underestimates residual disease levels when compared to MRD determined by polymerase chain reaction.

Conclusions: New FC markers for discriminating switched monocytoid blasts from nonmalignant monocytes are needed. Although monocytic switch has not been reportedly associated with higher incidence of relapse or poorer prognosis, the phenotypic changes challenge the current B-ALL therapeutic options.

Keywords: immunophenotype, minimal residual disease, monocytes

R74. INTERPRETATIVE READING OF RESULTS IN THE ERA OF DIGITAL MICROBIOLOGY

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Introduction: The automation of microbiology laboratories allows shortening diagnostic times by obtaining standardized microbial cultures, increasing the performance of microbial isolation on culture media by obtaining digital images, identifying bacteria and fungi at species level from culture (within minutes) or alongside with resistance genes directly from clinical isolates (within hours).

Methods: The aim of this study was to emphasize the importance of digitalization in microbiology, as well as to present several clinical cases whose efficient therapeutic approach was possible due to automation, but also to the correct interpretative reading of the results. Clinical isolates were sampled and the cultures were analyzed on WASPLab (Copan®), identifications were performed on MALDI-TOF (Bruker®), antibiotic susceptibility tests (ASTs) were performed on VITEK 2 (Biomerieux®), and the isolates were processed simultaneously on UNYVERO (Curetis®).

Results: Extensively drug resistant *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* were classified as "difficult to treat resistance" with limited therapeutic options. Interpretative ASTs reading and identification of resistance genes, together with additional susceptibility testing of these isolates, provided the optimal therapeutic solutions, represented by back-up antibiotics such as: aztreonam/avibactam, cefiderocol, colistin, etc., or antibiotic combinations.

Conclusions: In the era of digital microbiology, interpretative reading relies on the efficiency and speed provided by laboratory automation, but also on human intervention, that brings added safety, accuracy and critical thinking, allowing results to be adapted according to the clinical and epidemiologic context.

Keywords: *Acinetobacter baumannii*, automation, interpretive reading, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*

R75. INTEGRATING MOLECULAR TECHNIQUES INTO THE GENERAL LABORATORY FLOW

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Recent advances in molecular biology techniques accompanied with technological optimisation and development of standardised bioinformatic interpretation tools resulted in an unprecedented variety of clinical molecular assays in microbiology on the market. Integrated high-capacity diagnostic molecular platforms that provide open channels and introduction of high-priority samples into the workflow, have become a cornerstone of molecular laboratories today. In addition, integrated sample-to-answer assays allowing detection and quantification of viral nucleic acids allow rapid diagnostics within clinicaly relevant time. For example, the use of multiplex sample-to-answer assays that enable detection of genomic nucleic acids from a large number of viruses, bacteria and fungi in the cerebrospinal fluid within 1h have completely changed the timelines in the etiological diagnostics of central nervous system infections.

Point-of-care molecular assays allowed global dissemination of molecular technologies and represent an important part in global responses in various health emergencies as well as in infectious diseases elimination efforts. Population-based sequencing is the fundamental sequencing technology in clinical laboratories that provides reliable, clinically-validated results that can be easily interpreted by using well-established bioinformatics algorithms. High-throughput sequencing (HTS) technologies in clinical environment are increasingly used in various aspects of microbiology. The majority of HTS applications in virology are dedicated to viral identification, outbreak investigation with a particular emphasis on identification of new viral variants and the analysis of viral resistance to antiviral and antiretroviral drugs.

Validation and accreditation of HTS protocols and further development of interpretation algorithms (including those based on AI) will be essential for the more efficient integration of metagenomics into clinical laboratories.

Keywords: bioinformatics, high-throughput sequencing (HTS), microbiology, molecular diagnostics

C76. THE ADDED VALUE OF DIAGNOSING AND MONITORING WITH MOLECULAR TECHNIQUES

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Molecular techniques have been extensively developed and improved during recent years in order to respond to diagnostic needs in the field of virology and microbiology: rapidity, good performances in terms of sensibility and specificity, broad range spectrum/ syndromic testing.

Staring from our experience, we present several examples when starting from raw results generated by diagnosing and monitoring tests we could obtain added information about different pathogens and/or epidemics in Romania.

One illustrative example is the HIV-1 epidemic in Romania. In addition to national surveillance, genotyping testing can offer important information about circulating HIV-1 strains, transmitted drug resistance (TDR), transmission networks in risk populations identified among newly diagnosed cases. Beside its clinical significance for individual cases, monitoring transmitted drug resistance is also relevant for public health, having an impact on both initial regimens and preexposure prophylaxis (PrEP). Integrating information about transmission networks and resistant viruses circulation into prevention strategies design and eventually improve the evolution of this epidemic. Continuous molecular surveillance adds important insights into the HIV-1 epidemics dynamics in Romania and may contribute to design of targeted interventions in the near future.

Keywords: molecular surveillance, molecular technique, prevention strategy, public health

R77. TRACKING HOSPITAL-ACQUIRED INFECTIONS: APPLICATIONS OF NEXT-GENERATION SEQUENCING

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Introduction: Healthcare-associated infections (HAIs) rank among the most prevalent problems in healthcare facilities globally. The hospital microbiome is a mixed flora derived from the patients, visitors, and healthcare personnel. Microorganisms may then persist for extended periods of time on inanimate surfaces, colonize the patients and lead to infections. Due to their prevalence in hospitals and their role in a considerable number of hospital infections, ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species) are especially significant. Hence, there is a need to develop and implement a surveillance system to monitor the safety of hospital “microbiome” and how they contribute to certain HAIs. Next-generation sequencing (NGS) may be a useful and effective tool for these purposes. This study aimed to evaluate hospital-acquired infections by next-generation sequencing (NGS) technologies recovered from a multi-profile hospital in the Country of Georgia. We summarize the results of our recent studies using culture-based methods and Next-generation sequencing.

Methods: Microbiological contamination can be assessed by different methods, including culture isolation, ATP bioluminescence, and NGS. Sampling was performed using sterile swabs with Gel-Amies to collect microbes from surfaces. For many years, these techniques have been employed in hospital settings, primarily for the monitoring of high-risk areas (Dancer, 2014; D’Accolti et al., 2019). The samples were enriched with broth and incubated for 2–7 days at 37OC and at the appropriate temperature. NGS was used for the sequencing.

Results: The study was conducted as part of Infection Prevention and Control training, which was executed by the Walter Reed Army Institute of Research for four Georgian public hospitals in 4-8 November 2024. A total of 32 samples were collected from the Operating Room (10 samples) and Intensive Care Unit (22 samples). The results showed the presence of persistent contamination by gram-positive and gram-negative bacteria. Gram-negative *Enterobacterales* 50% (16/32) were identified as a prevalent contaminant, followed by Gram-negative non-fermenting bacteria 28.1(9/32) and gram-positive cocci 21.9(7/32). Epidemiological relationships among environmental samples were inferred on the basis of pairwise comparisons of ST profiles. Further research aimed to relate ST distribution patterns to environmental features. For an epidemiological survey following interpretations are proposed: (i) samples with an identical ST (i.e., identical gabR-SST, bssA-SST and dhaM-SST) contain very closely related strains and the sampling environment is most likely linked. (ii) Isolates with an identical ST (i.e., identical gabR-SST, bssA-SST and dhaM-SST) are most likely clones and belong to the same genotype.

Conclusions: Data suggests that NGS may provide deeper understanding of the microbiome contaminating the hospital environment and may have practical use in tracking HAI outbreaks. This information may also be used to implement targeted infection control measures to prevent further transmission. ST Profile analysis for environmental DNA allows us to track opportunistic pathogens, identify their origins and study their distribution pattern around the hospital. This method’s application to additional opportunistic pathogens may advance our understanding of their ecology and their contribution to hospital infections, which is crucial for epidemiological risk assessment and developing complex outbreak mitigation plans.

Keywords: environmental DNA, healthcare-associated infections, intensive care unit, molecular typing, operating room, opportunistic pathogens

C78. THE BENEFITS OF INTRODUCING AN INTEGRATIVE GENOMIC ANALYSIS: SURVEILLANCE OF AUTOCHTHONOUS *SALMONELLA ENTERITIDIS* FROM THE ONE HEALTH PERSPECTIVE

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Introduction: Salmonellosis remains a major zoonotic disease and public health burden despite regulations mandating preventive actions and monitoring systems. In Romania, most human cases are indigenous, and *Salmonella Enteritidis* is the most common serovar associated with them. This study compared the genomic characteristics of *S. Enteritidis* from Romania to assess the benefits of whole genome sequencing (WGS) data for detecting potential farm and food reservoirs and understanding transmission routes.

Methods: A collection of human, poultry, and food *S. Enteritidis* strains, gathered between 2023-2025, was subjected to WGS using Illumina platforms MiSeq and NovaSeq 6000. Bioinformatic analysis of the genomic sequences targeted antimicrobial resistance markers and cluster detection. It was performed with the commercial software Ridom SeqSphere+, and publicly available tools from the Centre for Genomic Epidemiology and the National Center for Biotechnology Information.

