

Congress Abstracts

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Analytical Quality and Laboratory Organization for Neonatal Diagnostics

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Laboratory diagnostics in neonatology particularly requires integrated management of pre-analytical, analytical, and post-analytical phases, with a focus on producing clinically informative reports in settings of high biological variability, as seen in newborns. Analytical quality depends not only on instrumentation, but also on the integrity of the biological matrix and the system's ability to detect and manage pre-analytical errors, often subtle yet clinically significant (1,2).

Pre-analytical processes are supported by trained laboratory personnel and automated systems that identify anomalies such as hemolysis, clotting, icterus, or insufficient volume. Proper integration of this information into the reporting process allows the addition of interpretive comments, enhancing the reliability and clinical value of the result. The combination of automation and expert review ensures consistently high analytical standards.

Although Point-of-Care Testing (PoCT) occurs outside traditional laboratory environments, it must include appropriate quality control procedures—particularly when coordinated by the central laboratory. Nevertheless, variability in sampling techniques and limited traceability in decentralized settings may increase the risk of error. Remote laboratory oversight is thus essential to ensure quality checks and result interpretation.

Capillary blood gas testing exemplifies these issues: non-standard matrices reduce comparability and complicate interpretation. To safeguard result validity, an Individualized Quality Control Plan (IQCP) should be implemented. This includes structured risk analysis, identification of variability sources, and definition of performance goals adapted to clinical requirements (3).

Training plays a pivotal role in PoCT safety. It is crucial not only during implementation, but also for preserving operator competence. Structured educational programs—offered via certified e-learning, simulations, and periodic assessments—ensure skill retention, reduce variability, and maintain adherence to quality standards. When combined with real-time alerts and documentation of pre-analytical conditions, training enhances diagnostic safety and decision-making.

Finally, the integration of middleware and AI tools has the potential to offer opportunities for responsive, data-driven neonatal diagnostics. However, these tools must be embedded within a robust framework of quality governance, ongoing monitoring, and strong clinical-laboratory collaboration.

In conclusion, the laboratory must evolve from a passive data provider to an active clinical partner, including in the context of neonatal diagnostics. Its expanded role involves interpreting results, delivering informative reports, and supporting clinicians with clear, relevant insights. By leveraging continuous quality improvement data through dedicated platforms, the laboratory can detect deviations early and contribute to timely, preventive actions. Moreover unified, quality-driven diagnostic network that integrates PoCT with central laboratory workflows is essential to provide safe, accurate, and clinically meaningful information for neonatal care.

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EFLM Science Division: science approaches to creating value-based laboratory medicine

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The EFLM Division “Science: Value-based Laboratory Medicine” is responsible for the EFLM projects to advance science, practice and value of laboratory medicine, aiming to improve patient outcomes through appropriate use and applications of in vitro diagnostic (IVD) data in health services and medical practice. The objectives are:

- Identify new and emerging IVD biomarkers and technological innovations, appraise evidence of their analytical and clinical performance, and provide recommendations and guidelines on how to implement them in clinical laboratory practice and integrative diagnostic strategies.

- Establish safety and quality standards to be met in delivering value to patients, clinicians, public health agencies and authorities through better test utilization, test-assisted clinical decision, integrated diagnostics, personalized (precision) diagnostics, and patient empowerment through remote monitoring, Direct-to-Consumer Testing (DTCT) and patient self-tests.

- Harmonisation of the Total Testing Process (TTP), through guidelines stating best practice in pre-analytical, analytical and post-analytical areas including (but not limited to) measurement units, reference intervals and decision limits, across the full continuum of the brain-to-brain loop of requesting, performing, reporting and using laboratory tests and test-based calculations for diagnosis and treatments through the full patient journey in the clinical pathway.

- Practical guidance to implement clinical and analytical test performance specifications, measurement uncertainty, and biological variation estimates in clinical laboratory practice. Deliver biological variation data to the global laboratory community.

- Facilitate digital transformation, A.I. applications and standardized health data coding to enable novel approaches to exchange and use diagnostic data being shared between laboratories, healthcare professionals, healthcare providers and patients.

- Organize collaborative projects and communications with IVD Industry and EQA providers, and engage in guideline development in co-operation with relevant clinical societies and multidisciplinary consensus groups.

- Respond to scientific, clinical and technical needs, opportunities, or (pandemic) emergencies by translating expert scientific and clinical evidence into advice for clinical laboratories, IVD Industry, European Regulatory and other key stakeholders to ensure the clinical benefit and safety of IVD tests on the market, and education of patients/consumers to ensure safe use of DTCT and appropriate interpretation of self-tests.

- Produce criteria and recommendations to implement sustainable practices in the medical laboratories by decreasing their deleterious environmental impact without compromising quality and patient safety.

- Develop a “value-score” of objective evaluation of quality in the TTP to accomplish an effective program of benchmark between clinical laboratories.

The EFLM Science Division manages the scientific projects through 20 Committees of experts working on the specific areas.

New frontiers in serological and biochemical diagnosis of synovial fluid

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Periprosthetic joint infections (PJI) are serious complications after joint arthroplasty, needing timely and accurate diagnosis. According to international guidelines, the identification of PJI should follow a comprehensive approach that integrates clinical evaluation with laboratory and imaging findings, incorporating major and minor diagnostic criteria. In the evolving landscape of diagnostics, beyond the traditional reliance on positive cultures, serological and biochemical biomarkers measured in both synovial fluid and serum have emerged as valuable tools for improving diagnostic accuracy, especially in cases where traditional biomarkers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) yield equivocal or borderline results. Synovial fluid testing, including the assessment of leukocytes, calprotectin, alpha-defensin and leukocyte esterase, has shown variable diagnostic performance. D-dimer has recently been proposed as a complementary biomarker for PJI. Although initially validated in coagulation disorders, its role in infection diagnostics is gaining recognition, with studies reporting diagnostic accuracy rates for PJI approaching 70%, sensitivity of 74%, and specificity of 79%. However, the diagnostic utility of several of these biomarkers may be compromised by systemic antibiotic therapy, which can attenuate inflammatory responses and lead to false-negative results. While serum biomarkers provide a convenient, minimally invasive initial screening modality, their sensitivity for detecting low-grade or indolent infections is also limited, reinforcing the clinical value of synovial fluid analysis, which offers a more localized reflection of intra-articular inflammation. Emerging biomarkers such as D-lactate, matrix metalloproteinases and tissue inhibitors of metalloproteinases are expanding the diagnostic arsenal in complex or culture-negative infections. Advances in ultrasound-

guided synovial biopsies and artificial intelligence-enhanced data interpretation, hold potential to transform early detection and therapeutic stratification in PJI management.

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European In Vitro Diagnostic Regulation (Reg. (EU) 2017/746 - IVDR): achievements and opportunities for improvement

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The implementation of Regulation (EU) 2017/746 (IVDR) on in vitro diagnostic medical devices marked a turning point in the European regulatory landscape, introducing stricter requirements to ensure device safety and performance. However, several operational challenges emerged during the initial implementation phase, prompting further regulatory adjustments by the European Union. The recently adopted Regulation (EU) 2024/1860 introduces an extension of the transitional periods to facilitate compliance and mitigate risks of device shortages.

This presentation provides an updated overview of the evolving regulatory framework, focusing on the key amendments introduced by Regulation (EU) 2024/1860 compared to the earlier Regulation 2017/746. Particular attention is dedicated to the extended transitional provisions applicable to legacy devices and the new obligations for manufacturers, especially concerning the notification duties in case of anticipated supply disruptions or discontinuations that could pose serious risks to patients or public health.

