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EDUW 2 – SYSMEX – Monday 12 June, 14.30-15.30

DETECTION OF CELL FUNCTIONALITY STATUS TO SUPPORT DIFFERENTIATION BETWEEN REACTIVE AND MALIGNANT LYMPHOCYTOSIS

J. Linssen [1]
[1]*Sysmex Europe, Germany*

Blood cell counts and cell differentiation based on morphology are valuable diagnostic tools. However, when it comes to pathological samples, determining cell functionality provides better information on the patient‘s status. Usually this involves special testing, which tends to be costly and time-consuming so information on cell functionality from routine blood testing could provide the needed information faster and more efficiently. By combining two fluorescence flow cytometric methods, the Sysmex XN-Series haematology analysers permit to differentiate cells based on their functionality, particularly in cases when it is hard to decide from a morphological perspective. The analysers' reagents interact with lipid components within cell membranes that play important roles in protein trafficking and cellular signaling. For example, elevated levels of lipid rafts in the cell membrane have been reported in metabolically active cells (e.g. malignant and reactive cells) compared to resting cells and immature cells. This allows to differentiate the maturity and activation state of cells, or to confirm the presence of a malignant condition. The two-step method classifies samples into one of three clearly defined groups: reactive, malignant and negative. A performance evaluation will be presented for the differentiation between reactive and malignant lymphocytosis.

EDUW 2 – SYSMEX – Monday 12 June, 14.30-15.30

THE EXTENDED INFLAMMATION PARAMETERS ALLOW THE CHARACTERISATION OF THE IMMUNE RESPONSE IN CHILDREN WITH BACTERIAL AND VIRAL INFECTIONS

M. Eveillard [1]
[1]*University of Nantes, France*

When a child is suspected of having an infection, rapid differentiation between various possible pathogenic causes is important. New haematological inflammation parameters, which are readily available from a routine blood laboratory test together with the complete blood count, provide early information about the inflammatory response of patients' immune system. Blood samples used for this study were collected from children between 1 month and 5 years old that were admitted to the emergency unit with fever. Samples were examined for C-reactive protein and procalcitonin, and with an XN-Series analyser with the Extended Inflammation Parameters. Novel neutrophil and red blood cell parameters were able to distinguish between children with infections and the reference group, while novel lymphocyte parameters allowed the differentiation between bacterial and viral infections in all children with fever. Thus, the complete blood count, which is the most-commonly performed laboratory test, can be extended to provide additional information, confirm the presence of infection in febrile children, and distinguish between bacterial and viral infections.

EDUW 3 – BIO-RAD – Monday 12 June, 15.45-16.45

APPLICATIONS OF DROPLET DIGITAL PCR SOLUTIONS IN THE CLINICAL LAB

S. Tzonev [1]
[1]*Digital Biology Center, Bio-Rad Laboratories*

Droplet Digital PCR (ddPCR) technology was first commercialized in 2011 and has gained rapid and wide adoption in research, translational and, increasingly, routine clinical settings. The digital nature of the technology implies substantial improvement in precision, accuracy, reproducibility, sensitivity and specificity versus traditional approaches.
This presentation will illustrate uses of ddPCR solutions in hematology and oncology, including liquid biopsy and monitoring of residual disease. Examples will discuss workflow, performance characteristics and comparison with other approaches. When precise and sensitive detection and quantification of specific, actionable genomic targets, DNA or RNA, is required, ddPCR offers the most advanced and economic solutions.

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EDUW 4 – WERFEN – Monday 12 June, 17.00-18.00

GLYCATED ALBUMIN: FROM LABORATORY MEDICINE TO CLINICAL PRACTICE

E. Dozio [1], E. Kilpatrick [2]
[1]*Department of Biomedical Sciences for Health, University of Milano, Milano, Italy*
[2]*Department of Pathology, Sidra Medical and Research Center - Doha, Qatar*

Diabetes mellitus (DM) is nowadays considered one of the top world issues affecting more than 385 million of people probably doubling in the next 20 years. About 9% of the total health expenditure of the European Countries is spent for DM management. Prevention and risk evaluation is still considered the best option for avoiding diabetes critical scenario.
Diabetes diagnosis and follow up are current challenges both for clinicians and laboratory doctors in addition to those for diabetic patients. Fasting Plasma Glucose (FPG) and HbA_{1c} evaluation are often used to monitor the glycemic control of diabetic patients, together with post-prandial glycemia and glycemic variability. Glycated Albumin (GA) is a short to intermediate term test useful to assess the glycemic control since it reflects glycemic status over the last 3 weeks. GA, being not affected by RBC life-span, may represent a real benefit for clinicians and patients.
Aim of this workshop is to review the potential of this new test, to highlight the clinical usefulness and the pathogenic role of GA. Literature review will show data and experiences collected in countries that already adopted GA, as well as results obtained in a recent multicenter evaluation. The contribution of qualified experts in the field will certainly stimulate the discussion between all the stakeholders (clinicians, laboratorians, patients, public health organizations and more).

EDUW 5 – ROCHE DIAGNOSTICS – Monday 12 June - 14.30/15.30

DIGITAL HEALTHCARE INNOVATION, SCIENTIFIC UPDATE ON CLINICAL DECISION SUPPORT

T. Jaeger [1]
[1]*Roche Diagnostics*

We are experiencing a period of remarkable progress in science and medicine. Keeping up with this progress is a challenge for researchers, physicians and patients alike. It is becoming increasingly difficult to navigate the wealth of healthcare information, identify relevant data and draw meaningful conclusions. The answer and our future is Digital Diagnostics.
These changes represent a great opportunity for laboratories. Building on an expertise in the diagnostic science and technology and leveraging an understanding of medicine, the clinical laboratory's value to the healthcare system and role in patient care can be elevated by embracing the opportunity associated with the digitization of healthcare information.
This workshop will describe the trends and advances in the digitization of healthcare information, advanced analytics and machine learning technologies that will lead to valuable decision support applications that can improve the quality, efficiency and cost of healthcare. The speakers will discuss how labs will be impacted by these trends and provide examples of digital diagnostic applications that are already being utilized or explored today.