Results: The comparison of the 3002 loci from the core genome provided an overview of the *Salmonella Enteritidis* population structure, derived mostly from the ST11 lineage. The phylogenetic tree revealed clusters of strains, some of which were suggestive of potential sources of human illness. More than half of the strains displayed fluoroquinolone resistance markers (gyrA mutations and/or the presence of qnrB). Resistance to other antimicrobial classes was sporadic. One human isolate from 2024 carried the acrB_R717L mutation, which confers resistance to azithromycin, a last-resort antibiotic for invasive salmonellosis.

Conclusions: Using genomic sequencing for real-time monitoring of *S. Enteritidis* circulation in the country can lead to the early detection and limitation of epidemiological events with economic impact. Organization of a national genomic database through collaboration between key human health and veterinary institutions is valuable for Romania and the European Union.

Keywords: antimicrobial resistance, genomic surveillance, Romania, *Salmonella Enteritidis*, whole-genome sequencing (WGS)

C79. CHARACTERIZATION OF CLINICAL ISOLATES OF *KLEBSIELLA PNEUMONIAE* USING BACTERIAL WHOLE GENOME SEQUENCING

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Introduction: *Klebsiella pneumoniae* (*K. pneumoniae*) is a Gram-negative bacillus that colonizes the digestive tract. It is one of the main bacteria responsible for healthcare-associated infections, usually with extensive antibiotic resistance, and sometimes pan-resistant.

Methods: In this retrospective study, the characteristics of 42 *K. pneumoniae* isolates from a hospital in Romania from 2022 to 2024 were investigated. Phenotypic antibiotic susceptibility testing was performed according to the EUCAST standard. Ion Torrent PGM/S5 and Illumina technologies were used for WGS. The analysis of the obtained data was performed with the commercial program Ridom SeqSphere+, the tools available on the Center for Genomic Epidemiology platform, the Galaxy Pasteur platform, PolyPhen-2 program. The establishment of the kinship relationships between the isolates was performed using the cgMLST method (2358 loci).

Results: A series of antibiotic resistance and virulence markers were noted. Combinations of two different carbapenemases were identified for 27 genomes: 2 genomes blaNDM+blaKPC, 25 genomes blaNDM+blaOXA-48, mutations in the ompK36 gene: ompK36_D135DGD (30 genomes), ompK36_D135DD (7 genomes). All genomes analyzed have genetic markers of resistance to fluroquinolones, penicillins and cephalosporins (e.g. blaTEM, blaOXA, blaCMY-6, blaCMY-16, blaCTX-M-15), aminoglycosides, macrolides, chloramphenicol, rifampicin, streptogramins, sulfonamides, trimethoprim, tetracyclines, and some of them also have genetic markers of resistance to colistin - changes in chromosomal genes. Nine genomes were identified that present genetic virulence markers associated with the hypervirulent phenotype: iucA/B/C/D, iutA, rmpA2, peg-344. They were classified into 8 ST types: ST 101, ST 15, ST 147, ST 383, ST 258, ST 307, ST 2096, ST 7120. The cgMLST analysis revealed 8 genetic clusters.

Conclusions: Diversity analysis of the batch of 42 *K. pneumoniae* genomes highlighted the existence of several multi-antibiotic-resistant clones, in some cases with multi-year persistence, and which present plasmids that can be easily transferred, not only within the same species, but also between members of the *Enterobacterales* family. A worrying aspect is the identification of hypervirulence genes in MDR genomes (an isolate ST 101 and the high-risk clone ST 383), which may have a major impact on public health.

Keywords: hypervirulent, *Klebsiella pneumoniae*, MDR, WGS

Acknowledgement: This study was carried out using funds from the research project PSCD EMERGENT.

C80. GENOMIC INVESTIGATIONS OF *ACINETOBACTER BAUMANNII* OUTBREAKS IN INTENSIVE CARE UNITS IN ROMANIA

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Introduction: *Acinetobacter baumannii* (*A. baumannii*), opportunistic pathogen associated with nosocomial infections, represents a serious threat in healthcare settings. *A. baumannii* has evolved in extensively drug-resistant (XDR) clones responsible for infections difficult to treat. Our study aimed to investigate molecular epidemiology and antimicrobial resistance of *A. baumannii* hospital outbreaks isolates.

Methods: Fourteen *A. baumannii* isolates were collected from two outbreaks. Isolates were identified using mass spectrometry MALDI-TOF MS. Antibiotic susceptibility testing was performed using standard methods. Detection of OXA-23, OXA-40/58, NDM carbapenemases was assesed with immunochromatography tests. Clonal relatedness was investigated using pulsed field gel electrophoresis (PFGE) and Bruker IR Biotyper. Isolates were subjected to whole genome sequencing (WGS) using Oxford Nanopore Technologies (ONT). Libraries were prepared using the rapid DNA barcoding protocol (SQK-RBK114.24) and sequenced on a MinION device. The sequence types (STs) were assigned according to the Pasteur multi-locus sequence typing (MLST) scheme. CgMLST was used to assess relatedness.

Results: All isolates presented a high level antimicrobial resistance to beta-lactams (penicillin and cephalosporin classes, carbapenems), aminoglicozides and fluoquinolones. For 13 isolates, lateral flow imunocromatographic tests revealed dual production of carbapenemases confirmed by genomic analyses. blaOXA-23 gene was detected in all isolates, 13 isolates (93%) presented blaNDM-1 gene. MLST analysis revealed that isolates belonged to ST570 and ST2. No plasmid replicons were detected and all resistance genes were integrated în the chromosome through composite transposons (based on Tn2006 and ISAba125 mobile genetic elements). Strains included genomically inserted bacteriophages, while some also included extrachromosomal bacteriophages.

Conclusions: This study provide a valuable insight into genomic landscape of *A. baumannii* nosocomial strains, emphasizing the importance of genomic surveillance data on effective control interventions and/or antibiotic stewardship.

Keywords: *A. baumannii*, antimicrobial resistance, multilocus sequence typing, whole-genome sequencing

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C81. THE IMPORTANCE OF CYTOMORPHOLOGICAL EXAM FOR THE DIAGNOSIS OF ACUTE LEUKEMIAS

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Introduction: Acute leukemia is an aggressive neoplasm of multipotent hematopoietic stem cells or partially differentiated progenitor cells. The leukemic trigger induces a profound change in the structure of cellular DNA, followed by maturation arrest, abnormal differentiation, clonal proliferation and accumulation of these cells in the bone marrow/ extramedullary (ganglions, spleen, liver, skin, CNS). Disorganization of the medullary microenvironment leads to severe bone marrow failure, which generates the clinical disorders of this condition. The aim of the present study is to identify distinctive morphological landmarks, which strengthen the specificity of cytological testing for the diagnosis of acute leukemias.

Methods: In this study, morphological examination of peripheral blood smears and bone marrow aspirate samples (May Grunwald Giemsa staining) was correlated with immunophenotypic study (flow cytometry), demonstration of clonality, molecular biology, biochemical or genetic tests.

Results: During January 2023 - April 2025, 258 cases of acute leukemia were diagnosed in our hospital (91.4% acute myeloid leukemia, 4.3% B-cell precursor acute lymphoblastic leukemia, 1.6% T-cell acute lymphoblastic leukemia and 2.7% mixed lineage acute leukemia). Quantification and identification of morphological abnormalities of blast cells are the most critical aspects of the medullogram. According to the WHO classification criteria, a percentage of blasts greater than 20% confirms the diagnosis of acute leukemia.

Conclusions: The cytomorphological examination of blood and marrow aspirate represents a complex step within the integrative diagnostic algorhythm of acute leukemias, which aims to guide the hematological diagnosis, the trajectory of paraclinical management (immunophenotyping, cytogenetic or molecular biology tests) and targeted therapy.

Keywords: blast, immunophenotyping, acute leukemia, medulogram

R82. DIAGNOSTIC CHALLENGES IN MYELOID NEOPLASMS WITH ATYPICAL CLINICAL AND MORPHOLOGIC FEATURES

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In the hematological clinical setting, atypical presentation of myeloid neoplasms may be occasionally encountered posing diagnostic challenges. Intricated myeloproliferative and myelodysplastic features in the peripheral blood and bone marrow, concomitant eosinophilia or monocytosis, negative results at the routine molecular tests, non-specific findings at the bone marrow biopsy, hinder the assignment to an established disease entity, according to the latest 2022 World Health Organization classification of myeloid neoplasms. Next-generation sequencing-based assays are needed in those conditions to support a proper diagnostic.

A few cases of myeloid neoplasms - chronic neutrophilic leukemia, atypical chronic myeloid leukemia, myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis, not otherwise specified, NPM1-mutated acute myeloid leukemia - will be described, highlighting the importance of integrating available hematological, morphologic and genetic data, with the results of more advanced molecular tests.

Keywords: atypical, diagnostic challenge, myeloid neoplasm

R83. FACTORS RELATED TO DISEASE PROGRESSION IN LOW-RISK MYELODYSPLASTIC NEOPLASMS

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Myelodysplastic neoplasms (MDS) include a wide spectrum of heterogeneous clonal stem cells disorders characterised by peripheral blood cytopenias, morphologic dysplasia in one or more myeloid lineages in the bone marrow with ineffective hematopoiesis, and an increased risk of conversion into acute myeloid leukemia (AML). The therapeutic approaches are currently based on the risk assessment provided by the Revised International Prognostic Scoring System (IPSS-R), that uses hematologic and cytogenetic data and is widely recognized as the standard prognostic tool in MDS.