However, from the recently published 2024 MedTech Europe survey,¹ persisting industry concerns are still detected, particularly regarding the capacity of Notified Bodies, the prologue and unpredictable timelines for the conformity assessment procedures and the associated costs. Indeed, the number of IVDR-designated Notified Bodies in Europe has increased to 18, this remains insufficient to meet the market's conformity assessment needs.

Future developments are also addressed, including the European Commission's targeted evaluation of the MDR and IVDR, aimed at collecting evidence to optimize the regulatory framework's effectiveness and efficiency and the recently announced revision of both regulations. In this context of regulatory evolution, the ongoing enhancement of the regulatory infrastructure, such as the completion and publication of the updated European Medical Device Nomenclature (EMDN) codes, the availability of supporting educational materials for stakeholders, as well as the development of Eudamed, is presented.

¹ MedTech Europe 2024 Regulatory Survey: key findings and insights, <https://www.medtecheurope.org/resource-library/medtech-europe-2024-regulatory-survey-key-findings-and-insights/>

Based also on the recent analysis proposed by Confindustria Dispositivi Medici,² the presentation concludes by outlining key priorities for the upcoming years: strengthening the capacity of Notified Bodies, enhancing sector competitiveness, streamlining certain administrative obligations, and ensuring the full functionality of the Eudamed database to support transparency and traceability in the European market.

INTEGRATIVE DIAGNOSTICS AND THE MEDICAL DIALOGUE IN LABORATORY MEDICINE

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Modern medicine is characterized by data-driven sophistication and personalization in virtually every area. Particularly, diagnostic disciplines, i.e. laboratory diagnostics (*in-vitro*) and medical imaging (*in-vivo*) have seen enormous advances since the early 2000s. Consequently, the diagnostic performance in detecting early health conditions, in monitoring and prognostication of clinical outcomes has tremendously improved clinical decision-making. These advances come with a “price tag”: a staggering increase of complex and often fragmented data separately deposited in their respective “specialty silos”. Often seen as a remedy, the compilation into electronic health record (EHR) platforms does little by itself as a countermeasure to overcome fragmentation or reduce data complexity. Indeed, volume and diversity of diagnostic results may overwhelm the diagnostic acumen of even the most dedicated and experienced clinician. Medical professionals depend on reducing data complexity and fragmentation to achieve qualified decision-making, and two different - not mutually exclusive - strategies directly come to mind:

1) no restrictions regarding complexity and fragmentation during the “stage of data acquisition” followed by a “stage of data processing” through machine learning algorithms and artificial intelligence (AI) tools to reduce complexity for a manageable number of few suggestions. This strategy extends the current approaches requires no improvement of diagnostic process quality; its diagnostic success being based on the power of the AI tool used (the “garbage-in-garbage-out problem”).

2) *a-priori* reducing data complexity and fragmentation by employing knowledge-based strategies contributed by the diagnostic disciplines and coordinated through “integrative enquiry and processing”.

Moving towards a “Integrative Diagnostics” will require stepwise changes to the process of the “diagnostic brain-to-brain loop”. Regularly, diagnostic test orders are separately addressed to different diagnostic disciplines that will generate and report their respective data independently requiring clinicians to assemble them *post hoc* into coherent pictures for clinical decision-making. A first major improvement in this process would be that (*in-vitro* and *in-vivo*) diagnostic disciplines after being confronted with separate diagnostic questions synchronize their individual results between them to produce a coordinated joint finding to be reported. Such an integrated answer is a product, the quality of which is strongly influenced by the quality of the diagnostic question. Further improving this strategy envisages addressing the clinical question directly at Diagnostic Medicine, where internal coordination firstly defines the investigations that need to be performed to answer the question. This strategy fulfils the definition of “Integrative Diagnostics” as a process rather than a product and could substantially strengthen Diagnostic Medicine in an improved medical dialogue.

Harmonization of measurement units: an essential step for comparability of laboratory information

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Harmonization of laboratory reports is a continuous challenge for laboratory professionals. The harmonization of measurement units, reference intervals, and nomenclature/ terminology, the three key factors characterizing laboratory

² The current challenges in Europe's Medical technology regulatory framework – Analysis and proposals from Confindustria Dispositivi Medici to revamp the competitiveness of the medical device sector in Europe, <https://www.confindustriadm.it/position-paper-revisione-mdr-ivdr/>

reports, must be achieved by sharing and adopting the recommendations as well as by following the suggestions by guidelines of the National and International Societies. The widespread acceptance of this approach is imperative, not only because harmonization of nomenclature and measurement units allow to minimize risk to patient safety but also considering the future “European Health Data Space” which will entail mandatory the accessibility and exchange of healthcare data. However, the results of a recent survey carried out from EFLM Committee: Harmonisation demonstrated that the community of the laboratory professional seriously underestimates the problem: some countries in Europe expressed little interest in this specific topic and 25 % of the countries failing to participate. In addition, although the data showed an overall and progressive, albeit slow, improvement in harmonization of reports provided by clinical laboratories in Europe, the real message arising from the data is that there is an urgent need for a change in attitude from all stakeholders involved in this process. In order to accelerate harmonization activities, National societies should be supported by European scientific bodies providing guidelines and specifying the time-frame for the update. The first step might consist in strongly encouraging EQA scheme providers to use only SI units in reporting results: EQA performance represent a fundamental prerequisite for ISO 15189 accreditation, and, according to the proposed strategy, laboratories should adopt the SI units to evaluate their analytical performance through the EQA scheme. A further step might be to oblige manufacturers (within the IVDR regulation) to exclusively include in their Instructions For Use (IFU), the SI units in their product description, in declaring the specific analytical performance and in reporting the proposed reference intervals. Currently, in the IFU of the main manufacturers of reagents and systems, SI units are reported in brackets, or named as “alternative” to the traditional units, the latter being identified as principal or “standard” units. In order to address this issue promptly, EFLM working groups and the official bodies managing the in vitro diagnostic medical device regulation requirements, are working together to plan the joint strategic activities to propose a pragmatic and sustainable approach enabling the rapid achievement of the harmonization of the three key issues in reporting results: measurements units, reference intervals, and nomenclature.

NT-proBNP in cardio-oncology: a role still under debated

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Progress in cancer therapy over the past decades improved long-term survival but increased cancer therapy-related cardiotoxicity. Many novel treatment options have been implemented with yet incompletely characterized cardiovascular side effects including heart failure, coronary artery disease, myocarditis and different heart conditions of varying severity. Diagnosis of potential cardiotoxic side effects that is essential for an optimal treatment, remains today challenging. Cardiac biomarkers measurements, particularly high sensitive troponins (hs-cTns) and natriuretic peptides (NPs) may provide a sensitive and early indicator of cardiovascular involvement from different diseases as evidenced by many studies carried out during several years. In particular, elevated natriuretic peptides (BNP/NT-proBNP) have been shown to predict manifest heart failure as well as the response to heart failure therapy in adult and pediatric cancer. Therefore, most recent published clinical guideline on cardio-oncology, recommends the inclusion of the measurement of natriuretic peptides (in association of hs-cTns) in baseline cardiovascular toxicity risk assessment of all patients with clinical history of previous cardiovascular disease or at risk from cancer therapy-related cardiac dysfunction. Of particular value from clinical point-of-view, seems to be the baseline measurement in patients with myeloma multiple of NT-proBNP, as recommended by specific clinical guideline, in that has proven a predictive marker for subsequent cardiovascular adverse events. Despite these assumptions and the strong pathophysiological and clinical evidences demonstrating the ability of cardiac biomarkers levels to provide a very early information on the onset and the development of cardiac disease, particularly heart failure that differently from myocardial damage may occur several times after treatment, several concerns still prevent the adoption in clinical practice of the described biochemical approach: the knowledge of adequate cut-points specific to diagnose cardiotoxicity as well as a better definition and agreement on the optimal timing of a sampling regimen may fill, to some extent, the knowledge gap that clinicians are faced until now, that makes the recommendations vague at best, according to the critical statement of several papers in the recent literature.