EDUW 5 – ROCHE DIAGNOSTICS – Monday 12 June, 14.30-15.30

DIGITIZED PATHOLOGY WORKFLOW AND TUMOR BOARD INTEGRATION. UTILIZING ALGORITHMS AS PART OF ROUTINE DIAGNOSTICS

P. Van Diest [1]
[1]*University Hospital of Utrecht*

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EDUW 6 – ABBOTT – Monday 12 June, 15.45-16.45

THE VALUE OF ACTIVE B12

D.J. Harrington [1]
[1]*Guy's and St. Thomas' (Viapath)*

Vitamin B_{12} (B_{12}) deficiency is common. Risk factors include restricted dietary intake of animal products, impaired gastric absorption, loss or inactivity of intrinsic factor (Addisonian pernicious anaemia), pancreatic insufficiency, impaired intestinal absorption (e.g. ileal resection in Crohn disease), multiple congenital factors and acquired drug effects. The prompt detection and correction of B_{12}-deficient states prevents megaloblastic anaemia and potentially irreversible neuropathy and neuro-psychiatric changes.
B_{12} status is typically assessed by measuring the total abundance of B_{12} in serum. However this test has low sensitivity and when used in isolation up to 45% of deficient patients may be overlooked. Moreover, the National Health Service Atlas of Variation in Diagnostic Services (Nov 2013) shows that the number of serum B_{12} tests ordered is five times greater in some parts of England compared with others. This degree of variation appears to be greater than can be explained in the prevalence of B_{12} deficiency and in part may relate to local protocols e.g. some may stipulate that B_{12} status is only to be evaluated when haematological indices indicate megaloblastic change. Crucially, ~20% of B_{12}-deficient patients show no discernable haematological diathesis. Existing strategies may delay the diagnosis of B_{12} deficiency. In a recent survey of 889 members of the Pernicious Anaemia Society, 304 individuals experienced symptoms of the disorder for up to a year before a diagnosis; 193 for two years; 173 for five years; and 40 patients for ten years or more. Serum B_{12} assays measure the sum of haptocorrin- and transcobalamin-bound (known as holotranscobalamin) B_{12} yet it is only holotranscobalamin that is taken up by cells to meet metabolic demand (Active B12). Receiver operator characteristic curves show Active B12 measurement to be a moderately more reliable marker of B_{12} status than serum B_{12}. Diagnostic utility is enhanced further when Active B12 is used in combination with a laboratory B_{12} status marker such as methylmalonic acid or total homocysteine that reflect the cellular utilisation of adenosylcobalamin and methylcobalamin respectively. Sequential assay selection algorithms or the combination of multiple markers into a single diagnostic indicator are both approaches that can be used to mitigate inherent limitations of each marker when used independently.

EDUW 6 – ABBOTT – Monday 12 June, 15.45-16.45

WHAT IS THE IMPACT OF ANALYTICAL PERFORMANCE OF AN HBA1C METHOD ON CLINICAL PRACTICE?

E. Lenters-Westra [1]
[1]*Clinical Chemistry Department, Isala, Zwolle, The Netherlands*

The central importance of HbA1c in monitoring glycemic control was highlighted by the Diabetes Control and Complications Trial (DCCT) and the UK Prospective Diabetes Study (UKPDS). These trials showed that improved glycemic control, as monitored by HbA1c, delayed the onset of diabetic complications. The publication of these trials has resulted in a large increase in the number of HbA1c requests received by clinical laboratories, and that high quality methods for HbA1c measurement were required to ensure accurate assessment of the glycemic status. The lack of international standardization resulted in the development of National Standardization Programs in several countries and the effect of these standardization programs was that the inter laboratory precision (CV) decreased from 30% before 2003 till ± 3.5% in 2017. A few years ago HbA1c has been advocated as a diagnostic marker for diabetes as a result of global standardization of the HbA1c assay and major improvements in analytical performance of different HbA1c methods made by the manufacturers. But how good should an HbA1c method be? and what is the impact of precision and bias on clinical practise?
In general it is assumed, that when an HbA1c method has a manufacturer National Glycohemoglobin Standardization Program (NGSP) certification, the analytical performance is adequate. Given the fact, that even HbA1c assays with poor analytical performance are certified, such an assumption should be challenged.

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In our reference laboratory the analytical performance of different HbA1c methods, point-of-care and laboratory methods, was investigated using certified CLSI protocols. Furthermore, the interpretation of HbA1c values among different health care professionals was investigated which produced, in combination with the outcome of the evaluation studies, remarkable results.
In this presentation I will use the results of some of our evaluation studies to show what the impact is of the analytical performance of an HbA1c method on clinical practise.

EDUW 7 – SEBIA – Monday 12 June, 17.00-18.00

FLC TESTING: FIXING THE PAST FOR A BETTER FUTURE

M. Drayson [2], J. Jacobs [1]
[1]*Radboudumc The Netherlands*
[2]*University of Birmingham*

Serum free light chains (sFLC) are sensitive biomarkers that are used as an important complementary test in the management of patients with monoclonal gammopathies. The sFLC assay has its complementary value in the context of screening, prognostic stratification, and monitoring of therapy responses. Since a long time, analytical limitations have been reported with the currently available nephelometry/turbidimetry techniques to measure sFLC. In this workshop, we present two new assays for sFLC quantification: Lateral flow/ competition inhibition and sandwich ELISA.

Seralite® FLC lateral flow technology: rapid, easy-to-operate FLC K/L quantitative measurement
Mark Drayson, M.D., PhD – Prof. Clinical Immunodiagnostics, Director Clinical Immunology Service – University of Birmingham - UK
Seralite® FLC Dual Kappa/Lambda (Seralite is an Abingdon Health product, Birmingham, UK*) is a 10 min lateral flow assay for the simultaneous quantification of free kappa and free lambda FLC levels and ratio in serum. Seralite utilizes extensively validated antibodies against human sFLC and the measurement is based on the competitive inhibition principle, making it immune against antigen excess issues. The assay incorporates a number of technical advances which are designed to overcome existing analytical problems in FLC testing. Results here presented support the suitability of Seralite to laboratory's routine and allow setting different important clinical cut-offs for measuring response and for distinction between myeloma and non myeloma AKI (Acute Kidney Injury) patients.
Various categories of sera were tested by Seralite and read on the ADxLR5 reader in a cohort of 576 light chain only (LCO) and 60 non-secretory (NS) cases, at diagnosis, maximum response to therapy and relapse.
20% of LCO patients had urine FLC levels below that recommended for measuring response but >97% of these had adequate sFLC levels (oligosecretory). Two fifths of NS patients (urine negative for FLC by immunofixation) had measurable sFLC levels and could be reclassified as oligosecretory myeloma. The recommended Seralite level of FLC for measuring response was established to be a FLC difference (dFLC) >20mg/L. Serum from 99 patients with acute dialysis dependent kidney injury (AKI) were analysed for sFLCs. A Seralite ′/≤ ratio range of 0.14–2.02 provided 100% sensitivity and 100% specificity for distinguishing between the 45 patients with myeloma and the non-myeloma related AKI patients. A Seralite dFLC also provided an optimal cut-off of 399 mg/L to distinguish between myeloma and non-myeloma AKI patients.
Seralite yielded high quality analytical performances in individual patients for diagnosis and in measuring response to therapy before proceeding to the next cycle and monitoring for relapse in LCO patients and for light chain escape. Seralite is a rapid test ideally suited for small lab activity, or for labs sending away their FLC measurements, in this way improving response time to clinician.
*Sebia has the exclusive distribution of Seralite worldwide, except in BeNeLux.