This presentation focuses on low-risk MDS (LR-MDS) as defined by IPSS-R score, distinguished by a relatively lower risk of leukemic transformation or death during the forthcoming period after diagnosis. This MDS category is also very heterogeneous as patients may experience different patterns of disease progression, including early exitus from severe cytopenias in the context of extra-hematologic comorbidities, without AML occurrence. The mutational profiles related to certain patterns of LR-MDS progression will be discussed along with other predictive factors such as male gender, comorbidities, transfusion needs, multilineage dysplasia, bone marrow fibrosis, and serum levels of ferritin and albumin.

A more refined stratification of LR-MDS patients using a combination of clinical, hematologic, histological, cytogenetic and molecular predictive factors will allow the improvement of the therapeutic decisions, leading to better disease outcomes.

Keywords: cytogenetics, low-risk myelodysplastic neoplasms (LR-MDS), mutational profile, prognostic factor

R84. GENOMIC LANDSCAPE OF PEDIATRIC ACUTE MYELOID LEUKEMIA – SINGLE CENTER EXPERIENCE

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Introduction: Pediatric myeloid malignancies, though rare, display remarkable genomic heterogeneity with direct implications for diagnosis, prognosis, and therapy. Integrating molecular profiling into clinical evaluation is crucial for personalized treatment and risk stratification.

Methods: We retrospectively analyzed 61 patients ≤18 years old diagnosed with acute myeloid leukemia (AML), myelodysplastic syndromes (MDS), or myeloproliferative neoplasms (MPN). Clinical, morphological, immunophenotypic, cytogenetic, and molecular data were integrated. Genomic characterization included targeted next-generation sequencing (NGS) panels (23 genes) and comprehensive profiling. Survival analyses were performed to assess prognostic significance of molecular and immunophenotypic markers.

Results: AML patients were older at diagnosis compared with MDS/MPN. Clinical differences included weight loss and bone pain in AML, versus higher hepatosplenomegaly in MPN. Immunophenotyping revealed mixed-phenotype acute leukemia in 15.9% of AML cases, and CD7 expression was strongly associated with inferior overall survival (median 14.4 months, $p=0.005$). Cytogenetic abnormalities were most frequent in AML (52.5%) and MDS (71.4%), with recurrent chromosome 7 abnormalities and KMT2A rearrangements. Gene fusions were detected in 36.8% of patients, most commonly RUNX1::RUNX1T1 and KMT2A::AF9. Functional classification of mutations highlighted RAS/MAPK pathway alterations as predominant in AML (36.4%) and MPN (88.9%). Overall, 81.4% of patients were classified as high-risk.

Conclusions: This single-center experience underscores the biological heterogeneity of pediatric myeloid malignancies. Key prognostic markers include CD7 expression, chromosome 7 abnormalities, and high prevalence of RAS/MAPK pathway mutations. Comprehensive genomic profiling provides critical insights for risk-adapted therapies and supports the integration of molecular stratification in clinical practice.

Keywords: acute myeloid leukemia (AML), CD7, immunophenotyping, KMT2A, pediatrics,

C85. NEXT-GENERATION SEQUENCING TESTING ON MYELODYSPLASTIC SYNDROME: A SINGLE-CENTER EXPERIENCE

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Introduction: Myelodysplastic syndromes (MDS) are a family of myeloid cancers with diverse genotypes and phenotypes .1 Although somatic mutations do not currently appear in prognostic scoring systems, testing by massively parallel sequencing (NGS) has revealed an increasing number of genetic abnormalities, including recurrent alterations in the TP53, DNMT3A, NRAS, NPM1, RUNX1, and FLT3 genes.2 This study aimed to evaluate the incidence and prognostic role of these abnormalities in patients newly diagnosed with MDS.

Methods: Bone marrow aspirates from 59 patients with MDS (26 female and 33 male) diagnosed between February 2024 and May 2025 at the Regional Institute of Oncology, Iași Romania were investigated for mutations using NGS (HEMEaccuTest™ kit). We compared the relationship between gene mutation status and laboratory characteristics, such as certain cytopenias, the revised international prognostic scoring system, MDS subtypes, karyotypes, AML development, and overall survival.

Results: After analyzing the results, 69% of the patients had at least one mutation and of these 42% had a normal karyotype. The genes that most frequently showed abnormalities were: ASXL1 (11.8%), TET2 (11.8%), SF3B1 (10.16%), BCOR (8.47%) and DNMT3 (8.47%). 71% of the patients who had mutations in ASXL1 progressed to AML.

Conclusions: The results obtained using NGS provide new information on the disease, which is important especially for patients who do not have cytogenetic abnormalities. Such studies help us to better understand the impact of various mutations in the evolution of MDS, which will lead to more targeted treatment.

Keywords: gene mutations, myelodysplastic syndrome (MDS), next-generation sequencing (NGS), prognostic factors

R86. NGS IN MALIGNANT HEMATOPATHIES – EXPERIENCE OF THE REGIONAL INSTITUTE OF ONCOLOGY IN NATIONAL HEALTH PROGRAMS

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The detection of genetic abnormalities is mandatory for the diagnosis, classification and post-therapeutic evaluation of malignant hematological diseases. Molecular biology techniques can provide information for establishing a precise diagnosis and, respectively, a personalized treatment.

The next-generation sequencing (NGS) technique is one of the most complete techniques, managing to simultaneously bring a very large number of information with diagnostic and prognostic value. To identify minor clones, it is necessary to obtain very high read depths, which leads to the need to select a limited number of markers that can be investigated simultaneously.

The current study includes over 350 patients diagnosed with different malignant hematological diseases in the Iași Regional Oncological Institute (IRO). Three different NGS kits, from different manufacturers, were used. The technologies used for library preparation, panels and dedicated software were compared. The mutations found were reported as tier1 to tier3 depending on the clinical significance. A complete evaluation of the patient with hematological malignancies, phenotypically, cytogenetically and molecularly, is strictly necessary to identify all markers with diagnostic value for treatment, prognosis and response assessment.

Keywords: molecular diagnosis, malignant hematopathies, NGS

C87. BETWEEN POLICY AND PRACTICE: ACCEPTING THE UNACCEPTABLE SAMPLES IN MICROBIOLOGY

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The EN ISO 15189:2022 standard provides clear requirements on when biological samples are considered compromised and should typically be rejected: incorrect identification of the patient or sample, insufficient sample volume, inadequate quality of the samples. However, real-world clinical situations often present challenges that may justify deviation from these strict standards. In particular, microbiology laboratories may encounter circumstances where rejecting a compromised sample could have significant negative consequences for the patient or public health. In such cases, laboratory professionals must weigh the risks and benefits of analyzing and reporting results from non-conforming samples.

This study aims to review the literature and current laboratory practices to identify specific pathologies and clinical and pre-analitical conditions where accepting non-conforming samples may be justified.

While the standard emphasizes the importance of pre-examination quality, there are exceptional clinical situations in which samples are either irreplaceable or urgently needed. These include, but are not limited to critical infections, suspected outbreaks, or cases involving vulnerable populations such as neonates or immunocompromised individuals. In such scenarios, rigid application of rejection criteria may delay diagnosis and treatment, potentially resulting in harm.

Furthermore, it explores technical and procedural adaptations that can enable laboratories to process such samples responsibly. These may include method validation under non-ideal conditions, implementation of interpretive comments to guide clinicians, and establishing referral laboratories equipped to handle challenging samples.

Ultimately, while compliance with standards remains essential, the laboratory’s role in patient care and safety requires a flexible, informed approach.

Developing formal policies to evaluate exceptions, mitigate risks, and ensure informed clinical interpretation is a necessary evolution in laboratory practice to support both individual patient outcomes and broader public health needs.

Keywords: compromised/ non-conforming samples, EN ISO 15189:2022 standard, patient care and safety, rejected samples

R88. HOW TO TACKLE THE PROCESS OF VERIFICATION AND VALIDATION OF A MICROBIOLOGY TEST?

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Introduction: Procedures of verification and validation are standard requirements of any novel microbiology test/equipment or laboratory-developed tests (LDTs) before introducing into daily practice. Determination of the performance features is an integral part of the quality assurance process performed in laboratories. The aims of the presentation is to offer a practical assistance for performing verification and validation of the microbiology assays/instruments in order to confirm reliable, acurrate and reproducible results compliant with the intended use.

Methods: It was based principally on the recommendations issued by the International Organization for Standardization (ISO) 15189:2023 and the European Commission's In Vitro Diagnostic Regulation (IVDR).

Results: The discussion is focused mainly on implementing a verification/validation plan, terms definitions. Moreover, arguments for selecting reference standard, relevant test samples, performance characteristics, acceptance criteria, solutions for solving discrepant results are mentioned.

Conclusions: This material may serve in planning and performing of these methods in order to implement successfully the recent version of the ISO 15189:2023 in microbiology laboratories.

Keywords: accuracy, ISO 15189:2023, IVDR, precision, reference range, reportable range

R89. CHALLENGES FACED BY BIOBANKS IN THE PROCESS OF PREPAREDNESS AND RESPONSE TO EMERGING AND RE-EMERGING INFECTIOUS DISEASES

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Preparedness and prompt response when (re)emergent pathogens cause epidemics rely on surveillance, testing and diagnostic, as well as proposal of treatments if they exist. Pandemics cannot be accurately predicted. So, as part of an effective ongoing surveillance program, a broad range of pathogens should be continuously deposited. In the longer term research efforts need to be redirected towards understanding the pathogen and discovering useful tools to fight against it.