Clinical Risk Management Tools in Laboratory Medicine

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Clinical risk in laboratory medicine refers to the potential for errors during the diagnostic process to cause patient harm. Errors may occur at any stage—from pre-analytical (e.g., patient misidentification, sample collection, transport) to post-analytical phases (e.g., incorrect or delayed reports, improper communication). Such errors can lead to significant adverse outcomes, including misdiagnosis, inappropriate treatment, delayed therapy, patient distress, increased healthcare costs, and in severe cases, death (1).

The Institute of Medicine estimates that diagnostic errors, including laboratory-related ones, cause 44,000–98,000 deaths annually in the US. Sample identification errors result in over 160,000 adverse events yearly. While, errors in BRCA genetic testing exposed 20 patients to potential harm, with at least one significant clinical consequence. Most pre-analytical errors cause report suspensions or delays, often with limited clinical impact, whereas undetected analytical and post-analytical errors are more dangerous—7.6% of reported errors are linked to serious clinical outcomes (2,3).

Despite its impact, clinical risk in Laboratory Medicine is still underestimated—not only compared to other clinical fields but also by lab professionals. A 2016 survey by the joint SIBioC–SIE group, targeting laboratories in the Tuscany Region, revealed heterogeneous risk perception. While some laboratories fully acknowledge the criticality of sample identification errors, others regard them as marginal. This inconsistency reflects cultural and organizational differences and highlights the need for standardized practices and a shared safety culture (4).

The integration of clinical risk management tools is therefore pivotal to ensuring the quality and safety of diagnostic services. The implementation of international standards such as ISO 15189 and ISO/TS 22367, which advocate for quality management and risk assessment, has yielded measurable improvements, including reductions in analytical errors, enhanced performance in external quality assessments (EQA), decreased incidence of unsuitable samples, and fewer adverse events. In accredited laboratories, weekly complaints have decreased by over 70%, and blood sample contamination rates have declined from 16% to 4% (5).

Automation technologies and barcode-based traceability systems have also demonstrated efficacy in minimizing identification errors. Laboratory information management systems ensure comprehensive traceability throughout the testing process and facilitate more effective internal audits. Concurrently, continuous personnel training, coupled with fostering a safety culture and implementing non-punitive incident reporting systems, promotes ongoing quality improvement and error prevention.

Finally, effective, structured communication between laboratories and clinicians—especially about critical value management—is essential for timely, appropriate clinical responses. In conclusion, integrating international standards, technology, comprehensive training, and a culture of safety forms a strong framework to enhance laboratory quality and safety, ultimately protecting patient outcomes.

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DIAGNOSTIC METHODS FOR NEONATAL HYPERBILIRUBINEMIA IN THE LEVEL III NEONATAL UNIT OF THE MARCHE REGION

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Neonatal hyperbilirubinemia is a common and clinically relevant condition. Prompt and accurate assessment of bilirubin levels is essential to prevent complications such as kernicterus. At the “G. Salesi” Children’s Hospital in Ancona, the only level III neonatal care center in the Marche region, nearly 1600 newborns are admitted annually and routinely undergo monitoring for hyperbilirubinemia.

In clinically stable term and near-term newborns, bilirubin levels are measured within the first 48 hours of life using point-of-care (POC) capillary blood devices (55 µL) equipped with a secondary reading channel to account for interference from free hemoglobin. Blood is collected from the heels in heparinized capillaries, centrifuged, and analyzed using a bilirubinometer, which provides plasma bilirubin levels that correlate well with total serum bilirubin (TSB). Alternatively, a transcutaneous bilirubinometer is used. Timing, frequency, and duration of monitoring depend on predefined risk factors (e.g., positive Coombs test), clinical signs of jaundice, and TSB values. In newborns requiring intensive care, TSB is measured from capillary blood (65 µL) using blood gas analyzers, which automatically upload results into the Laboratory Information System (LIS), enabling timely, data-driven clinical decisions.

In physiological or uncomplicated jaundice, bilirubin measurements rarely extend beyond day 14 of life and are sufficient to guide therapeutic decisions, without additional diagnostic work-up. If jaundice persists beyond 14 days of life (prolonged jaundice), further evaluation is warranted to determine whether it reflects unconjugated or conjugated hyperbilirubinemia. In these cases, a venous blood sample collected in a gel-separation tube is sent to the central laboratory for total and fractionated bilirubin analysis. Micro-cups are routinely used to allow testing even from low-volume samples. When unconjugated hyperbilirubinemia is suspected, additional investigations may include complete blood count, G6PD activity, urine dipstick, and serum albumin. For conjugated hyperbilirubinemia, supportive markers include GGT, ALP, transaminases, ammonia, INR, bile acids, α -1 antitrypsin (level and phenotype), PCR for congenital infections, and expanded metabolic screening. All bilirubin devices, both POC and laboratory-based, undergo daily calibration and internal quality control. Nursing staff are specifically trained to maintain POC analytical performance consistent with laboratory standards. Bilirubin values are plotted on reference nomograms to guide therapeutic decisions such as phototherapy or, when necessary, exsanguino-transfusion. An automated system linking LIS data to the neonatal electronic health record, together with the integration of clinical decision-support tools and potential expansion to peripheral settings, is currently under evaluation.

In our experience, the key to effective management of neonatal hyperbilirubinemia lies in close collaboration between the neonatal unit and the central laboratory, supported by regular review of diagnostic devices.

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Measured and Estimated GFR: State of the Art

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Accurate assessment of glomerular filtration rate (GFR) remains central to the diagnosis, staging, and management of chronic kidney disease (CKD). The 2024 Kidney Disease Improving Global Outcomes (KDIGO) guidelines provide substantial updates to CKD evaluation and management, with direct implications for clinical laboratories, particularly in Europe. These guidelines emphasize the harmonization of CKD testing, the use of regional equations, and the need for standardized, traceable biomarker measurements.

Creatinine-based estimated GFR (eGFR_{Cr}) continues to be the first-line approach due to its practicability; however, it is limited by non-GFR determinants such as muscle mass, diet, and ethnicity. The 2024 KDIGO guidelines promote the combined use of serum creatinine and cystatin C (eGFR_{Cr-cys}) to enhance diagnostic accuracy and reduce individual-level imprecision. Cystatin C, being independent of muscle mass, supports the use of sex- and race-neutral equations. However, standalone cystatin C-based estimation has not consistently demonstrated superior performance unless combined with creatinine.

In the European context, the European Kidney Function Consortium (EKFC) equations, developed in 2021, are particularly well-suited. These equations use the Q-value (population median creatinine) to recalibrate eGFR estimates across diverse age groups and ethnic backgrounds. Compared to the CKD-EPI 2021 race-free equation, the EKFC model shows superior accuracy in European populations and supports application across the lifespan. A parallel EKFC equation using cystatin C has also been developed, maintaining the same mathematical structure and promoting harmonized, race- and sex-free GFR estimation.