SebiaFLC assay: a novel ELISA FLC assay, bringing diagnostic coherence**
Joannes (Hans) F.M. Jacobs, Ph.D., M.D. - Laboratory Specialist Medical Immunology, Radboudumc – The Netherlands
During this workshop, the data from the first evaluation of the SebiaFLC assay (Sebia, Lisses, France), issued from a co-development between Sebia and the Radboudumc , will be presented as a novel platform to measure sFLC in routine diagnostic use.
The SebiaFLC assay for the determination of sFLC kappa (′) and sFLC lambda (≤) is based on the sandwich ELISA technology, using polyclonal antibodies. Assay interference, reproducibility, lot-to-lot variability, and linearity were assessed. Reference ranges were calculated from 208 blood bank control sera. Method comparison and preliminary clinical validation was conducted by retrospective analysis of 501 patient sera. Quantitative results of the SebiaFLC assay were compared to the Freelite assay (The Binding Site, Birmingham, UK) performed on a BNII analyzer (Siemens, Marburg, Germany). Quantitative differences

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between both assays were further compared to measurable involved FLC (iFLC) peaks on Serum Protein Electrophoresis (SPE) in 53 sera.
Reference ranges of the SebiaFLC assay were for κFLC 5.2-15.3 mg/L, λFLC 8.2-18.1 mg/L and κ/λFLC-ratio 0.37-1.44. We observed good sensitivity (1.5 mg/L) and linearity in both polyclonal and monoclonal sFLC samples and no antigen excess occurred in any of the tested samples. Reproducibility of the SebiaFLC assay varied between 6.7% and 8.1% with good lot-to-lot consistency. The method comparison with Freelite in all 709 sera showed the following correlations: κFLC R=0.94, λFLC R=0.92 and κ/λFLC-ratio R=0.96. The clinical concordance of the κ/λFLC-ratio of both methods was 94%. Significant quantitative differences were observed with higher Freelite iFLC concentrations in sera with relatively high sFLC concentrations (slopes: κFLC=0.66, λFLC=0.57 and κ/λFLC-ratio=0.63). The SebiaFLC assay concentrations were in the same range as the iFLC concentrations obtained by SPE, bringing coherence with the reference technique. Freelite iFLC concentrations were consistently higher, with a mean 12-fold overestimation compared to SPE.
The SebiaFLC assay is an improved platform for sensitive and accurate sFLC measurements. The SebiaFLC assay showed good clinical concordance with Freelite and a superior coherence with the reference technique, electrophoresis. Further studies are warranted to confirm the clinical value of the SebiaFLC assay.
** The SebiaFLC assay, is fully automated, using the DAS AP22 ELISA processor (DAS, Tivoli, Italy) offering full walkway capability and data processing option on Phoresis, the Sebia proprietary software.

EDUW 8 – ABBOTT – Monday 12 June, 14.30-15.30

DEVELOPMENT OF A NOVEL ACUTE CORONOARY SYNDROME ALGORITHM

M. Than [1]
[1]*Emergency Medicine, Christchurch, New Zealand*

For patients coming to the Emergency Department suspected of Acute Coronary Syndrome (ACS) if not determined by clinical findings and ECG to be having a heart attack, clinicians rely on further information from cardiac biomarkers like Troponin. High sensitivity troponin providing so much information today with gender differences and notable impact due to age as well as the shortening of serial sampling strategies, it has become even more important to consider all of this information when evaluating the patient for ACS. Thus we have developed a comprehensive algorithm that considers all of these variables in an objective manner per each presenting patient. This makes for a more robust algorithm than a manual decision tree algorithm as is utilized today.

EDUW 8 – ABBOTT – Monday 12 June, 14.30-15.30

PROCALCITONIN: A MARKER FOR SEPSIS DIAGNOSIS AND ANTIBIOTIC STEWARDSHIP

P. Schuetz [1]
[1]*Kanstonsspital Aarau*

The limitations of clinical signs and microbial techniques for the diagnosis of bacterial infections are eminent. The use of Procalcitonin provides a promising novel approach to better diagnose infection and for antibiotic stewardship. Interpretation of Procalcitonin levels must always comprise the clinical setting and the assay characteristics, particularly the setting specific cut off ranges and functional assay sensitivities. The higher the risk of a patient, the more cautious physicians must be and empirical antibiotic therapies must be considered despite low biomarker levels. Still, measurement of highly sensitive PCT embedded in a clearly defined setting and prospectively validated with clinical algorithms can significantly improve the diagnostic certainty and safety of patients, and still reduce the (over-) utilization of antimicrobial therapy. Today, this concept has been proven for LRTI and for sepsis in the intensive care unit. For other infections, disease and setting specific cut-off ranges must be validated and proposed and intervention studies conducted to tackle the existing vicious cycle of diagnostic uncertainty, antibiotic overuse and emerging multi-resistance.

EDUW 9 – ROCHE DIAGNOSTICS – Monday 12 June, 15.45-16.45

ANGIOGENIC MARKERS IN PREECLAMPSIA: FROM CLINICAL EVIDENCE TO IMPLEMENTATION IN ROUTINE

S. Verlohren [1]
[1]*Charite University Medicine Berlin*

Preeclampsia is a potentially life-threatening syndrome for the mother and the fetus with high variability in the dynamics of the clinical course. The tools routinely used for diagnosis, blood pressure and urine protein

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measurement, have low sensitivity and specificity for predicting the course of the disease and the associated adverse outcomes.
An imbalance of the angiogenic markers soluble fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PlGF) has been implicated in preeclampsia pathogenesis. High sFlt-1/PlGF ratios are observed even before disease onset, showing potential as a new predictive tool.
PROGNOSIS, a multicenter/prospective/double-blind/non-interventional study, investigated the sFlt-1/PlGF ratio measured by Elecsys® fully automated immunoassays for short-term prediction of preeclampsia and maternal/fetal adverse outcomes in women with suspected preeclampsia at gestational week 24–37. A single cut-off value of 38 was validated: a low sFlt-1/PlGF ratio (≤38) predicts absence of preeclampsia/eclampsia/HELLP syndrome for 1 week after the measurement, and a high sFlt-1/PlGF ratio (>38) predicts diagnosis of preeclampsia/eclampsia/HELLP syndrome within 4 weeks. The correlation of low and high sFlt-1/PlGF with absence and presence, respectively, of maternal/fetal preeclampsia-related adverse outcomes within 1 and 4 weeks was also demonstrated.
When preeclampsia is suspected, there is a high clinical need for reliable short-term prediction to optimize prenatal care. Providing rapid results for the angiogenic markers levels and their ratio to the obstetricians greatly supports their assessment of the severity and progression of the disease and their decision making for patient management. It is important that the clinicians and the laboratory work together for the implementation of the markers in routine, in order to define the source of funding for the test, the best way to report the results and provide guidance for interpretation.