In this process the role of biobanks might prove determining. Biobanks are designed as safe harbours for collection of biological samples. But they also have an important role in archiving associated knowledge, techniques, and tools.

Biobanks should perform a watchful selection and containment of pathogens, should have an unique mode of access to resources (preferably through a secured website), should have a strong quality system allowing the distribution of quality controlled material and logistics to distribute quickly and efficiently the material all over the world (through a specially-designed Material Transfer Agreement). Risk management and risk mitigation in the case of disasters and unexpected occurences such as (re) emerging pathogens should also be focused at in the planning for biobank infrastructure and processes.

Grouping of different biobanks in consortia or networks is a good option, but it requires reorganization of the activity of the global science community (including public health, fundamental research and private companies). The so-called pillars of preparadness have to be addressed, and all the challenges faced by each of them should be carefully analyzed and overcome. Logistics should be well developed, as in the case of consortia, researchers have to deal with both global and local threat.

Sustainable biobanking networks for diseases of epidemic/pandemic potential (including the famous disease X) are obviously needed today, and will continue to be needed in the future.

Keywords: biobank, preparedness, (re)emergent pathogens, sustainability

C90. *MYCOPLASMA HOMINIS* AND *UREAPLASMA UREALYTICUM* IN TIRANA: A REVIEW OF PREVALENCE AND ANTIMICROBIAL RESISTANCE IN UROGENITAL INFECTIONS

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Introduction: *Mycoplasma hominis* and *Ureaplasma urealyticum* are cell wall-deficient organisms that may act as opportunistic pathogens in the lower urogenital tract. They are implicated in various infections, including urethritis, cervicitis, bacterial vaginosis, and are associated with pregnancy complications and infertility. Accurate diagnosis and effective treatment are complicated by asymptomatic colonization and rising antimicrobial resistance. Here, we aimed to assess the prevalence and antimicrobial susceptibility of *M. hominis* and *U. urealyticum* among patients in Tirana from January to October 2024.

Methods: A total of 2,715 patients (2,231 females and 484 males), aged 17–75 years, were evaluated. Pathogens were identified using Mycotest culture methods and molecular techniques. Antibiotic susceptibility was determined using Mycotest ST (Bioprepare).

Results: Of all samples, 44.86% (n=1,218) tested positive for at least one pathogen, with a higher prevalence in females (82.84%). *U. urealyticum* was isolated in 717 cases and *M. hominis* in 501. Infections were more common among young women with low vaginal pH, positive KOH tests, presence of clue cells, and reduced lactobacilli. High resistance to lincomycin and strong sensitivity to doxycycline were noted.

Conclusions: The data highlight the clinical significance of routine screening and targeted antimicrobial therapy guided by susceptibility patterns to manage *M. hominis* and *U. urealyticum* infections effectively and prevent complications .

Keywords: Albania, antimicrobial resistance, *Mycoplasma hominis*, prevalence, *Ureaplasma urealyticum*

C91. BACTERIOLOGICAL URINALYSIS: FROM ROUTINE CLASSICAL METHODS TO LAST GENERATION PROCEDURES

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Introduction: It is estimated that urinary tract infections affect approximately 150-250 million people globally annually, generating over 5 billion EURO in healthcare costs. Rapidity and accuracy of diagnosis are essential prerequisites for therapeutic success. In Romania, both microbiology laboratories with minimal equipment and laboratories with excellence or reference level of equipment operate.

Methods: The Science Direct, Web of Science, Scopus, Ovid, Wiley databases were searched using the keywords: urinary tract infections, modern microbiological diagnostic methods, POC (Point of Care) methods, methods in laboratories with limited resources.

Results: Diagnostic methods for urinary tract infections can be classified into two large categories: methods that involve sample processing in the laboratory and increasingly diversified rapid methods that can be used at home or POC methods. The advantages and disadvantages of traditional methods, currently most widely used, as well as of the rapid methods applicable in the laboratory or of the POC methods, including those that can detect the pathogenicity mechanisms of microorganisms present in urine, are compared and highlighted.

Conclusions: Recent advances in laboratory diagnostics, such as molecular, immunological methods, proteomics, nanotechnologies, etc. can be used in laboratories with special equipment to shorten the time required to obtain clinically relevant information. For routine laboratories that do not have automated methods, we propose a minimal classical algorithm, which allows the correct identification and use of an appropriate antibiotic panel for the main bacterial species frequently encountered in the etiology of urinary tract infections.

Keywords: bacteriological urinalysis, diagnostic method, point-of-care testing (POC), urinary tract infection (UTI)

C92. ESKAPE AND EMERGING FUNGAL PATHOGENS IN BLOODSTREAM INFECTIONS: A HOT ZONE OF ANTIMICROBIAL DRUG RESISTANCE

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Introduction: Bloodstream infections (BSIs) are a medical emergency leading to high morbidity and mortality worldwide. The extended ESKAPE acronym consists of notoriously nosocomial pathogens with a critical impact on BSIs (E: *Enterococcus faecium*, S: *Staphylococcus aureus*, S: *Stenotrophomonas maltophilia*, K: *Klebsiella pneumoniae*, A: *Acinetobacter baumannii*, P: *Pseudomonas aeruginosa*, and E: *Enterobacterales* group). The aim of the study was to assess the distribution and resistance profiles of ESKAPE and emerging fungal agents in BSIs episodes.

Methods: The retrospective analysis included all consecutive patients diagnosed with BSIs episodes in a Romanian hospital from August 2022 to August 2024 using the BacT/Alert 3D 120 instrument (bioMérieux SA, Marcy l’Etoile, France). The microbiological diagnosis and the antimicrobial susceptibility testing was principally based on conventional phenotypic methods, Vitek 2 Compact System (bioMérieux SA, Marcy l’Etoile, France), the Micronaut MIC-Strip Colistin and the Micronaut-AM plates (Merlin Diagnostika GMBH, Bornheim-Hensel/Bruker Daltonics GmbH, Bremen, Germany).

Results: Out of 821 species isolated, n=298 (36.29%) and n=10 (1.21%) were ESKAPE and yeasts members, respectively. *K. pneumoniae* (n=78; 26.17%) and *S. aureus* (n=70; 23.48%), versus *Candida parapsilosis* (n=4) and *Candida auris* (n=2) were the top two BSIs pathogens in each category. The antimicrobial resistance rates included 66.66% carbapenem resistance in *K. pneumoniae* and 90.90% in *A. baumannii* isolates, while oxacillin resistance was encountered in 30.0% of *S. aureus strains*. The total number of *E. faecium* strains doubled in the second year of the study and the vancomycin resistance (VRE) was 42.10%. Out of 55 Gram-negative ESKAPE strains tested, no resistance to cefiderocol was detected.

Conclusions: The study underscores the concerning occurrence in our hospital of carbapenem-resistant *K. pneumoniae* and *A. baumannii*, as well as VRE and *Candida auris* isolates. It is of utmost importance the continuous monitoring of all emerging challenges and implementation of antimicrobial stewardship practices.

Keywords: antimicrobial resistance, bloodstream infections, *Candida auris*, difficult-to-treat resistance, emerging infections, ESKAPE

C93. LABORATORY DIAGNOSIS OF TUBERCULOSIS: FROM MICROSCOPICAL EXAMINATION TO GENOME SEQUENCING

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Tuberculosis (TB) remains a challenge as clinical and laboratory diagnostic as well. The laboratory methods have developed in an unimaginable way in terms of information and time for result release. Tuberculosis is a major global public health issue, with more than 5 milion new cases occurring every year. These facts determined the researchers to discover new methods that are quicker compared to classical microbiological techniques.

Classical TB diagnostics is based on medical history, tuberculin skin test, chest Xrays, smear microscopy and growth. For patient survival, rapid determination of tuberculosis and its susceptibility towards drugs is a sharp need. Revolution in diagnosis was introduced by GeneXpert system- with its variants Ultra and XDR, that generates the result in 60 minutes with information on presence of Mycobacterium tuberculosis and detection of Rifampicin resistance. It is a point of care device that can be operated with minimal laboratory infrastructure requirement in a mobile van to reach long distance areas.

Besides that, other molecular diagnostic methods are used in diagnostic: whole genome sequencing (WGS) which offer details about starin relatedness and epidemiological survey of outbreaks, RFLP (random fragment lengths polymorphism), Spolygotyping- direct sequence repeats, MIRU-VNTR – Mycobacterial Identification Repetitiv Unit-VNTR variable number of tandem repeats.

In conclusion, for over 100 years, the microscope, microbial culture, and immunodiagnostics served as cumulative sources of laboratory data for tuberculosis diagnostic. These techniques remain gold standards for many pathogens, and there is little reason to expect that their role will disappear. What has changed dramatically in recent decades are complementary diagnostic strategies stemming from the advent of molecular biology. In tuberculosis diagnosis the turnaround time decreased at 2 hours compared to 60 days in classical method. This is converted in life saving, early treatment and decreasing the hospital costs. It will be an unlimited tool for achieving the goal "End TB".