Despite these advancements in estimation, measured GFR (mGFR) remains essential in specific clinical scenarios, such as atypical body composition, therapeutic drug monitoring, kidney donor evaluation, and discordant biomarker results. The 2024 KDIGO guidelines encourage the use of exogenous markers like iothexol to measure GFR where eGFR is inadequate. Iothexol plasma clearance, while considered a robust reference method, poses practical challenges due to its complex pre-analytical and analytical requirements, including blood sampling timing, assay standardization, and curve-fitting methodology. Recent evidence supports simplified multi-sample and one-sample protocols, which offer acceptable precision when supported by validated correction formulas and modeling techniques.

Future priorities include the global standardization of creatinine and cystatin C assays with traceability to international reference materials, harmonization of GFR reporting formats, and further validation of regional eGFR equations. Additional directions involve integrating muscle mass or body composition data into eGFR models, exploring novel filtration markers, and employing artificial intelligence to refine GFR estimation. Standardized definitions and management of discordances between creatinine and cystatin C values also remain critical to improving patient outcomes.

Primary Aldosteronism: biochemical diagnostic approach

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Primary aldosteronism (PA, or hyperaldosteronism) is a syndrome caused by excessive and inappropriate aldosterone (ALD) production and is the most common form of endocrine hypertension (HT). The Endocrine Society suggests a three-tiered diagnostic approach for PA that includes initial testing, confirmation, and subtyping. The initial screening is recommended in high-risk patients for PA, that is those with resistant HT, HT with adrenal incidentaloma, HT and hypokalaemia, HT and sleep apnoea, family history of early-onset HT or stroke (<40 years), and hypertensive first-degree relatives of patients with PA.

Aldosterone-renin ratio (ARR), constituting serum ALD concentration in ng/dL (or pmol/L) and plasma renin activity (PRA) in ng/mL/h (or pmol/L/min) or direct renin concentration (DRC) in mU/L (or ng/L), is a widely used screening method for PA.

ARR testing requires standardization of the sampling conditions and careful consideration to potential confounders specific procedures to properly prepare patients for specimen collection. Additionally, a variety of factors must be accounted for when interpreting results.

However, there is a lack of consensus on a universal cut-off for the ARR and some apply this ratio in conjunction with a plasma ALD concentration of 10 ng/dL or more (≥ 277 nmol/L). Furthermore, the ARR is denominator dependent (renin) and risks misinterpretation as laboratories have different lower detection limits for renin levels, and slight variations in renin can cause significant changes in the ratio.

Except for patients with spontaneous hypokalaemia, suppressed renin, and serum ALD concentration of 20 ng/dL or higher (≥ 555 pmol/L), all guidelines, following a positive screen, recommend confirming the diagnosis by demonstrating nonsuppressibility of ALD with a dynamic test (oral sodium load, saline infusion, captopril challenge, or fludrocortisone suppression test). There is substantial variation and lack of consensus on protocols, interpretation of results, and categorical levels that indicate a “positive” or “negative” result. Moreover, there is insufficient evidence to recommend one strategy over another.

Studies analysing the new generation of laboratory assays (liquid chromatography-tandem mass spectrometry or 2-site sandwich chemiluminescent immunoassay) have revealed lower ALD cut-offs compared with conventional radioimmunoassays, emphasizing the need for recalibration of the screening and confirmatory thresholds based on the assay type.

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PoCT Micro-Methods: A Solution For Multiple Clinical Settings, A Challenge For The Laboratory

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The use of Point-of-Care Testing (POCT) based on the analysis of micro-samples of capillary blood represents an increasingly important diagnostic strategy for the timely management of critically ill patients. The ability to perform hematology, metabolite, blood gas and electrolyte tests from extremely small sample volumes (approximately 10–250 μ L) minimizes the risk of iatrogenic anemia, which is particularly relevant in neonatology units, and significantly reduces the stress associated with repeated venous sampling. The implementation of miniaturized analytical systems enables near-immediate results, optimizing clinical decision-making processes and facilitating early, targeted therapeutic interventions. Clinically, these advantages translate into improved management of complex conditions such as metabolic imbalances, neonatal hypoglycemia, respiratory distress, and tissue oxygenation monitoring. However, the use of capillary blood introduces significant preanalytical challenges, including difficulties in standardizing collection techniques, risk of hemolysis, clotting and sample dilution with lymphatic fluid, due to improper handling. Blood gases are more prone to ambient air contamination, especially if samples are not carefully collected. Physiological differences between capillary and venous blood may lead to analytical discrepancies, requiring rigorous and continuous accuracy verification. The heterogeneity of personnel performing POCT necessitates structured training programs, certified competence, and periodic audits to ensure data quality and reliability. Within this framework, the clinical laboratory plays a pivotal role in governing POCT, balancing technological innovation and rapid clinical decision-making with strict quality assurance to maximize clinical benefits and minimize diagnostic risks. The widespread adoption of POCT micro-methods, increases the complexity of ensuring analytical

accuracy, as capillary blood samples are inherently more prone to preanalytical errors. Dissemination of POCT devices across different clinical units necessitates a robust governance model, incorporating standardized protocols, user training, competency assessments, and comprehensive internal and external quality control programs. Financial sustainability also emerges as a laboratory-level challenge, as decentralized testing often entails higher per-test costs, increased maintenance expenses, and logistical burdens related to reagent supply chains and device calibration. These factors collectively redefine the laboratory's role from a centralized testing hub to a multidisciplinary governance entity responsible for ensuring diagnostic reliability, clinical safety, and cost-effectiveness across distributed care environments. Addressing these challenges requires laboratories to embrace a leadership position, leveraging innovation, staff education, and advanced quality management systems to fully realize the clinical potential of POCT micro-methods while safeguarding diagnostic excellence.

Laboratory tests in the management of hemorrhages in emergency situations

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Laboratory testing plays an essential role in bleeding management in emergency settings, offering essential diagnostic and prognostic information that guides clinical decisions for improving patient outcomes. Hemorrhages, whether internal or external, vary in severity and are categorized into four classes based on the percentage of blood volume lost, each with specific clinical presentations. Class I is often asymptomatic, while Class IV is life-threatening and requires immediate intervention. A vast array of laboratory tests supports the evaluation of hemorrhagic patients. Complete Blood Count (CBC) is one of the most frequently used tools, helping identify anemia through hemoglobin levels. The so-called basic metabolic panel typically includes sodium, potassium, bicarbonate, blood urea nitrogen (BUN) and creatinine, and provides useful insights into metabolic function and electrolyte imbalance, which can be altered in patients with significant blood loss. Coagulation tests such as APTT, PT and fibrinogen reflect clotting ability, crucial in trauma cases or in patients on anticoagulants, in whom measuring the plasma level of anticoagulants (especially direct oral anticoagulants) may be warranted. ROTEM, thrombelastography and thrombin generation assays offer valuable insights into the real-time functionality of coagulation system during hemorrhages. Specifically, ROTEM and thrombelastography enable rapid, point-of-care assessment to guide targeted transfusions, while thrombin generation assays help evaluating global hemostatic capacity in complex or unclear bleeding disorders. Serum lactate levels may be used to assess tissue perfusion and metabolic stress, as elevated blood lactate predicts poor prognosis. In cases where initial tests indicate abnormalities, further specific tests may be warranted (e.g., C-reactive protein and D-dimer). Lastly, the interpretation of test results must be done cautiously and in the clinical context. Although certain findings, like low hemoglobin, indicate ongoing hemorrhage, normal values may not exclude serious internal bleeding, especially in early or compensated phases. This diagnostic uncertainty highlights the importance of always integrating laboratory test results with clinical evaluations, imaging and patient history. Additionally, some laboratory results may be misleading or unnecessary in certain scenarios, prompting concern over excessive testing that prolongs stays in the emergency room without improving care.