EDUW 9 – ROCHE DIAGNOSTICS – Monday 12 June, 15.45-16.45

NATRIURETIC PEPTIDES IN ERA OF ARNI DRUGS: THE LAB MATTERS

A. Bayes-Genis [1]
[1]*Universitat Autonoma de Barcelona*

Heart failure (HF) affects 1-3% of the general population and approximately 10% of the elderly. Chronic HF patients have frequent shortterm readmission rates, counting more than one quarter of patients that are readmitted within 30 days. Healthcare spending for chronic HF accounts for 1-2% of total healthcare expenditure in developed countries. Natriuretic peptides (NP) have become a laboratory tool with significant implications in the diagnosis, prognosis and treatment of patients with suspected or confirmed HF. The use of NPs affects various healthcare settings (outpatient consultations, emergency department, hospitalization and laboratory) and by various primary care and specialized professionals. The proper use of NPs has implications for patients and for the healthcare system, especially considering the epidemic nature of HF. Recently a new class of drug in HF management was introduced, in over 10 years, which lead to the question of suitability of NP for monitoring of these patients treatment. New class of drugs is called angiotensin receptor neprilysin inhibitors (ARNI), and it presents the combination of NEP inhibitors and angiotensin II receptor blockers. LCZ696 (now known as sacubitril/ valsartan and marketed by Novartis under the name of Entresto) is the first-in-class. Similar to conventional therapy, sacubitril-valsartan suppresses the RAAS system, but then unlike the conventional therapy, sacubitril-valsartan enhances the protective neurohormonal NP system by blocking BNP degradation. In PARADIGM-HF trial, combined inhibition of the angiotensin receptor and neprilysin with LCZ696 experienced 20% reduction in cardiovascular death or hospitalization for HF ($P < 4.0 \times 10\text{-}7$) and 16% reduction in all-cause mortality ($P < 0.001$). Levels of both urinary cyclic GMP and plasma BNP were higher during treatment with LCZ696 than with enalapril; the increases in cyclic GMP reflect the fact that the peptides whose levels are enhanced by neprilysin inhibition act through enhancement of cyclic GMP. In contrast, in comparison with enalapril, patients receiving LCZ696 had consistently lower levels of NTproBNP (reflecting reduced cardiac wall stress) throughout the trial. The contrasting effects of LCZ696 on the 2 types of natriuretic peptides represents an important finding, because the levels of the 2 peptides characteristically parallel each other
during the course of heart failure. However, because BNP (but not NTproBNP) is a substrate for neprilysin, levels of BNP will reflect the action of the drug, whereas levels of NTproBNP will reflect the effects of the drug on the heart. With regards to biomarker assessment in the post-PARADIGM era, BNP may not be a suitable heart failure biomarker in patients treated with sacubitril/valsartan, because it is a NEP substrate, and BNP levels rise with treatment. By contrast, NTproBNP, not a NEP substrate, better reflects the unloading of the heart with treatment. Switching to NT-proBNP as a natriuretic peptide biomarker may be recommended in patients treated with sacubitril/valsartan.

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EDUW 9 – ROCHE DIAGNOSTICS – Monday 12 June, 15.45-16.45

THE NOVEL BIOMARKER-BASED ABC-BLEEDING RISK SCORE FOR PATIENTS WITH ATRIAL FIBRILLATION

Z. Hijazi [1]
[1]*Uppsala University Sweden*

Atrial fibrillation (AF) is the most common persistent arrhythmia, which increases in prevalence with higher age. AF confers a five-fold increased risk of stroke and a two-fold increased risk of mortality. Treatment with oral anticoagulants reduces this risk substantially although at a cost of increased risk of major bleeding.
The benefit of oral anticoagulation in AF is therefore based on a balance between reduction in ischemic stroke and increase in major bleeding. The aim with the biomarker research was to improve the risk prediction of stroke and bleeding in patients with AF. A new biomarker-based risk score for major bleeding was developed and internally validated in 14 537 patients with AF randomised to apixaban versus warfarin in the ARISTOTLE trial and externally validated it in 8468 patients with AF randomised to dabigatran versus warfarin in the RE-LY trial. Plasma samples for determination of candidate biomarker concentrations were obtained at randomisation. Major bleeding events were centrally adjudicated. The predictive value of biomarkers and clinical variables were assessed with Cox regression models. The most important predictors for major bleeding were the concentrations of the biomarkers growth differentiation factor-15 (GDF-15), high-sensitivity cardiac troponin T (cTnT-hs) and hemoglobin, age, and previous bleeding. The new proposed ABC-bleeding score was consisted of Age, Biomarkers [GDF-15, cTnT-hs, and hemoglobin], and Clinical history [previous bleeding]), yielded a higher c-index than the conventional HAS-BLED and the newer ORBIT scores for major bleeding in both the derivation cohort. ABC-bleeding score also yielded a higher c-index score in the the external validation cohort. Interpretation The ABC-bleeding score, using age, history of bleeding, and three biomarkers (haemoglobin, cTn-hs, and GDF-15 or cystatin C/CKD-EPI) was internally and externally validated and calibrated in large cohorts of patients with atrial fibrillation receiving anticoagulation therapy. The ABC-bleeding score performed better than HAS-BLED and ORBIT scores and should be useful as decision support on anticoagulation treatment in patients with atrial fibrillation. These results has been published in The Lancet 2016.

EDUW 11 – SIEMENS – Monday 12 June, 14.30-15.30

EARLY DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION

C. Prof. Mueller [2], M. Plebani [1]
[1]*Department of Laboratory Medicine at the University Hospital of Padova*
[2]*University Hospital of Basel, Switzerland*

Patients with symptoms suggestive of acute myocardial infarction (AMI) account for about 10% of all emergency department consultations. ECG and cardiac troponin (cTn) form the diagnostic cornerstones and complement clinical assessment. A limitation of former generation cTn assays is the “troponin-blind” period within the first hours after the onset of AMI resulting from poor sensitivity and delayed detection of increased circulating cTn levels. This has had two important consequences: first, uncertainty among patients and physicians in patients presenting within the first hours of AMI onset, and second, the clinical need for serial sampling for 6-12 hours. The later leads to delayed detection and treatment of AMI, and interferes with the evaluation of alternative diagnoses contributing to dangerous and expensive crowding in the emergency department.
Recently developed hs-cTn assays provide a new window to the heart and enable precise measurements of cTnT and cTnI blood concentrations around the 99th percentile and even in the normal range, which was not possible with prior generations of tests. Their analytical superiority translated into clinical superiority in the early diagnosis of AMI.
Evolution of the analytical performances of troponin (cTn) assays, from conventional or classical assays to the sensitive and high sensitive assays has impacted the interpretation of elevated cTn results and led to earlier diagnostic protocols.
With the introduction of high sensitive troponin assays, the time interval to the second measurement of cTn can be significantly shortened. This is the main clinical benefit of these assays and may result in substantial reduction in time to decision and therefore total treatment.
Laboratorians are tasked with understanding the improved performance capabilities of high sensitive troponin assays and how to assist their institutions with an elegant transition to new testing protocols

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EDUW 15 – A. MENARINI – Tuesday 13 June, 14.30-15.30

A GALLERY OF IMAGES BY PHASE CONTRAST AUTOMATED MICROSCOPY

R. Falbo [1], M.R. Sala [1], C. Soldi [1], P. Brambilla [2]
[1]*ASST-Monza, Ospedale di Desio, Desio, Italy*
[2]*ASST-Monza, Ospedale di Desio, Desio, Italy and Università Milano Bicocca, Dipartimento di Medicina e Chirurgia, Monza, Italy*