Keywords: classical methods, GeneXpert, genome sequencing, tuberculosis diagnostic

C94. *TOXOPLASMA GONDII* INFECTION AND PSYCHIATRIC DISEASES

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Toxoplasma gondii is an obligate intracellular protozoan parasite with a global distribution. Although *T. gondii* infection is typically asymptomatic in immunocompetent individuals, the parasite may cause overt clinical disease in a small proportion of those infected and a life-long latent infection in neuronal and muscular tissues.

The neurotropism of the parasite characterized by long-term presence of the protozoan within the brain provides opportunity for manipulation of the host's behavior. Infected rodents have been shown to no longer fear cats, rendering them easier prey and thus potentially increasing the risk of infection and parasite's chances of sexual reproduction.

In humans, behavioral changes associated with toxoplasmosis include decreased reaction times, which could be linked with the results of studies on infected individuals being more likely to be involved in traffic accidents and/ or low level of novelty seeking. In the past years, these has led to an increased interest on the potential role of *T. gondii* in the etiology of psychiatric diseases, including schizophrenia and major depression.

Schizophrenia and depression can be exacerbated by immunological events similar with those noted during toxoplasmosis. It is not clear whether the causal link is directly attributable to the protozoan or to the immune response it generates. Suggested mechanisms responsible for the changes in human behavior involve tryptophan metabolism and the hypothalamic-pituitary-adrenal axis. *T. gondii* has been shown to influence dopamine synthesis by upregulating enzymes like tyrosine hydroxylase. Such changes in neurochemical signaling and immune activity have been associated with higher rates of schizophrenia and depression in *T. gondii* seropositive individuals, suggesting a plausible link between the parasite and these psychiatric diseases.

Recent studies indicate an association between *T. gondii* and psychiatric morbidity in Western Romania. These reports highlight the need for further multidisciplinary collaboration and may open a new research area with major clinical and public health ramifications.

Keywords: major depression, psychiatric diseases, schizophrenia, *Toxoplasma gondii*, toxoplasmosis

P30. WHOLE EXOME AND WHOLE GENOME SEQUENCING: EXPERIENCE OF THE REGIONAL CENTER FOR MEDICAL GENETICS MUREȘ

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This presentation outlines the infrastructure and genetic testing services offered by the Regional Center for Medical Genetics Mureș (CRGM), with a focus on next-generation sequencing (NGS) techniques. It compares gene panel testing with whole exome sequencing (WES) and whole genome sequencing (WGS), highlighting their respective advantages and limitations.

Based on the center's experience and literature data, over 160 patients are investigated annually using WES/WGS, with this number growing due to advancing knowledge and decreasing costs. Patients from various medical specialties are referred, particularly from neurology, psychiatry (including epilepsy, autism spectrum disorders, and ADHD), cardiology, oncology, immunodeficiencies, and infertility.

The use of NGS has led to a precise genetic diagnosis in approximately 60% of cases. The study emphasizes the importance of selecting the appropriate genetic testing method based on its specific benefits and limitations. WES and WGS have proven valuable, especially when larger structural genetic causes cannot be identified by lower-resolution techniques.

Keywords: next-generation sequencing (NGS), whole-exome sequencing (WES), whole-genome sequencing (WGS)

P31. DETECTION OF SOMATIC VARIANTS IN ACUTE MYELOID LEUKEMIA USING NEXT-GENERATION SEQUENCING – COMPARISON WITH REFERENCE METHODS

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Introduction: Next-generation sequencing (NGS) detects genomic variants (short insertions/deletions, single nucleotide variants, copy number variations) and identifies mRNA expression of gene fusions in patients with acute myeloid leukemia (AML).

Methods: We analyzed DNA and total mRNA (extracted using the QiaSimphony system, DSP DNA Mini and PAXgene Blood RNA reagents, Qiagen) from peripheral blood or bone marrow aspirates of 31 patients with AML and one healthy donor. From the study group, 28 patients had previously been tested using classical methods for the presence of fusion mRNA, FLT3-ITD and NPM1 mutations. Samples were prepared using the Oncomine Myeloid reagents (covering 40 genes and 29 gene fusions), processed with the IonChef instrument, and sequenced using the Ion GeneStudio S5 (ThermoFisher Scientific). Primary data analysis was performed using the Torrent Suite v5.18 platform, secondary analysis was done on the Ion Reporter v5.20 online platform, and tertiary analysis (the significance of the identified variants) was conducted by consulting open-access tools and databases (ClinVar, Franklin, Cosmic etc.) and the Oncomine Knowledgebase Reporter application.

Results: In the analyzed group, 7 and 5 patients showed FLT3-ITD and NPM1 mutations, respectively, previously detected using classical molecular techniques. Fusions detected by RT-PCR were also identified using NGS, with one exception showing discordant results. A total of 93 mutations and 5 fusions were identified (using the Oncomine Variants v5.20 filter), with an average of 3 mutations per patient. Results are analyzed and several clinically relevant mutations are discussed.

Conclusions: NGS and PCR provide comparable results, with NGS offering more comprehensive information. Interpreting the clinical significance of the identified variants remains the main challenge in using NGS in our laboratory.

Keywords: acute myeloid leukemia, next-generation sequencing (NGS), somatic variants

P32. TRBC1/TRBC2 FLOW CYTOMETRY: A RELIABLE METHOD FOR ASSESSING T-CELL CLONALITY AND DIAGNOSING T-CELL NEOPLASMS – OUR EXPERIENCE IN ALBANIA

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Introduction: T-cell neoplasms represent an uncommon and heterogeneous group of lymphoid malignancies. Their diagnosis and classification primarily rely on histopathological examination and immunohistochemical profiling. However, the absence of distinctive histopathological features, overlapping cytomorphological characteristics, immunophenotypic variability, and a broad spectrum of clinical presentations significantly complicate accurate diagnosis and subclassification. Here, we aimed to evaluate the use of TRBC1 and TRBC2 monoclonal antibodies in flow cytometric immunophenotyping (FCI) for the detection of T-cell clonality in clinical samples.

Methods: In this study, a 6-color DxFLEX Flow Cytometer (Beckman Coulter) was utilized for leukocyte immunophenotyping. The sample size consisted of 30 patients between January 2023 and March 2025 referred to our laboratory from the Hematology and Infectious Diseases departments. The average age was 64,5 years old, consisting of 53% males and 47% females. Samples were collected from bone marrow or peripheral blood using EDTA tubes. Immunophenotyping was performed using appropriate markers for the cell populations present in these samples. When aberrant T-cell populations were detected, anti-TRBC1 and anti-TRBC2 antibodies were added to evaluate clonality.

Results: Among the 30 patients studied, 14 cases were exhibited as monoclonal proliferation of mature T-cell lineage, while 16 cases were non-monoclonal. In the monoclonal cases, TRBC1 expression was positive in the pathological T-cell lymphocyte population in 6 (42.8%) cases and absent in 8 (57.1%) cases. In these 8 cases, TRBC2 expression was positive, confirming T-cell clonality. In the remaining 16 cases, the TRBC1/TRBC2 ratio in the T-cell lymphocyte population was normal, indicating polyclonality. The leukocyte immunophenotyping data were consistent with the final diagnosis in all cases.

Conclusions: Incorporating anti-TRBC1 and anti-TRBC2 antibodies into FCI, significantly enhances the detection of T-cell clonality and provides valuable support in the diagnostic work-up of T-cell malignancies.

Keywords: clonality, flow cytometry, immunophenotyping, T-cell lymphoma, TRBC1, TRBC2

P33. LDH, FERRITIN AND ESR AS LABORATORY INDICATORS OF DISEASE ACTIVITY IN MYELODISPLASTIC SYNDROMES

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Introduction: Myelodysplastic Syndromes (MDS) are a heterogeneous group of clonal hematopoietic stem cell disorders characterized by ineffective hematopoiesis, peripheral cytopenias, and an increased risk of progression to acute myeloid leukemia (AML). In recent years, attention has shifted toward easily accessible laboratory biomarkers that may reflect underlying disease activity, inflammation, and marrow turnover. Among these, Lactate Dehydrogenase (LDH), serum ferritin, and the erythrocyte sedimentation rate (ESR) have shown potential utility, yet their role in MDS monitoring remains under-explored.

Methods: We conducted a retrospective observational study involving 80 patients diagnosed with MDS between 2020 and 2025 in Albania. Demographic, clinical, and laboratory data were collected from patient records, including: age, gender, and MDS subtype, hematological parameters (hemoglobin, WBC, platelets, bone marrow blast percentage), and biochemical markers (LDH, serum ferritin, and ESR). Data were analyzed using SPSS. Statistical significance was defined as $p < 0.05$.

Results: Key findings from the statistical analysis are as follows: LDH levels were moderately and significantly positively correlated with bone marrow blast percentage ($r = 0.42$, $p < 0.005$), suggesting that higher LDH may reflect increased cellular turnover and disease activity. Serum ferritin levels demonstrated a moderate correlation with LDH ($r = 0.31$, $p = 0.007$), reinforcing the association with disease activity and inflammation. ESR was moderately correlated with ferritin ($r = 0.28$, $p = 0.02$), and displayed a negative trend with hemoglobin ($r = -0.21$), indicating a potential link between inflammatory state and the severity of anemia in MDS patients.