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Strategic Selection of Point-of-Care Testing (POCT) Devices: A Multidimensional Approach to Decentralized Diagnostics in Complex Clinical Settings

Erica Rampoldi

The appropriate selection of Point-of-Care Testing (POCT) devices is a strategic and multidimensional process that must consider clinical, organizational, economic, and regulatory aspects. At the center of this process is the assessment of clinical need, which remains the most important criterion. Selecting the right POCT device involves identifying which tests are required—such as glucose, blood gas analysis, bilirubin, or C-reactive protein—and clearly understanding the context in which the device will be used, including emergency departments, intensive care units, outpatient clinics, home care, or non-clinical outreach settings. Additionally, the type of operator—whether healthcare professionals, nurses, or trained non-medical staff—must be considered to ensure proper implementation and use.

A challenging example for clinical laboratories is the use of capillary blood, which presents specific issues that can affect its reliability, especially in laboratory settings, due to several factors:

Capillary blood can be less reliable than venous blood for certain tests due to:

- **Clotting tendency:** Capillary samples clot quickly if not collected and mixed properly with anticoagulants.
- **High viscosity:** The small volume and higher concentration of cellular components can affect analyte measurements.
- **Inconsistent mixing:** It is harder to ensure homogeneous distribution of cells and plasma, which can lead to variability in results.
- **Contamination risk:** Squeezing the puncture site can dilute the sample with tissue fluid, skewing results.

However, capillary blood is widely used and accepted in many contexts—especially in neonatology and point-of-care testing—when proper technique and equipment are applied.

For example, in NICUs, POCT enables rapid diagnostic results, which is critical for managing time-sensitive conditions in neonates. Various bilirubin measurement devices are available, each differing in method, gestational age suitability, invasiveness, response time, accuracy, data management, maintenance needs, certifications, and cost. While all non-invasive transcutaneous devices are limited to use in infants of ≥ 35 weeks' gestation, only one supports measurements in those < 35 weeks. Some devices stand out for their quick response time, low maintenance, and moderate cost, making them ideal for neonatal follow-up and outpatient settings. In contrast, the device that uses a minimally invasive capillary method—though costlier per test—offers very high serum correlation and is better suited for early diagnosis and hospital confirmation.

Furthermore, POCT is especially valuable in crisis areas—such as war zones and low-income countries—where access to centralized laboratories is limited. It enables rapid, on-site diagnosis and monitoring with minimal infrastructure, helping to deliver timely care and improve patient outcomes in resource-constrained settings.

New Standard Operating Procedures of the SIBIOC Drug-Toxicology Working Group on toxicological investigations in cases of violence”

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Victims of drug-facilitated violence (DFV), including sexual assault and other coercive acts, require precise and reliable toxicological investigations to ensure both clinical care and forensic validity. Despite increasing reports of drug-facilitated crimes (DFCs), standard procedures for the detection of substances involved remain inconsistent across Italian regions. In

response, the Drug-Toxicology Study Group (GS Farmaco-Tossicologia) of the Italian Society of Clinical Biochemistry (SIBIOC), in collaboration with the Istituto Superiore di Sanità, developed a set of Standard Operating Procedures (SOPs) for the detection of psychoactive substances in biological matrices. These protocols aim to support healthcare and forensic personnel in emergency departments and reference laboratories when managing suspected DFV cases.

The procedures emphasize early and standardized collection of biological specimens—blood, urine, and hair—ensuring the chain of custody and medico-legal validity from the point of patient admission through to analytical testing. Biological sampling should ideally occur within 48 hours post-incident and before any pharmacological intervention. For delayed reporting, hair analysis offers retrospective detection, including through micro-segmental analysis, which enables daily resolution of substance exposure and detection of low-dose administrations.

All analyses must follow validated procedures based on chromatographic techniques coupled with mass spectrometry (GC-MS, LC-MS/MS, or HRMS), in accordance with ISO 17025 and international regulatory standards. The use of internal standards and external quality assurance programs further guarantees analytical reliability. The document also addresses logistical aspects of sample transport and storage, recommending freezing for biological fluids and ambient conditions for keratin matrices. Interpretation of toxicological findings must consider pharmacokinetics, matrix-specific detection windows, and contextual clinical information. Special attention is given to distinguishing endogenous from exogenous analytes, particularly in the case of gamma-hydroxybutyrate (GHB). By designating regional reference laboratories and harmonizing toxicological approaches, this protocol enhances the capacity to generate reproducible and legally robust toxicological evidence, ultimately supporting both judicial outcomes and the protection of victims' rights.

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New psychoactive substances and gender-based violence

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Chemical submission (CS) refers to the involuntary administration of psychoactive substances intended to impair a victim's resistance or memory of events representing a form of violence, increasingly associated with crimes such as sexual assault, robbery, and other opportunistic offenses. In recent years, it has gained global attention due to a rise in reported cases and its notable impact on public health and safety. Despite the growing media attention, CS remains widely unrecognized and underreported, posing significant challenges for prevention, detection, and forensic investigation. Alcohol often contributes to drug-facilitated sexual assaults and is frequently used with other substances to amplify effects. Commonly found substances in these cases include benzodiazepines, gamma-hydroxybutyrate (GHB), ketamine, and various Z-drugs. These compounds are usually easily accessible, effective in small doses, and have no detectable taste or color, making oral administration—especially through beverages—the preferred method. After ingestion, they may cause effects such as sedation, disinhibition, and confusion. These effects both facilitate committing an assault and make diagnosis and investigation more difficult. These compounds exert a rapid effect on the central nervous system, resulting in impairments in

motor skills, memory, and decision-making abilities. Victims often struggle to clearly remember the event, making medical and legal responses more difficult. Recent trends show a rise in the misuse of prescription and over-the-counter drugs, such as antihistamines, sedatives, and antipsychotics. This, along with new psychoactive substances (NPS) like synthetic cathinones (e.g. 4-MEC, MDPV, 3-MMC), complicates the issue. These “designer drugs” mimic illegal substances while avoiding regulation, making detection and control harder. Unlike traditional date rape drugs, some NPS do not cause complete memory loss, leaving victims dazed but still conscious. This condition can be intentionally exploited by perpetrators. Cathinones in combination with sedatives such as **doxylamine** and alcohol have been identified in DFSA cases, increasing the level of unpredictability and risks of these mixtures. Other substances identified in such contexts include **phosphodiesterase inhibitors**, **zopiclone**, **flunitrazepam**, **2CB**, **mephedrone**, **PMA**, and **PMMA**. These agents are known for their psychoactive or amnesic effects and are often classified as “**date rape**” drugs. Their presence in forensic analyses underscores the urgent need for enhanced toxicological screening and tailored prevention strategies. In conclusion, CS presents a growing and complex challenge at the intersection of law, medicine, and public health. The wide range of substances involved, their accessibility, and the difficulty in detection highlight the importance of multidisciplinary efforts, improved screening tools, and increased public awareness to prevent and prosecute these crimes more effectively.

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PHYSICAL AND PSYCHOLOGICAL EFFECTS OF GENDER-BASED VIOLENCE FOLLOWING DRUG USE: WHAT COULD THE EPIGENETIC PROFILE TELL US?

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Gender-based violence (GBV) and substance abuse are deeply interconnected public health issues with significant and enduring physical and psychological consequences. Survivors of GBV, particularly women, are at increased risk of using psychoactive substances as a coping mechanism, which can, in turn, intensify trauma-related symptoms and hinder recovery.