Urinalysis is one of the most frequent tests performed in the clinical laboratory. In the recent past, urinalysis was labor intensive and subject to variability. The advent of automated systems has eased the burden and generated standardization. The introduction of phase contrast microscopy into the automated cuvette-based system has greatly enhanced the ability to differentiate the details of each element found within the urine sediment. The purpose of the investigation was to apply the cuvette-based automated phase contrast microscopy to routine urinalysis samples in order to appraise those with both common and salient elements of the sediments and create a gallery of images for reference purposes.
A total of 600 urinalysis samples arriving to the clinical laboratory of Desio Hospital were anonymously and sequentially analyzed, after routine testing, on the automated cuvette-based phase contrast microscopy system sediMAX conTRUST2 (A. Menarini, Florence, Italy). Images were selected for representative elements such as: cells, casts, crystals, mucus, lipids, organisms, and contaminants.
Two hundred and fifty out of 600 samples were completely lacking any remarkable particle. All the remaining 350 samples had different combinations of the elements studied within the urine sediment. In particular, with the automated cuvette-based phase contrast microscopy, we were clearly able to distinguish dysmorphic red blood cells from isomorphic ones, renal tubular epithelial cells from deep transitional epithelial cells, and hyaline or mixed casts from the surrounding background. An image library of these was created.
The introduction of phase contrast microscopy into the automated cuvette-based analyzer further enhances urinalysis performance. The characteristic feature of each sediment particle is sharper and easier to distinguish. We initiated the creation of a reference library of images useful for the identification of the elements we may find within the urine sediment.

EDUW 15 – A. MENARINI – Tuesday 13 June, 14.30-15.30

LATEST IMPROVEMENTS ON AUTOMATED URINE SEDIMENT MICROSCOPY

G. Bayer [1]
[1]*Development Department of 77 Elektronika, Budapest*

The sediMAX instrument is an automated urine sediment analyzer, which uses the patented cuvette-based automated microscopy with particle recognition, i.e. the so-called UriSed Technology. It was developed by 77 Elektronika and it is distributed by Menarini. It appeared on the market in 2008 and until today Menarini sold close to 1000 sediMAX instruments in 10 European countries. To obtain even more accurate results, the measurement technology has been further developed. The further developed technology provides both bright-field microscopy and phase contrast microscopy, which has multiple advantages. The sophisticated image evaluation module takes not only the bright-field (as it did it before), but also both the bright-field and phase contrast images from each field of view into account. This way there is more information for the evaluation and more accurate results can be obtained. This technique improves the detection of several particle types and makes the differentiation between different Red Blood Cell (RBC) types possible. RBC sublcassification is a new direction in the field of automated urine sediment analysis. Due to the further developed automated urine sediment microscopy technology there are significant improvements in the measurement results:- The recognition rate of the different RBC sublcasses increased by more than 20% with lower or the same error (misidentification) rate as before- The recognition rate of the Yeast cells increased by more than 15% with lower or the same error (misidentification) rate as before- The recognition rate of the Hyaline Casts increased by more than 10% with lower or the same error (misidentification) rate as before- The recognition rate of the Non-squamous Epithelial Cells increased by more than 10% with lower or the same error (misidentification) rate as before.

EDUW 15 – A. MENARINI – Tuesday 13 June, 14.30-15.30

THE CLINICAL RELEVANCE OF SOME URINARY SEDIMENT PARTICLES SHOWN BY SEDIMAGE

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In recent years, sediMAX instrument has become increasingly encountered in clinical laboratories worldwide. Users especially like the quality of the digital images provided by cuvette based microscopy (CBM), associated to robust automation. Digital images may be stored and used for continuous education of medical laboratory technologists (MLTs), or may be sent to colleagues via email to request a specific advice. In order to allow continuous education on urinalysis using sediMAX, the sedimage platform, a database on urine sediment images encountered with sediMAX, was recently created. Interesting sediment images may be sent to sedimage platform for the benefit of sediMAX users' community. In our laboratory, sediMAX was used since 17th January 2011 and more that 150.000 urine sediments were performed on the instrument. During this 6 years timespan, many clinically important sediment particles were encountered and transmitted on the sedimage platform. Encountered particles included notably cystine crystals, red blood cell (RBC) casts, renal tubular epithelial cells, and lipids. Other interesting, rarely described particles, such as daisy-shaped crystals, were also seen in our laboratory.
Cystine crystals are hexagonal shaped structures that are pathognomonic for cystinuria, a genetic cause of urine lithiasis that occurs in approximatively 1 of 7000 births. While cystinuria should be suspected in patients presenting a urine lithiasis in childhood or adolescence, diagnosis of cystinuria may also occur at older ages. RBC casts are strongly suggestive of glomerular hematuria and glomerulonephritis. These casts may be encountered with dysmorphic red blood cells such as acanthocytes. Lipiduria may take the form of free lipid droplets, oval fat bodies, or fatty casts. Presence of lipids in urine is frequently associated with nephrotic syndrome. One of the greatest advantages of sediMAX is the quality of its digital images that may be stored and used for continuous education. Sedimage is an interesting platform beneficial to sediMAX users' community. Sedimage currently includes clinically important urine sediment particles that must be recognized by every operator performing urine sediment analysis.

EDUW 15 – A. MENARINI – Tuesday 13 June, 14.30-15.30

"SEDIMAGE": A NEW WEBSITE EDUCATIONAL PROGRAMME FOR THE USERS OF AN AUTOMATED URINARY SEDIMENT ANALYZER.

G.B. Fogazzi [1], G. Garigali [1]
[1]Clinical and Research Laboratory on Urinary Sediment, U.O. di Nefrologia, Dialisi e Trapianto di rene, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano – Italy.

Automated urinary sediment (U-sed) analyzers are widely used in the developed world today. Among the available instruments, sediMAX is based on a unique technique which supplies black and white "whole-field" images, which are similar to those obtained with bright field manual microscopy.
"sedimage" is an original educational website programme conceived for sediMAX users with the following aims 1. to set up an ongoing database of images submitted by the registered persons and selected by the two scientific editors (FGB and GG); 2. to report on the relevant papers on U-sed published in the international journals; 3. to offer an educational tool in which the particles and urinary profiles shown are identified, commented and shared with the participants in order to improve their knowledge on - and their interest in – U-sed examination.
The selected images are organized into a "gallery" which includes the different types of cells, casts, lipids, crystals, microorganisms, contaminants, and eight main urinary profiles.
To date (October 2016), "sedimage" has 233 registered persons from 17 different countries (15 European and 2 non European). Sixty-one images have been selected and uploaded in the gallery (crystals, 22; cells, 14; casts, 8; microorganisms, 8; contaminants, 3; lipids, 1; urinary profiles, 5), which have been submitted from 10 different laboratories belonging to 6 European countries (Italy, 4; Spain, 2; Austria, Belgium, France, and Hungary, 1 each). Each image is shown with the name and institution of the image supplier, a legend, and a space ("discussion room") for possible comments.
As to scientific literature, "sedimage" contains the e-version of the book "The urinary sediment by sediMAX" (authored by FGB and GG), which was published in 2012, and the power points lectures presented at an international symposium on urinary sediment, which was held in Rome in December 2014.
"sedimage" is an innovative educational website tool which aggregates professionals from different countries around U-sed, a basic but still important test for the diagnosis of the diseases of the kidney and of excretory urinary tract.