Conclusions: LDH, ferritin, and ESR demonstrate statistically significant correlations with clinical and hematological indicators of disease in MDS. These markers could serve as useful adjuncts in the evaluation and follow-up of patients. Further prospective studies are needed to validate their prognostic and longitudinal utility in larger and more diverse patient cohorts.

Keywords: ESR, ferritin, inflammation, laboratory biomarker, LDH, myelodysplastic syndrome

P34. CO-OCCURRENCE OF RING SIDEROBLASTS MYELODYSPLASTIC SYNDROME (MDS-RS) AND MULTIPLE MYELOMA (MM) IN THE ABSENCE OF PRIOR CHEMOTHERAPY

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Introduction: Multiple myeloma (MM) and myelodysplastic syndromes (MDS) are distinct clonal hematologic disorders. The concurrent occurrence of both conditions in a single patient, particularly in the absence of prior chemotherapy or radiotherapy, is exceedingly rare. Such cases may point to shared pathogenetic mechanisms or underlying genomic instability at the level of hematopoietic stem cells.

Methods: We report the case of an 80-year-old female with a history of type II diabetes mellitus and a diagnosis of MDS with ring sideroblasts (MDS-RS) established in 2017. The disease course was complicated by progressive renal failure and recurrent infections.

Results: In 2024, the patient presented severe anemia and elevated proteinuria. Bone marrow aspirate revealed 48% plasmacytic infiltration, trilineage dysplasia, ring sideroblasts, and negative cytogenetics for del(5q). Serum electrophoresis showed a single monoclonal lambda band, and imaging studies (CT) identified osteolytic lesions. These findings confirmed a diagnosis of concomitant multiple myeloma. The patient was initiated on bortezomib-based therapy, achieving complete hematologic remission.

Conclusions: The co-occurrence of MM and MDS without prior chemotherapy is rare and may suggest common pathogenic pathways or genetic instability at the stem cell level. Due to the rarity and complexity of such cases, further research is essential to develop optimal diagnostic and therapeutic guideline.

Keywords: multiple myeloma, myelodysplasia, plasma cells, renal failure, ring sideroblasts

P35. EVALUATION OF HEMOGLOBIN ELECTROPHORESIS PROFILE IN ANEMIC PATIENTS

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Introduction: Anemia is a significant global public health issue, particularly affecting young children, pregnant women, and postpartum women.Hemoglobinopathies are common inherited monogenic disorders that significantly affect the structure and function of hemoglobin. The WHO estimates that at least 5% of the global population carries hemoglobin mutations. The aim of this study was to evaluate the frequency of hemoglobinopathies among anemic patients over a one-year period (October 2023 – October 2024).

Methods: The study included 2,468 anemic patients, of whom 1,994 were female and 474 were male. Blood samples were collected via venipuncture and placed in K3 EDTA vacuum tubes. Hemoglobin electrophoresis was performed using the Sebia Capillary 3 Octa analyzer, an advanced platform for hemoglobin variant detection. The test identified various hemoglobin fractions, including HbA1, HbA2, HbF, HbS, HbC, among others. Anemia diagnosis and classification (mild, moderate, severe) were based on WHO guidelines.

Results: Out of 2,468 patients, 648 (26.25%) showed hemoglobin variants. Gender distribution: 409 (63.1%) were female, and 239 (36.9%) were male. Most common variant: Beta Thalassemia minor was identified in 607 patients (93.67% of hemoglobinopathy cases). Age distribution: The highest frequency was observed in patients over 40 years of age (234 cases). Anemia severity: 55.86% of patients with hemoglobin variants had moderate anemia. Mean hemoglobin level: 9.2 g/dL in patients with hemoglobin variants.

Conclusions: The findings indicate that hemoglobinopathies, particularly Beta Thalassemia minor, are a significant underlying cause of anemia. This has critical implications for public health, as patients are often misdiagnosed with iron deficiency anemia and treated with iron supplements. The high prevalence of variants in patients over 40 years old suggests delayed diagnosis, highlighting the need for earlier screening—especially in anemic individuals with unclear etiology.

Keywords: anemia, beta thalassemia minor, hemoglobin electrophoresis, screening

P37. THE ROLE OF BLOOD SMEAR CYTOLOGY IN THE ETIOLOGICAL DIAGNOSIS OF INFLAMMATORY COLITIS

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Introduction: The term colitis includes numerous clinical forms, which differ depending on the etiology or pathogenetic mechanisms, some having an acute or chronic evolution. Infectious colitis can have multiple causes, bacterial, viral, parasitic or fungal, and the detection of the pathogen in stool culture sometimes becomes difficult in certain situations, due to the early introduction of antibiotic therapy. Thus, any information provided by other investigations, such as the cytological examination of the blood smear, can play a key role in the diagnostic algorithm.

Methods: We present the case of a 75-year-old female, who presents to the doctor for abdominal pain, moderate fever and diarrheal stools with mucus and blood. Blood count and blood smear (May-Grünwald-Giemsa stained) are performed, which is interpreted according to the Recommendations of the International Council for Standardization in Hematology (ICSH).

Results: The blood count indicates moderate leukocytosis (23,760/µl), moderate anemia (Hb: 9.9 g/dL) and mild thrombocytopenia (145,000/µl.). Blood smear reveals a leukemoid reaction, neutrophilia with left deviation of the granulocyte series up to the blasts (6%), lymphopenia with reactive lymphocytes. The erythrocyte series presents extremely marked disorder, with orthochromic normoblast (1%) with dysplastic changes, anisocytosis with normocytes and microcytes, normochromia, expressed polychromasia, extremely marked poikilocytosis with frequent schistocytes (7.6%), codocytes, acanthocytes, elliptocytes, ovalocytes, microspherocytes, rouleaux formation. The platelet series presents anisocytosis with macrothrombocytes, bizarre-shapes platelets, platelet aggregates. A gastrointestinal panel is performed by PCR, which detects the presence of STEC- Escherichia coli producing Shiga-like toxin stx 2.

Conclusions: In this case, the peripheral blood smear brought an important contribution to the diagnosis, by highlighting schistocytes, posing the problem of a microangiopathic hemolytic anemia, respectively, of a hemolytic uremic syndrome of infectious cause, which was later confirmed by the detection of STEC stx2 by PCR.

Keywords: Escherichia coli – STEC stx1/stx2, hematological changes, inflammatory colitis, schistocytes

P38. IN VITRO CLOTH-INDUCED PSEUDOTHROMBOCYTOPENIA: "THE PHYSIOLOGICAL GIANT AND THE MORPHOLOGICAL DWARF"

Carmen Delianu[1,2], Loredana Liliana Hurjui[1,2], Claudia Cristina Tarniceriu[1,2], Roxana Iancu[1,2], Ion Hurjui[1], Larisa Ghemis[1], Liliana Georgeta Foia[1,2]

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Introduction: A critical state of thrombocytopenia is represented by pseudothrombocytopenia, an in vitro event resulting from platelet clumping under the influence of the anticoagulant ethylenediaminetetraacetic acid (EDTA).

Methods: Within the Department of Hematology of the “Sf. Spiridon” Hospital in Iași, between January and December 2024, we conducted a study on subjects presenting with a complete blood count (CBC) where platelet (PLT) recorded low values. The patients were divided into two groups: L1 (n=68) in which the presence of platelet aggregates was highlighted on the peripheral blood smear and the number of platelets on sodium citrate was evaluated, and L2 (n=400) subjected to transvasation procedure and subsequent accidental presence of clot identification.

Results: Out of the 68 samples with platelet aggregates (L1) following citrate verification, genuine thrombocytopenia was identified in 20 patients and pseudothrombocytopenia was confirmed in 44 patients, for 4 patients the determination being not repeated. Of the total of 400 samples from L2, in 283 (70.75%) the clot was observed in the postanalytical vacutainer stopper, and in 117 (29.25%) the clot was identified using the transfer procedure. The sampling and implicitly the CBC determination were then repeated, from the total of L2 subjects, 222 (55.5%) had the PLT count within the normal reference range, 80 (20%) displayed genuine thrombocytopenia, while for 98 (24.5%) the resampling was not possible.

Conclusions: Pseudothrombocytopenia may be the result of the accidental presence of an in vitro clot that was not identified preanalytically, with part of the leukocytes, erythrocytes and numerous platelets accumulating in the fibrin network, hence leading to false results. In this context, taking into account the particularities and role of the accidentally present clot, one can say that although morphologically it is small, the functional impact can be dramatic, like that of a "physiological giant". The use of postanalytical re-verification procedures, such as the transvasation used in our study, could be a guarantee to avoid exposing the patient to additional investigations, a false thrombocytopenia diagnosis or therapeutic failure.

Keywords: in vitro clot, pseudothrombocytopenia, thrombocytopenia, transvasation

P39. OXIDATIVE STRESS ASPECTS IN PATHOGENESIS OF PULMONARY TUBERCULOSIS

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Introduction: Pulmonary tuberculosis remains a major cause of morbidity and mortality globally. According to data published by the World Health Organization for 2022, approximately 10.3 million people were affected by TB, of which 8 million were men and 2.3 million were women. During the course of the disease the human body activates multiple biological mechanisms, including oxidative stress (OS) reactions, as part of the immune response against tuberculosis infection.