The role of memory in resilience following GBV is complex and multifaceted. Whether recalling or repressing traumatic experiences fosters resilience depends on several factors, including an individual's psychological coping style, availability of social support, and the timing and nature of the trauma. When survivors could remember and process their experiences in a safe and supportive context, such as therapy, they are more likely to integrate the trauma into their life narrative, potentially fostering post-traumatic growth and psychological resilience. Conversely, persistent suppression or dissociation of traumatic memories can impede emotional processing, increasing the risk of chronic post-traumatic stress disorder (PTSD), somatic symptoms, and substance dependence. Research has shown that adults with a history of childhood sexual abuse, especially those with incomplete or repressed memories, often exhibit elevated levels of anxiety and dissociative symptoms later in life [1].

Recent advances in epigenetics have opened new pathways for understanding the biological mechanisms underlying these long-term effects. Epigenetic modifications, such as DNA methylation and histone acetylation, can be influenced by both trauma and substance use, leading to altered gene expression associated with stress regulation, neuroplasticity, and immune function. These molecular changes may contribute to enduring mental health conditions such as PTSD, depression,

anxiety, and functional somatic syndromes, even years after the original trauma. For example, differential methylation of genes involved in the stress response and neural adaptation, including *NR3C1* and *BDNF*, has been observed in women exposed to intimate partner and sexual violence, suggesting a molecular signature of GBV's long-term psychological impact [2].

Furthermore, epigenetic research indicates that trauma memory, whether retained or suppressed, may be linked to structural and functional changes in key brain regions such as the hippocampus and amygdala, further influencing an individual's vulnerability or resilience to psychological distress. This emerging field highlights the potential of epigenetic profiling as a tool for identifying individuals at higher risk, tailoring therapeutic interventions, and evaluating treatment outcomes. By integrating biological, psychological, and social frameworks, this approach offers a more comprehensive understanding of the interplay between GBV, substance abuse, and trauma recovery, paving the way for innovative prevention and personalized healing strategies.

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The role of the laboratory in the control of the Total Testing Process

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The management of hemorrhagic emergencies in hospital settings requires a prompt, multidisciplinary approach based on objective evidence. In this context, thromboelastography (TEG) represents a fundamental diagnostic tool for the dynamic assessment of coagulation, allowing for rapid clinical stratification and targeted guidance for appropriate therapy. However, the growing use of these devices in decentralized locations - such as operating rooms, intensive care units, and emergency departments - poses new challenges in ensuring quality, appropriateness, and the integration of test results into the clinical decision-making process.

Although the laboratory is not always directly involved in the technical execution of these decentralized tests, it retains a strategic and indispensable role in the entire process governance. This role extends across multiple dimensions: from providing support in assessing the appropriateness of test use and its integration into clinical diagnostic pathways, to method validation and contribution to the training of clinical personnel, and up to the oversight of internal quality control and the management of external quality assessment (EQA) programs. The current regulatory framework, including Regulation (EU) 2017/746 (IVDR) and UNI EN ISO 15189:2024, reinforces the principle of shared responsibility in the management of point-of-care testing (POCT), emphasizing the need for formalized and shared procedures between the laboratory and clinical departments.

In this context, POCT governance must be structured within an organizational model that ensures compliance with regulatory requirements and patient safety. It is essential to define clear responsibilities, establish an authorization system for operators, ensure periodic and traceable training, implement maintenance and verification plans for equipment, and integrate results into laboratory information systems (LIS). The laboratory must also ensure ongoing monitoring of analytical performance through specific quality indicators and actively participate in defining the clinical usage criteria for the test.

Furthermore, the implementation of shared protocols, result traceability, periodic performance verification, and the creation of interdisciplinary discussion forums are key elements in ensuring the appropriate use of TEG results and reducing the risk of misinterpretation, which could lead to inappropriate therapeutic decisions.

In this framework, Laboratory Medicine plays a strategic role in the integrated management of hemorrhagic emergencies. Its active participation in multidisciplinary teams is essential to promote a culture focused on quality throughout the diagnostic process and to establish a reliable and sustainable governance system for decentralized devices.

Diagnosis of red cell disorders

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Congenital hemolytic anemias (CHAs) comprise a group of very heterogeneous and rare disorders caused by alterations in structure, transport functions, metabolism, or defective production of red blood cells (RBCs) (Bianchi & Mohandas 2025). Since the pathophysiology of some rare forms is poorly understood, these disorders represent a group of diseases that still lack easy-to-apply tools for diagnosis, clinical management, and patient stratification.

The laboratory diagnostic pathway of congenital hemolytic anemias was historically based on sequential steps using a panel of functional analyses that investigate the RBC membrane and metabolism. The first step relies on hematological tests (complete blood count, red cell indices, hemolysis markers), peripheral blood smear examination, osmotic fragility tests and eosin-5-maleimide (EMA) binding test. The second includes biochemical tests such as quantitative assay of RBC enzymes activity, analysis of RBC membrane proteins, and specialized investigations requiring instruments available only in reference Centers, as ektacytometry (King *et al.*, 2015). The molecular characterization of the affected genes was usually, up to some years ago, the last step allowing the definitive confirmation of the diagnosis. Despite this, even after extensive and complete investigation, the differential diagnosis of these disorders may be difficult, and some patients remain undiagnosed with a consequent negative impact on clinical follow up, risk of inappropriate therapeutic decisions and lack of access to new specific treatments.

The advent and recent progresses on next generation sequencing (NGS) technologies has radically changed the diagnostic approach to CHAs, often placing the genetic analysis as a first line screening tool; different NGS strategies have been developed in the last years including targeted NGS panels and clinical/whole exome sequencing (WES), with a progressive reduction of costs that allowed their routinely use (Roy *et al.*, 2022). Targeted-NGS panels have been developed and applied by several groups. Custom panels include different numbers of genes and have been reported to have a wide range of diagnostic efficacy (38-90%) depending on the number of genes included and on the characteristics of the patients studied. Variants of uncertain clinical significance (VUSs) represent one of the main causes of inconclusive diagnoses. When identified in genes associated with the suspected phenotype, these variants cannot be classified as causative without supporting functional and/or familial studies to confirm their pathogenicity. For this reason, it is recommended that such analyses be performed in Reference Centres where functional tests for the diagnosis of congenital haemolytic anaemias (CHAs) are also available.

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Everything you always wanted to know about writing a paper but were afraid to ask

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Although writing a scientific article is a primary aspiration for many scientists and researchers, it remains a complex task, needing attention to several critical elements for maximizing the likelihood of success, i.e., the chance of acceptance in peer-reviewed journals. A well-drafted manuscript starts with meticulous and reliable data analysis. Employing appropriate statistical methodologies is essential not only for ensuring scientific validity, but also for highlighting findings that are both relevant and innovative. Visual components, such as tables and figures, are welcome but should be clear and self-explanatory to facilitate comprehension. The structure of a scientific manuscript should follow a logical and coherent progression. It is usually advantageous to begin with the results section, as this helps to clarify the main findings and guide the development of the remaining sections. The methods section, though frequently underestimated, must include a detailed

account of study design, participant characteristics, experimental procedures, statistical approaches and ethical approval. This transparency is essential to allow replication and to validate the robustness of the research. The introduction should be concise and focused, providing only the necessary context to frame the research question; excessive reviews of prior literature or redundant background information may create the impression that the problem has already been resolved. Instead, the introduction should highlight existing gaps in knowledge or areas of controversy to justify the need for the study. The discussion is the most critical section of the manuscript, where interpretation of findings should take precedence. Authors must relate their results to current evidence, offer plausible biological or clinical interpretations, and articulate conclusions with caution, especially when data are preliminary or not conclusive enough. While acknowledging study limitations is important, overemphasizing them prematurely may bias reviewers and readers. Titles and abstracts, although typically written last, are crucial for capturing the interest of editors, reviewers and potential readers. The title should be concise but informative, reflecting the key study outcomes. The abstract should focus on main results and conclusions, limiting background content to the essential. Strict adherence to the target journal's formatting and stylistic guidelines is essential. Authorship must be determined ethically, in accordance with the International Committee of Medical Journal Editors (ICMJE) criteria. The use of artificial intelligence tools in manuscript preparation should be transparent, with contributions clearly disclosed as part of the ethical publishing process. Finally, the selection of an appropriate journal is a strategic decision. Authors should consider the journal's aims, readership, impact factor and editorial policies.