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EDUW 16 – RANDOX LABORATORIES – Tuesday 13 June, 15.45-16.45

MEETING ISO 15189 REQUIREMENTS FOR UNCERTAINTY OF MEASUREMENT

M. Fick [1]
[1]*Randox Laboratories*

This talk explores ISO 15189:2012 requirements relating to Uncertainty of Measurement in the clinical laboratory. The presentation will focus on several key elements including; what is measurement uncertainty, how to calculate measurement uncertainty and tools available to assist with this process.

EDUW 17 – FUJIREBIO – Tuesday 13 June, 17.00-18.00

MAKE EXCELLENCE ROUTINE: REVIEWING A HS-TROPONIN I ASSAY, WPTH THIRD-GENERATION STANDARDIZED ASSAY AND THE FIRST FULLY AUTOMATED ALZHEIMER'S LABORATORY TESTS

M. Plebani [3], E. Cavalier [2], K. Blennow [1]
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[2]*Department of Clinical Chemistry, University of Liège, CHU Sart-Tilman, Liège*
[3]*Department of Laboratory Medicine, University-Hospital of Padova, Padova*

Fujirebio is a leader in providing in vitro diagnostics testing solutions, and a pioneer in automated chemiluminescence methods. This educational workshop will review newly developed assays in three different areas, namely the 3rd generation whole PTH (wPTH), high sensitivity (hs)-Troponin I and Alzheimer Disease biomarkers on the Lumipulse G platform.
The Lumipulse G hs-Troponin I assay was launched by Fujirebio in December 2016 and completes the Lumipulse G systems cardiac panel. The assay is based on a two-step sandwich immunoassay concept and meets all of the published performance criteria to be classified as a high sensitivity method. We will present in detail the excellent clinical and analytical performance characteristics of the assay as demonstrated during the pre-launch external clinical validation phase. The Lumipulse G whole PTH assay was launched by Fujirebio in August 2016. The assay is based on the one-step sandwich immunoassay concept. The workshop will present detailed insight into the analytical performance as well as the clinical performance of the Lumipulse G whole PTH assay, mainly for patients with chronic renal failure. We will also explain the interest of the standardization of the assay to reference material/method (WHO IS 95/646). Under the INNOTEST® brand name, Fujirebio pioneered the field of neurodegenerative disease testing by commercializing the first in vitro diagnostic biomarkers for Alzheimer's Disease, consisting of INNOTEST® ELISAs for detection of →-amyloid and Tau. The steadily growing acceptance of the clinical value of Alzheimer biomarkers, coupled with the expectation of new therapies sets the stage for the fully automated processing of CSF samples. The workshop will review Fujirebio's INNOTEST® ELISA biomarkers, and report on the performance of the first biomarkers to be launched on the Lumipulse G automated analyzers.

EDUW 18 – ABBOTT – Tuesday 13 June, 14.30-15.30

EVALUATION OF ALINITY IMMUNOASSAY AND CLINICAL CHEMISTRY ASSAYS BY CLSI PROTOCOLS AND WITH COMPARISON TO ARCHITECT

S. Ruetten [1]
[1]*Abbott Diagnostics, Lake County Illinois, USA*

To determine the analytical performance of several analytes on Abbott's next-generation Alinity clinical chemistry and immunoassay systems in human serum/plasma and urine using the latest modernized CLSI based protocols from internal Design Verification, Design Validation, and external studies. Performance was evaluated against analyte specific specifications, product user needs, medical clinical requirements, and customer expectations. Commutability with on market systems such as the ARCHITECT was performed for precision, linearity, and method comparison. An assay's measuring interval was defined by the range with acceptable performance for bias, imprecision and linearity. Analytical performance was performed for the clinical chemistry potentiometric and photometric systems, and Immunoassays using Chemiluminescent Microparticle Immunoassay (CMIA) technology. Results were collected for Sodium, Potassium, Chloride, Glucose, Cortisol, bHCG, Free T4, Syphilis TP, and HIV Ag/Ab assays. Using Integrated Chip Technology (ICT), a solid-state flow through Ion Selective Electrode (ISE) module, the total imprecision, linearity, and defined measuring intervals were determined and results versus an on-market comparator assay demonstrated a slope of 0.99 – 1.05 and r = 1.00. Using CMIA technology, total imprecision, sensitivity, and linearity results along with the defined measuring intervals were determined to be comparable to an existing system. Results

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versus the on-market comparator assay demonstrated a slope of 0.99 – 1.01 and r = 1.00. For the Syphilis evaluation, donor specificity was 99.98% for the tests of record (TOR). Clinical specificity was at 100.00% with 5119 negative donor specimens and 531 negative hospitalized patient specimens.
Using Abbott's next-generation chemistry analyzer Alinity c, excellent precision, linearity, and correlation with an on-market comparator assay were achieved. Representative immunoassays utilizing CMIA technology tested on Abbott's next-generation immunochemistry analyzer Alinity i demonstrated acceptable precision, sensitivity, and linearity. Method comparison data showed excellent agreement with an on-market comparator assay.

EDUW 18 – ABBOTT – Tuesday 13 June, 14.30-15.30

THE TOTAL COST OF OWNERSHIP OF THE ALINITY PLATFORM AND SERVICES, AND HOW ALINITY DELIVERS MEASURABLY BETTER HEALTHCARE PERFORMANCE

L. Gray [1]
[1]*Abbott Laboratories*

The next generation of Laboratories need to do more tests faster and in smaller spaces with little downtime for maintenance. Listening to the customer created the Alinity platform that contains improvements over previous generations that can be explained in footprint reduction, speed, and platform health monitoring. Alinity was built from the ground up in relation to footprint and platform health monitoring to limit space constraints and Laboratory downtime. In addition, Alinity provides business solution services to help the Laboratory analyze data. These areas decrease the total cost of ownership over previous generations without compromising healthcare.

EDUW 19 – SYSMEX – Tuesday 13 June, 15.45-16.45

INTEGRATED URINALYSIS BASED ON STRIP ANALYSIS AND FLOW CYTOMETRY

J. Delanghe [1]
[1]*Dept of clinical chemistry, Ghent University, Belgium*

Advances in CMOS technology for test strip reading and improvements in urinary flow cytometry have improved analytical sensitivity and have allowed an increased precision in urinalysis instruments. This technological evolution has created new perspectives for a more refined and expanded urinalysis.
A UC-3500 test strip reader (Sysmex, Kobe, Japan) using 11-parameter strips was used in combination with a dedicated urinary flow cytometer (UF-5000, Sysmex). Albuminuria was assayed on a BN II nephelometer (Siemens), urinary creatinine on a Cobas 6000 (Roche).
The mechanical coupling of both analysers allow a swift urine specimen handling. The test strips performed well and were characterised by low CV values. The quality of the test strip data was validated by additional analysis of reflectance data (which do not belong to the normal output of the instrument), which match very well with the corresponding data generated by flow cytometry (e.g. erythrocyte count vs. peroxidase, leukocyte count vs. leukocyte esterase, ...). The test strip based creatinine correlated well with the classical colorimetric Jaffe method. Albuminuria correlated well with nephelometrically quantified albumin ($r>0.94$). Analytical sensitivity for albuminuria was low, so that urinary albumin: creatinine ratios may be calculated.
Recent technological advances have opened new perspectives in urinalysis. Strip and flow cytometry are complementary. The combination of quantitative test strip analysis and flow cytometric data will allow the development of highly performant expert systems in the future.