Methods: The prospective study was carried out within the Pneumology Institute "Chiril Draganiuc" in Chisinau during the years 2019-2024 and approved by the decision of the Research Ethics Committee of the State University of Medicine and Pharmacy "Nicolae Testemițanu" no. 31 of 18.05.2019. The study involved 118 people: 31 women (26.3%) and 87 men (73.7%). The people were divided into 2 groups: group L1- patients with TB until treatment, group L2 – patients with TB after treatment. NO (nitric oxid) and GR (glutation redus) levels were assessed in blood serum by spectrophotometric method. The data were analyzed using R-studio and Phyton.

Results: In the L1 group the NO values were 92.66 µM/L, compared to 107.4 µM/L in the case of the L2 group patients, a fact that constitutes an obvious increase in the NO level in theL2group ($p \leq 0.010$). In theL1group, the GR values were 704.6 nM/s.L ($p \geq 0.9$) versus 298.2 nM/s.L in L2 ($p \leq 0.001$), a fact that constitutes a significant decrease in antioxidant activity in the case of patients in theL2 group.

Conclusions: The results of there search demonstrated that after the anti-TB treatment, the level of NO increased and the level of GR decreased, a phenomen on that indicates the persistence of oxidative stress after treatment. The levels of NO and GR in patients with tuberculosis can serve as biomarkers in the process of monitoring the evolution of the disease.

Keywords: nitric oxide (NO), oxidative stress (OS), pulmonary tuberculosis (TB), reduced glutathione (GR)

P40. EVALUATION OF CONCORDANCE AND DISCORDANCE BETWEEN GENOTYPIC AND PHENOTYPIC METHODS IN THE DETECTION OF MDR-TB AND PROGRESSION TOWARD XDR-TB

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Introduction: Multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) represent a major global public health concern, associated with high mortality, prolonged treatment duration, and significant challenges in transmission control. Early and accurate detection of drug resistance is crucial for initiating appropriate therapy and limiting the spread of resistant strains. This study compares phenotypic and genotypic drug susceptibility testing methods, highlighting the concordance and differences observed between them.

Methods: This retrospective study included 66 clinical isolates of *Mycobacterium tuberculosis*, of which 29 were classified as MDR-TB. Drug susceptibility testing was performed using the proportion method on Löwenstein-Jensen medium and the genotypic GenoType MTBDRplus assay. Resistance was evaluated for first-line drugs (isoniazid – INH, rifampicin – RIF, streptomycin – STR, ethambutol – EMB), as well as for second-line agents including fluoroquinolones and injectable aminoglycosides.

Results: The concordance between the two methods was 94.74% for RIF and 95.16% for INH. Discordant results were observed in 3 cases for RIF and 2 cases for INH, where isolates were genotypically sensitive but phenotypically resistant. The phenotypic resistance rates were: 84.85% for INH, 46.97% for RIF, 48.48% for STR, and 30.30% for EMB. Among the 29 MDR-TB isolates, 41.37% showed resistance to fluoroquinolones, and 31.03% also to aminoglycosides, being classified as XDR-TB. Additionally, 22.73% of MDR-TB isolates were resistant to all four first-line drugs.

Conclusions: The GenoType MTBDRplus assay provides rapid and clinically valuable results for the detection of resistant strains, but it cannot fully replace phenotypic testing. The combined use of genotypic and phenotypic methods, alongside genomic sequencing, is essential for comprehensive diagnosis and individualized treatment in MDR/XDR-TB cases.

Keywords: drug susceptibility testing (DST), extensively drug-resistant tuberculosis (XDR-TB), GenoType MTBDRplus, genotypic testing, multidrug-resistant tuberculosis (MDR-TB), phenotypic testing

P41. DYNAMICS OF ANTIBIOTIC RESISTANCE IN THE PERIOD 2019–2023 FOR *ESCHERICHIA COLI* ISOLATED FROM VARIOUS BIOLOGICAL PRODUCTS COLLECTED FROM PATIENTS IN THE MEDICAL AND SURGICAL WARDS OF A HOSPITAL UNIT

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Introduction: Antibiotic resistance is a particularly significant problem both in Romania and globally. Monitoring antibiotic resistance in various bacterial pathogens involved in human infections provides valuable information for the development of strategies to combat multidrug resistance (MDR).

Methods: Bacterial identification and antibiotic susceptibility testing were performed using the Vitek 2 Compact automated analyzer, along with identification and antibiogram cards: identification cards for Gram-positive cocci, identification cards for Gram-negative bacilli, and antimicrobial susceptibility testing cards AST-N204, AST-N222, AST-P592. Results were interpreted according to CLSI standards.

Results: Between 2019 and 2023, a total of 8,319 biological samples were analyzed in the medical and surgical wards of the hospital unit, of which 5,860 (70.4%) were urine cultures. Following bacteriological analysis, 2,900 bacterial strains were identified, with 1,204 (41.5%) being *Escherichia coli*. For the *E. coli* strains isolated and identified, resistance to Ampicillin remained consistently high throughout the five-year period (mean: 51.5%). Significant resistance rates were also observed for Trimethoprim/Sulfamethoxazole (28.6%) and Ciprofloxacin (25.4%). The proportion of extended-spectrum beta-lactamase-producing strains (ESBL+) ranged from 9% (in 2021) to 17.6% (in 2020), while multidrug resistance (MDR) was reported in an average of 17% of the isolates. The year 2020 recorded the highest percentages of both ESBL+ and MDR strains, most likely in the context of the COVID-19 pandemic.

Conclusions: The study highlights the persistence of high levels of antibiotic resistance in *E. coli*, with moderate fluctuations throughout the analyzed period. The findings support the continued need for active microbiological surveillance, regular updates to therapeutic guidelines, and strict antibiotic stewardship measures, tailored to the local specifics of the hospital.

Keywords: antibiotic resistance, ESBL, *Escherichia coli*, multidrug resistance

P42. ANTIMICROBIAL RESISTANCE PROFILE OF *ESCHERICHIA COLI* STRAINS IN HOSPITALIZED PATIENTS AT THE REGIONAL INSTITUTE OF GASTROENTEROLOGY AND HEPATOLOGY CLUJ-NAPOCA: A CUMULATIVE ANTIBIOGRAM ANALYSIS

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Introduction: Antimicrobial resistance in *Escherichia coli* is a major problem in treating nosocomial infections, affecting the efficacy of empirical therapy. Monitoring susceptibility of isolates from hospitalized patients is essential to choose appropriate treatment and prevent the spread of resistant strains.

Methods: This retrospective study included 154 clinical *Escherichia coli* isolates collected between February and November 2024, exclusively from hospitalized patients at the Regional Institute of Gastroenterology and Hepatology Cluj-Napoca. Specimens analyzed included urine, blood, and secretions relevant for gastrointestinal and hepatic infections. Antimicrobial susceptibility testing was performed using Vitek 2 Compact analyzer, with results interpreted according to EUCAST guidelines. The cumulative antibiogram was generated using the Myla software (bioMérieux). Tested antibiotics covered a wide range, including ampicillin, trimethoprim, ciprofloxacin, third-generation cephalosporins, carbapenems, amikacin, and piperacillin/tazobactam.

Results: High resistance rates were found for ampicillin (~85%), trimethoprim (~75%), ciprofloxacin (~70%), and amoxicillin/clavulanic acid (~60%), indicating reduced efficacy for empirical therapy. Third-generation cephalosporins showed moderate resistance (40-60%), reflecting a significant prevalence of ESBL-positive strains. Carbapenems maintained very high susceptibility (>95%). Amikacin (~92% susceptible) and piperacillin/tazobactam (~85% susceptible) also retained clinical efficacy.

Conclusions: The resistance profile of *E.coli* in hospitalized patients at the institute highlights the need for using local cumulative antibiograms to optimize empirical therapy. Strengthening antimicrobial stewardship measures is also essential to prevent further resistance development.

Keywords: antimicrobial resistance, cumulative antibiogram, *Escherichia coli*, hospitalized patients, stewardship

P43. VENTILATOR-ASSOCIATED PNEUMONIA CAUSED BY *ACINETOBACTER* IN INTENSIVE CARE PATIENTS

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Introduction: Ventilator-associated pneumonia (VAP) caused by *Acinetobacter* spp. is a major public-health challenge in intensive-care units, amplified by extensive antimicrobial resistance.

Methods: We performed a retrospective study of 965 tracheobronchial aspirates collected in 2024 from mechanically ventilated patients. Bacterial isolation and antibiotic-susceptibility testing followed EUCAST guidelines. For each isolate, the Multiple Antibiotic Resistance (MAR) index was calculated, and the quarterly dynamics of carbapenemase-producing strains were analysed statistically.

Results: *Acinetobacter* spp. was isolated from 242 samples, giving a VAP prevalence of 25.1 %. Most cases occurred in patients aged ≥50 years (79.3 %). Resistance rates exceeded 90 % to cefepime, ceftazidime, cefotaxime, piperacillin-tazobactam and carbapenems (imipenem 92.6 %, meropenem 92.0 %); 95 % of isolates produced carbapenemases. Colistin remained active against 97 % of strains, whereas tigecycline was active against 52 %. The mean MAR index was 0.85 (± 0.06), with a significant rise in carbapenemase-positive strains from the first to the fourth quarter ($p < 0.05$).