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Laboratory Diagnosis of Disseminated Intravascular Coagulation (DIC)

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The laboratory diagnosis of Disseminated Intravascular Coagulation (DIC) relies on a combination of clinical symptoms, identification of the underlying disease, and specific laboratory tests that reflect widespread activation of coagulation and fibrinolysis. The clinical features primarily depend on the underlying cause of DIC. A combination of several laboratory parameters is analyzed as part of a diagnostic algorithm, as no single test result alone can definitively confirm or exclude the diagnosis. These parameters include global tests of hemostasis such as **prothrombin time (PT)** and **activated partial thromboplastin time (aPTT)**, which initially indicate coagulation activation and, later in the process, consumption of coagulation factors. Other essential parameters are **platelet count**, **fibrinogen level**, and **markers of fibrin degradation** (such as **D-dimer** or **soluble fibrin monomer**), which reflect activation of both coagulation and fibrinolysis. A normal result for these markers can help rule out DIC. None of these markers are considered in isolation; instead, a combination of results over time is particularly helpful in determining the presence and progression of DIC. **Decreased levels of antithrombin and protein C** are frequently observed in patients with DIC, although their measurement is not included in standard diagnostic algorithms. New tests are being investigated for their potential utility in DIC, and additional assays may be useful depending on the suspected cause and their local availability. For example, **Thrombin Generation Test** parameters, such as **lag time** and **peak thrombin**, have been identified as predictors of mortality in DIC. Finally, it is important to note that specific laboratory profiles may be more indicative of certain pathological mechanisms. For instance, **hyperfibrinolysis** is typically characterized by **very low fibrinogen levels** combined with **very high concentrations of fibrin degradation products (FDPs)**.

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Diagnosis of red cell disorders

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The laboratory diagnostic pathway of congenital hemolytic anemias was historically based on sequential steps using a panel of functional analyses that investigate the RBC membrane and metabolism. The first step relies on hematological tests (complete blood count, red cell indices, hemolysis markers), peripheral blood smear examination, osmotic fragility tests and eosin-5-maleimide (EMA) binding test. The second includes biochemical tests such as quantitative assay of RBC enzymes activity, analysis of RBC membrane proteins, and specialized investigations requiring instruments available only in reference Centers, as ektacytometry (King *et al*, 2015). The molecular characterization of the affected genes was usually, up to some years ago, the last step allowing the definitive confirmation of the diagnosis. Despite this, even after extensive and complete investigation, the differential diagnosis of these disorders may be difficult, and some patients remain undiagnosed with a consequent negative impact on clinical follow up, risk of inappropriate therapeutic decisions and lack of access to new specific treatments.

The advent and recent progresses on next generation sequencing (NGS) technologies has radically changed the diagnostic approach to CHAs, often placing the genetic analysis as a first line screening tool; different NGS strategies have been developed in the last years including targeted NGS panels and clinical/whole exome sequencing (WES), with a progressive reduction of costs that allowed their routinely use (Roy *et al*, 2022). Targeted-NGS panels have been developed and applied by several groups. Custom panels include different numbers of genes and have been reported to have a wide range of diagnostic efficacy (38-90%) depending on the number of genes included and on the characteristics of the patients studied. Variants of uncertain clinical significance (VUSs) represent one of the main causes of inconclusive diagnoses. When identified in genes associated with the suspected phenotype, these variants cannot be classified as causative without supporting functional and/or familial studies to confirm their pathogenicity. For this reason, it is recommended that such analyses be performed in Reference Centres where functional tests for the diagnosis of congenital haemolytic anaemias (CHAs) are also available.

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The Laboratory in the Diagnosis of Prediabetes

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Prediabetes is a metabolic condition characterized by blood glucose levels that are elevated above normal but do not meet the criteria for diabetes (1). It is a critical warning stage in the progression toward type 2 diabetes and is associated with increased cardiovascular risk and early microvascular complications (2). Identifying individuals with prediabetes allows for

the implementation of targeted lifestyle and therapeutic interventions that can delay or prevent the onset of diabetes and its complications.

The laboratory is central to the identification and monitoring of prediabetes. Three key tests are used in clinical practice: fasting plasma glucose (FPG), the 2-hour plasma glucose (2h-PG) following a 75g oral glucose tolerance test (OGTT), and glycated hemoglobin (HbA1c). Prediabetes is defined according to the American Diabetes Association (ADA) guidelines by one or more of the following results: FPG between 100–125 mg/dL (5.6–6.9 mmol/L), 2h-PG between 140–199 mg/dL (7.8–11.0 mmol/L), or HbA1c between 5.7% and 6.4% (39–46 mmol/mol) (3). World Health Organization (WHO) defines impaired fasting glucose (IFG) at higher glucose concentrations (110–125 mg/dL, 6.1–6.9 mmol/L) (1). FPG is preferred over the OGTT due to its ease of execution, lower cost, and greater patient acceptability. Every marker captures different aspects of glucose metabolism and may identify overlapping but non-identical populations.

The clinical value of diagnosing prediabetes lies not only in its predictive power for type 2 diabetes but also in its association with other conditions such as metabolic syndrome, non-alcoholic fatty liver disease, and increased cardiovascular morbidity. Individuals with prediabetes are often asymptomatic, making laboratory testing the only reliable method of detection.

Accurate measurement requires strict adherence to preanalytical and analytical protocols. For glucose measurements, venous plasma is preferred over whole blood or capillary samples due to better standardization. In-vitro glucose concentrations decrease by 5–7% per hour due to glycolysis so is mandatory to use a rapidly glycolytic inhibitor such as granulated citrate buffer containing tube or to centrifuge immediately tubes after sample collection (3). HbA1c has lower pre-analytical variability compared to FPG, but any condition that reduces RBC survival or decrease RBC age falsely lowers HbA1c test results. Furthermore several haemoglobin variants can interfere with some assay methods.

Laboratory identification of prediabetes enables timely patient education, structured lifestyle modification programs, and consideration of pharmacological strategies in selected high-risk cases. These approaches have been shown to reduce progression to type 2 diabetes by up to 58%.

In summary, prediabetes is a modifiable condition whose detection hinges on robust and standardized laboratory testing. The role of the clinical laboratory in recognizing and monitoring prediabetes through validated glycemic markers is an essential step in combating the global diabetes epidemic and reducing its clinical and economic burden.

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Intelligenza Artificiale e Medicina di Laboratorio: come sta cambiando il nostro modo di lavorare?