EDUW 19 – SYSMEX – Tuesday 13 June, 15.45-16.45

THE MODULAR WAY OF URINALYSIS – COMPLETE WORKFLOW WITH MAXIMUM FLEXIBILITY

F. Dupont [1]
[1]*Sysmex Europe GmbH*

With the new UN-Series, Sysmex introduced a truly modular and fully automated system in its urinalysis portfolio, including analysers for chemistry and particle analysis as well as a sophisticated work area management software. With fluorescence flow cytometry at the heart of the analysis, Sysmex is advancing further in terms of delivering quality of results and diagnostic significance while enhancing lab efficiency.
The new UN-Series offers these advances by raising the bar in terms of technology. Additional diagnostic parameters enabled by new smart algorithms within the analyser software will further empower clinicians to

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efficiently and accurately diagnose kidney disorders.
We will present an overview of all new features of this series and its components.

EDUW 21 – ROCHE DIAGNOSTICS – Tuesday 13 June, 14.30-15.30

CELL-FREE DNA TESTING FOR FETAL ANEUPLOIDY: BIOLOGY & TECHNOLOGY

F.R. Grati [1]
[1]*Graduate School of Medical Genetics University of Milan*

During the talk an overview of the main cfDNA technologies will be performed: Massive parallel shotgun sequencing (MPSS), digital analysis of selected regions (DANSR) and targeted SNP-counting. The description of the different biological sources of discordant results by cfDNA testing will be also given. A particular discussion will be performed on the implications of the presence of feto-placental mosaicisms on the rates of discrepant results by cfDNA testing and on the choice of confirmatory prenatal diagnostic procedure after a high risk cfDNA testing result.
As a result of participating in this activity, the participant will be able to:
- assess statistical principles of screening tests
- evaluate the differences among the different cfDNA Technologies
- differentiate the maternal and fetal biological reasons for discordant results
- interpret the meaning of a high risk cfDNA testing result and consequently counsel the expectant woman

EDUW 21 – ROCHE DIAGNOSTICS – Tuesday 13 June, 14.30-15.30

CLINICAL RESEARCH APPLICATIONS USING NGS-BASED TESTING OF LIQUID BIOPSY SAMPLES IN LUNG CANCER

J. Palma [1]
[1]*Roche Diagnostics*

Advances in NGS technologies are delivering on the promise of personalized medicine with significant clinical benefits for cancer patients and towards a better understanding of disease pathogenesis. Liquid biopsies in NSCLC have been shown to 1) help diagnose high-risk patients with potentially actionable mutations, 2) function as a complement for limited tissue, 3) identify patients responsive to targeted therapy, and 4) identify patients that develop resistance during treatment. This presentation will focus on clinical research applications using the AVENIO ctDNA Analysis Kits as a sensitive research tool for the detection of mutations in plasma from NSCLC patients and its potential utility for the prediction of treatment response and the detection of resistance mutations.

EDUW 22 – ROCHE DIAGNOSTICS – Tuesday 13 June, 15.45-16.45

ADVANCED HIV 4TH GENERATION SCREENING TESTS AND NEW OPPORTUNITIES FOR HIV DIAGNOSTICS

J. Verheyen [1]
[1]*Institut für Immunologie und Genetik Kaiserslautern*

HIV screening and testing guidelines continue to evolve with changes in testing technologies. Advanced HIV 4th generation screening assays not only detect, but also report HIV antigen and antibody results separately. This brings more transparency to positive screening results to guide the selection of confirmatory methods and has the potential to speed up confirmation and communication of acute HIV infection.

EDUW 22 – ROCHE DIAGNOSTICS – Tuesday 13 June, 15.45-16.45

CHALLENGES IN CLINICAL PRACTICE AND LABORATORY DIAGNOSIS OF SYPHILIS TODAY

M. Janier [1]
[1]*Hopital Saint-Louis*

There are two different Syphilis algorithms used in clinical and laboratory practice and additionally another algorithm has been suggested recently by ECDC.
Both clinicians and diagnostic laboratories are confused on which algorithm to use. Future trend is the reverse algorithm based on treponemal testing because of its higher sensitivity and specificity.

EDUW 22 – ROCHE DIAGNOSTICS – Tuesday 13 June, 15.45-16.45

ZIKA VIRUS: AN EMERGING INFECTIOUS DISEASE

J.E. Levi [1]
[1]*University Sao Paulo Brazil*

An ongoing Zika virus outbreak occurs in various regions worldwide. Although the primary transmission route of Zika virus is via the Aedes mosquito, cases of intrauterine, perinatal, sexual, laboratory-acquired and transfusion-associated transmission of Zika virus have been reported. This is of concern due to an association between Zika virus infection and adverse pregnancy and fetal outcomes, including microcephaly, neurological complications and Guillain-Barré syndrome.

EDUW 24 – SIEMENS – Tuesday 13 June, 14.30-15.30

BENEFITS OF USING THE ENHANCED LIVER FIBROSIS TEST (ELF) TEST™* IN NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) IN PRIMARY CARE

A. Srivastava, Phd [2], E. Prof. Powell, Phd [1]
[1]*Princess Alexandra School of Medicine. The University of Queensland, Brisbane, Queensland*
[2]*University College London (UCL) Institute for Liver and Digestive Health, London, UK*

The National Institute for Health and Care Excellence (NICE) has recommended use of the ELF test to test for and monitor advanced liver fibrosis in people diagnosed with NAFLD. Cost-comparison analyses assessing the impact of the ELF Test in the risk stratification of patients with non-alcoholic fatty liver disease in primary care. (Srivastava). Risk factors for NAFLD have reached epidemic proportions. A minority of at-risk individuals develop significant liver disease needing specialist referral. Identifying this group is a primary care challenge. Non-invasive liver fibrosis tests enable identification of NAFLD patients with advanced fibrosis, who may benefit from early specialist referral to limit complications of cirrhosis. Serum biomarkers for risk stratification in nonalcoholic fatty liver disease (Powell). NAFLD is the most common liver disorder seen by primary care physicians in Australia. There is limited awareness of identifying patients at-risk of advanced liver disease and little guidance on triaging for further investigation. Early identification of NAFLD subjects with advanced fibrosis is important because these people require specialist care.
We have constructed an analytical model to examine potential cost implications of this strategy on an intention-to-treat basis. (Srivastava) Serum biomarker panels for risk stratification of NAFLD in primary care and non-hepatology specialist clinics to examine subjects at high risk of liver-related complications will be examined. (Powell)
Our cost consequence analysis indicates that NAFLD patients in primary care settings, non-invasive tests are clinically and cost effective. (Srivastava). We hypothesize the ELF test will reliably classify subjects with high or indeterminate scores on simple algorithms. (Powell).
This study demonstrated potential clinical and cost benefit of employing non-invasive markers of liver fibrosis in a primary care setting. Analyses suggest these strategies increase cirrhosis detection rates and reduce secondary care referrals of low risk cases. (Srivastava). We hypothesize that implementing this test in clinical practice will permit more specific risk stratification of NAFLD patients and reduce the number of subjects requiring invasive investigation. (Powell)
*Not available for sale in the U.S. Product availability may vary from country to country and is subject to varying regulatory requirements.