Conclusions: Multidrug-resistant *Acinetobacter* VAP narrows effective therapy to colistin and a limited range of reserve agents. Strengthening antimicrobial stewardship, infection-control measures, selective oropharyngeal decontamination and rigorous ventilator hygiene, together with continuous molecular surveillance, are essential to reduce mortality and limit nosocomial transmission of VAP.

Keywords: *Acinetobacter* spp, antimicrobial resistance, colistin, intensive care, ventilator-associated pneumonia

P44. PREVALENCE OF *BORDETELLA PERTUSSIS* INFECTION IN CHILDREN FROM SIBIU REGION

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Introduction: Whooping cough is an extremely contagious respiratory disease, which can be severe in infants and children, therefore prevention through vaccination is very important. Many countries have been facing an increase in the incidence of the disease in recent years, generated by the fact that the vaccination rate in children is decreasing, and immunity after vaccination is temporary, 5-10 years. About 90% of cases of whooping cough have *Bordetella pertussis* as etiology, the diagnosis of the disease becoming much easier by using serological tests of the IgA anti-*Pertussis* type, their positivity being suggestive of a recent infection. The present work aims to determine the prevalence of *Bordetella pertussis* infection according to age, environment of origin and sex in patients hospitalized at the Pediatric Clinical Hospital in Sibiu, during the period, April-December 2024, corroborated with data from the literature.

Methods: In this retrospective study, 295 children hospitalized in the Pediatric Hospital were analyzed with suspicion of whooping cough. IgA anti *Bordetella pertussis* dosage was performed on the DiaSorin Liason analyzer, from serum. Variables such as gender and environment of origin were studied according to age groups (<1 month, 1 month–1 year, 2–9 years, 10–17 years and >18 years).

Results: Analyzing the results obtained, it was found that 50 patients out of 295 tested, 17%, presented positive IgA, The most affected was the age group 2 – 9 years, 29 out of 50, followed by children <1 year., 15 out of 50. The distribution by gender and environment of origin did not show any statistically significant difference ($p = 0.398$).

Conclusions: Infants and children up to 9 years of age represent the most vulnerable population to *Bordetella pertussis* infection, therefore promoting vaccination is a public health priority.

Keywords: *Bordetella pertussis*; children, respiratory disease, Sibiu

P45. PREVALENCE OF *MYCOPLASMA PNEUMONIAE* INFECTION IN CHILDREN FROM SIBIU REGION

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Introduction: *Mycoplasma pneumoniae* is one of the most common causes of community-acquired pneumonia in school-age children and adolescents. Modern diagnosis involves serological testing to identify IgM antibodies that appear one week after the onset of symptoms. The present study aims to determine the variation in the prevalence of *M. pneumoniae* infection according to age, sex and month of infection in patients admitted to the Pediatric Clinical Hospital of Sibiu, during the period, April-December 2024, corroborated with data from the literature.

Methods: In this retrospective study, 1069 children diagnosed with pneumonia were analyzed. IgM anti *M. pneumoniae* assay was performed on the DiaSorin Liaison analyzer, from serum. Variables such as gender and month of infection were studied according to age groups (<1 month, 1 month–1 year, 2–9 years, 10–17 years and >18 years).

Results: Analyzing the results , we found that 38.54% of patients tested positive for IgM anti-*M. Pneumoniae*. An increased seropositivity was recorded in May, June, September and October. The most affected age group was 2-9 years (25.72%). The distribution by gender did not show any statistically significant difference between the two groups ($P = 0.287$).

Conclusions: More than 1/3 of pneumonias diagnosed in preschool children were caused by *M. pneumoniae*. The existence of IgM serological Kit makes diagnosis much easier.

Keywords: children, IgM, *Mycoplasma pneumoniae*, Sibiu

P46. A HIDDEN ENEMY: UNDERSTANDING CANDIDEMIA IN CRITICALLY ILL PATIENTS

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Introduction: In recent decades, the prevalence of invasive fungal infections has steadily increased within clinical settings. Among these, infections attributed to *Candida* species have emerged as particularly concerning due to their persistence and severity. Critically ill patients are a particular category characterised by a life-threatening condition associated with vital organs dysfunction that requires intensive monitoring and mechanical or pharmaceutical support. They are the most vulnerable population to candidemia as they cumulate several independent risk factors.

Methods: A retrospective study was conducted to analyze the characteristics of 50 patients with *Candida* spp. positive blood cultures hospitalised over a period of 17 months in an emergency hospital. The laboratory diagnostic protocol included microscopy, culture, automated identification of yeasts (MALDI-TOF and Phoenix BD) and antifungal susceptibility testing. *Candida* score including the updated Sepsis 3.0 definition was assessed for all the patients.

Results: The study group included 41 adult patients with mean age of 59 years and 9 preterm infants. Candidemia occured more frequently in Intensive Care Unit patients (36%, 18/50), the rest of patients being admitted in Neurology, Internal medicine, Nephrology and Newborn Intensive Care Unit departments. Stroke, bronchopneumonia, cardiac and renal failure, deep vein thrombosis or malignancies were the main underlying pathologies in adults. 80.48% of adult patients (33/41) had previous or concomitant bacterial infections and the average duration of antibiotherapy before candidemia was 17 days. The mean duration of hospitalization until candidemia onset was 24 days for ICU patients and 15 days for non-ICU with significant difference ($p=0.041$) between the two means. In ICU patients, *Candida* score was semnificatively higher compared to non-ICU patients ($p=0.001$). Notably, C-reactive protein levels were elevated in all cases (>0.5mg/dl), while procalcitonin was increased (>0.5ng/ml) in 24 of 35 tested patients when the diagnostic of candidemia was made.

Conclusions: By understanding the unique vulnerabilities of critically patients and implementing strategic preventive measures, the risk of candidemia can be mitigated. Also, vigilant monitoring and detection through blood cultures can preemptively identify this threatening condition.

Keywords: blood cultures, *Candida* score, candidemia

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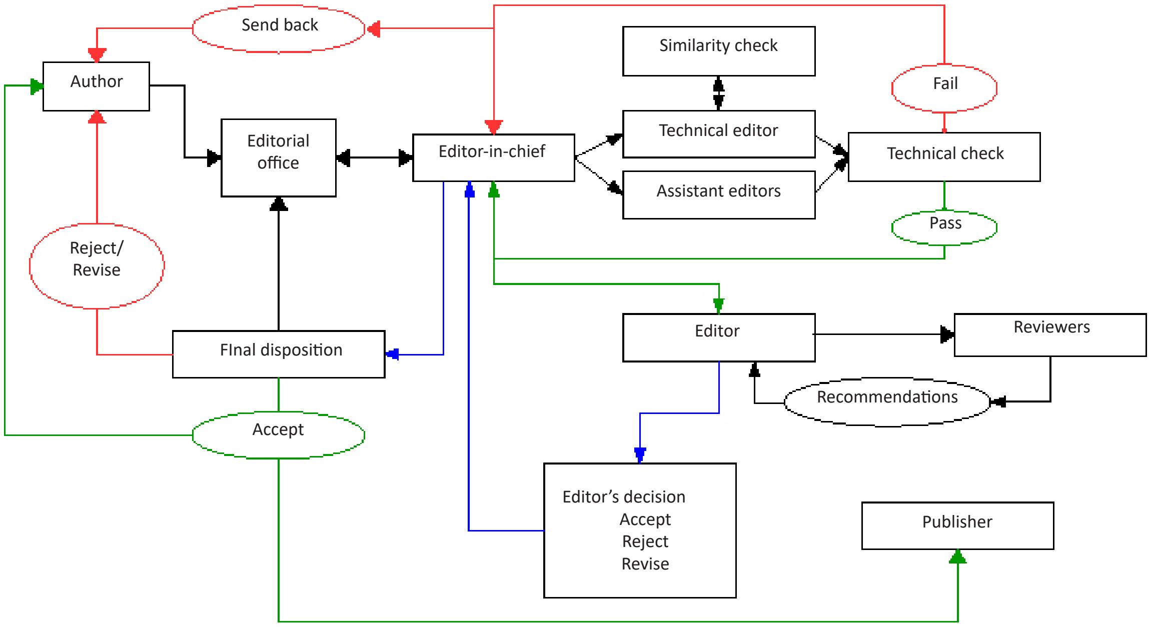

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Authors should consult someone proficient in the English language, if they feel it is necessary. If the manuscript is not conform to accepted standards of English usage, the manuscript will be rejected.

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Material and methods have to be described in enough detail to permit reproduction by other teams. The same product names should be used throughout the text (with the brand name in parentheses at the first use). **Results** should be presented concisely. Tables and figures should not duplicate text. The **discussion** should set the results in context and set forth the major conclusions of the authors. Information from the Introduction or Results should not be repeated unless necessary for clarity. The discussion should also include a comparison among the obtained results and other studies from the literature, with explanations or hypothesis on the observed differences, comments on the importance of the study and the actual status of the investigated subject, unsolved problems, and questions to be answered in the future. In addition to the customary recognition of non-authors who have been helpful to the work described, the **acknowledgements** section must disclose any substantive conflicts of interest.

Abbreviations shall be preceded by the full term at their first apparition in text. A list of all abbreviations used shall be made at the end of the article.

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