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Artificial intelligence (AI) is often described as a disruptive force in laboratory medicine, yet its actual impact on routine clinical workflows remains limited. Despite the growing attention in scientific sessions and literature, the daily operations in most clinical laboratories still rely on traditional forms of automation—rule-based validation, LIS-driven processes, and sample tracking systems—that, although efficient, do not constitute AI in its proper sense. Advanced methods such as deep learning, natural language processing, or predictive clinical modeling are rarely embedded in routine diagnostics. This disconnect between narrative and reality is driven by fragmented and poorly integrated data infrastructures, limited digital competencies, organizational silos, and the lack of clear regulatory frameworks. However, outside the boundaries of direct clinical application, AI has already become a transformative tool in the broader ecosystem of laboratory medicine. In research and development, AI supports data curation, statistical analysis and data visualization at unprecedented speed and

scale. In academic writing and scientific communication, it assists non-native English speakers in producing fluent, high-quality texts. As an educational resource, AI enables accelerated learning, and continuous knowledge updating for laboratory professionals. These domains demonstrate that AI is not merely a future promise but an active and present enabler of productivity, precision, and accessibility. The challenge, therefore, is to bridge the gap between this reality and the clinical setting, shifting from passive expectations to active integration. AI will not autonomously reshape laboratory medicine: it is up to us to redesign our practices, infrastructures, and roles to unlock its potential.

Modernizing the clinical laboratory: challenges and opportunities in procurement processes and acceptance testing within public healthcare institutions

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The centrality of the patient in laboratory medicine is reflected in the laboratory's ability to provide useful diagnostic information for more effective clinical decision-making, reducing time and unnecessary waste. Laboratory efficiency should be sought in the ability to ensure measurable clinical outcomes, using tools that guarantee sustainability, compliance with the ethics of clinical-diagnostic processes, and patient empowerment. From this premise, it's evident that procurement specifications for reagents and healthcare technologies in laboratory medicine should be structured as contractual models linked to clinical value, which is the ultimate purpose of the procurement. The objectives of such procurements should result from needs assessments carried out by multidisciplinary teams to defining requirements and quality indicators. The main indicators that should be requested include: verification of analytical performance characteristics, time to diagnosis, diagnostic error rates, environmental sustainability rates, and stakeholder satisfaction. These key performance indicators (KPIs), when integrated into the tender specifications, become tools for periodic assessment of the clinical and strategic validity of the supply. The implementation of clinically value-oriented procurement procedures in the public sector faces various regulatory, technical, and organizational limitations. The first obstacle is represented by the principles of the Public Procurement Code and by EU provisions regarding transparency and equal treatment of economic operators. These principles require to define award criteria which must always be objective, measurable, and non-discriminatory. A significant challenge lies in the difficulty of translating the concept of "clinical value" into technical criteria and scoring systems that are clearly measurable and legally defensible. An additional procedural constraint is the obligation to ensure equal treatment among economic operators. Including the largest possible number of suppliers in the evaluation process could lower the predefined quality standards. From a managerial perspective, evaluating KPIs requires public healthcare organizations to develop internal competencies — administrative, technical, and clinical — to monitor results and to draft potential disputes or apply contractual penalties. Not all healthcare facilities currently have the resources or the necessary expertise to conduct technical-clinical audits or to properly interpret the data provided by diagnostic systems. In many cases, healthcare information systems are still not sufficiently integrated to allow timely and automatic measurement of the clinical or economic indicators required to assess the actual impact of diagnostics on care pathways. While representing a necessary and strategic evolution that must be pursued, the adoption of Value-Based Procurement in diagnostics within public healthcare organizations remains a challenge requiring careful legal, technical, and organizational planning, significant investment in internal competencies and advanced information systems, to ensure the full success of value-oriented procurement processes.

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Pathogenesis of Disseminated Intravascular Coagulopathy (DIC)

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Disseminated intravascular coagulation (DIC) is a potentially life-threatening syndrome characterized by uncontrolled activation of the coagulation system. This syndrome is associated with a high risk of macrovascular and microvascular thrombosis and progressive consumptive coagulopathy, which leads to an increased risk of bleeding. Various pathological conditions can trigger DIC (primarily sepsis, cancer, trauma, and gynecological conditions). Disseminated intravascular coagulation (DIC) was defined by the ISTH in 2001 as “an acquired syndrome characterized by intravascular activation of the coagulation system with loss of localization resulting from various causes. It can initiate and cause damage to the microvasculature, which, if sufficiently severe, can lead to organ dysfunction.” The syndrome is characterized by the simultaneous presence of two key enzymes of the hemostatic system: thrombin, which causes microvascular thrombosis associated with organ dysfunction (MODS), and plasmin, which induces the consumption of coagulation factors and platelets, thus contributing to hemorrhagic consumption coagulopathy. Indeed, since the 1990s, studies have highlighted the significant role of cytokines in the pathogenesis of DIC, leading to a new paradigm of reciprocal interaction between coagulation and inflammation, followed by the creation of new cytokine-based pathogenic pathways in DIC. Even more recently, in the 2000s, the significant role of neutrophil extracellular traps (NETs) and histones (derived from the nuclear content of damaged cells) has been demonstrated, influencing the pathogenesis of DIC through immunothrombosis, with dysregulated immunothrombosis promoting pathological thrombosis in DIC. Histones and cell-free DNA, which comprise NET components, are further implicated in the pathogenesis of MODS in DIC. In addition to NET formation (NETosis), necrosis and regulated cell death, such as pyroptosis, have been identified as the main sources of tissue factors that are important initiators of DIC. Coagulation, the kallikrein-kinin system (KKS), and complement pathways interact with each other and play a critical role in the pathogenesis of DIC. Inflammation and coagulation in innate immunity are tightly coupled to maintain homeostasis against insults by confining and repairing tissue injury. Dysregulation of these systems leads to DIC associated with bleeding and MODS, which may allow for a more updated definition of DIC as “dysregulated immune coagulation.”

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Governance tools in the professional renewal process supporting Biomedical Laboratory Scientists.

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The ultimate goal of value-based laboratory medicine is to maximize the clinical effectiveness of laboratory testing in improving patient outcomes, while optimizing resource utilization and minimizing unnecessary costs (1). Laboratory testing plays a pivotal role in clinical decision-making, including diagnosis, therapeutic selection, and treatment monitoring. In recent years, the demand for laboratory services has increased significantly, accompanied by expectations for improved service accessibility and reduced turnaround times. These demands are compounded by growing economic pressures related to cost containment, workforce shortages, and the continuous evolution of professional competencies driven by technological advancements.

The role and competencies of Biomedical Laboratory Scientists have evolved substantially over time. Although initially defined by the Italian Ministerial Decree 745/94, the professional profile has progressively adapted in response to both legislative changes regulating professional practice and the ongoing development of educational and training programs (2).

Effective human resource management is essential not only to ensure the quality of healthcare services but also to safeguard financial sustainability, as personnel costs represent a major component of healthcare expenditure.

A core responsibility of middle management is the coordination and administration of operational processes and associated personnel, utilizing standardized methodologies capable of accurately estimating full-time equivalents (FTEs). Tools such as Activity-Based Management (ABM) facilitate the generation of objective and analytically robust data, derived from precise quantitative measurements, including productivity metrics and task execution times. (3).

At the same time, middle managers must recognize the fundamental importance of the human factor, positioning themselves as leaders and facilitators capable of enhancing each team member's expertise and individual strengths. Coordinating healthcare professionals in the current environment requires a complex blend of interpersonal skills, leadership qualities, and coaching abilities, which are essential for supporting an increasingly autonomous and highly skilled workforce (4).

In this context, it is imperative that middle managers and laboratory medicine professionals integrate their technical competencies ("hard skills") with transversal competencies, also referred to as "soft skills", which include personal, interpersonal, and communication abilities and have become essential for effectively managing renewal processes in support of the professional development of Biomedical Laboratory Scientists.

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