EDUW 26 –MINDRAY – Tuesday 13 June, 17.00-18.00

EVALUATION OF MINDRAY BC-6800 BODY FLUID MODE FOR AUTOMATED CEREBROSPINAL FLUID AND SEROUS BODY FLUIDS CELL COUNTING

S. Buoro [1]
[1]*Clinical Chemistry Laboratory, Hospital Papa Giovanni XXIII, Bergamo, Italy*

Cell counting in cerebrospinal fluid (CSF), Ascitic and pleural fluids provides important diagnostic information in various medical conditions. Historically, this procedure had been performed manually. However, the performance of the manual method vary because of differences in the skills and experience of the technologists. The manual method is also labor intensive and time consuming. In contrast, the Performance of an automated method is more consistent. Clinical specimens were collected and assessed with BC-6800-BF

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and optical microscopy. The study includes the evaluation of limit blank (LoB), limit detection (LoD), limit quantitation, (LoQ), carryover, linearity, and diagnostic concordance between the two methods. BC-6800-BF offers rapid and accurate cell counts in clinically relevant concentration ranges. The use of BC-6800-BF may allow to replace routine optical counting.

EDUW 28 – BIO-RAD, Wednesday 14 June, 14.30-15.30

ANALYTICAL PERFORMANCE FOR PRECISION IN MEDICAL LABORATORIES: STATE-OF-THE ART IN 2015

A. Vassault [5], D. Collin-Chavagnac [2], R. Grelat [4], F. Scherrer [3], J. Gras [1]
[1]*Clinique Saint-Luc Bouge, Belgium*
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[3]*Laboratoire BioRhone, France*
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[5]*Université Pierre et Marie Curie, 75005 Paris, France*

In clinical laboratories, state-of-the-art refers to the best technical performance that is achievable today for a specific analyte. Recently, the Milan classification about analytical performance specifications (APS) stated that state-of-the-art is one of the three models available to set APS for clinical laboratories. However, few data are currently available about state-of-the-art performance for precision. The objective of this workshop is to define 2015 state-of-the-art precision for analytes that are frequently requested in medical laboratories.
More than 2 billion results from quality control measurements performed in 2015 were assessed. These data were extracted from the international database of Unity inter-laboratory comparison program (Bio-Rad, Hercules, CA, USA). Data included the day-to-day precision expressed as coefficient of variation at the concentration level of the different quality control materials used by the participants. Medians of CVs were calculated for respectively percentile 50, 90 and 95 of the results for each analyte at different levels of concentration. We have analyzed state-of-the-art performance for precision for 252 analytes that are frequently requested in medical laboratories.
For each analyte, state-of-the art precision observed in 2015 is compared to state-of-the art precision reported in 1999 by SFBC (Ann Biol Clin 1999; 57(6): 585) and to analytical performance specifications based on biological variation. Observations included that for some analytes, precision is constant over the analytical measuring range, while for others, precision is dependent on the concentration level. For several analytes, precision seems to have improved significantly in 2015 as compared to 1999. Finally, we have also observed significant differences in the precision achieved by different methods used for assaying the same analyte.
In this workshop, we will report state-of-the art performance for precision, as observed in 2015 for frequently requested analytes. These 2015 state-of-the art precision values are based on the exploitation of a database containing more than 2 billion results from laboratories worldwide. State-of-the art values discussed in this workshop may be used by clinical laboratories to set analytical performance specifications in case of the absence of biological variation data, as proposed by the Milan consensus conference on analytical goals.

EDUW 31 – RANDOX LABORATORIES – Wednesday 14 June, 14.30-15.30

A RAPID, AUTOMATED MULTI-ANALYTE BIOCHIP ARRAY FOR EARLY STROKE DIAGNOSIS

J. Curry [2], K. Makris [1]
[1]*Clinical biochemistry Department, KAT General Hospital*
[2]*Randox Laboratories*

Stroke is the second leading cause of death globally (WHO). Acute ischaemic stroke, which accounts for 87% of all stroke cases, can be treated by thrombolysis and early administration (within 3-4 hours of symptoms onset) can help limit stroke damage and disability. However, inappropriate administration of thrombolytic therapy can cause serious adverse effects, including intracranial haemorrhage. Hence, there is an unmet clinical need for a rapid and highly sensitive test that will complement existing CT scanning approaches and facilitate the definitive identification of ischaemic stroke patients. Previous studies have reported Glutathione S-Transferase-Pi (GST-Pi), Nucleoside Diphosphate Kinase A (NDKA), Parkinson Protein 7 (PARK7), Glial Fibrillary Acidic Protein (GFAP), D-Dimer, Interleukin 6 (IL-6) and Heart Fatty Acid Binding Protein (H-FABP) as plasma markers for early diagnosis of stroke and for differentiation between ischaemic and haemorrhagic stroke. The aim of this study was to develop a biochip array for the simultaneous determination of these seven biomarkers in a single plasma sample. An array of chemiluminescent sandwich immunoassays was developed for application to the fully automated Evidence Evolution analyser. The capture

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antibodies were immobilised on the biochip surface at discrete test sites. Plasma samples from stroke patients on admission (within 6 hours of onset of neurological symptoms) and controls were analysed. The Mann-Whitney t-Test was applied to determine statistical significance ($p<0.05$) of the results. Randox Laboratories Limited will present its unique, proprietary, multiplexing, biochip array technology and how this has been applied to development of the stroke array, which facilitates simultaneous determination of GSTP-Pi, NDKA, PARK7, GFAP, D-Dimer, IL-6 and H-FABP in a single plasma sample. Furthermore, it will present the dedicated, Evidence biochip analyser platform, on which this array will be made available, the technical performance characteristics of the array and some preliminary data demonstrating clinical utility of the array as a stroke diagnostic.

Clinical evaluation of an automated multi-analyte biochip array for early stroke diagnosis
An observational study was designed in order to evaluate the utility of an automated multi-analyte biochip array for the early diagnosis of stroke. Patients admitted to the emergency department of our hospital, within six hours from the onset of neurological symptoms, were evaluated for inclusion into the study. Only patients presenting with stroke for the first time were included. Patients with malignancies, recent history of traumatic brain injury, chronic or end stage liver and renal disease were excluded.
Stroke was diagnosed by focal, neurologic symptoms that persisted for >24hours and was confirmed by computed tomography (CT) scan. All patients underwent CT-scan upon admission and at 72 hours after the stroke onset. In each patient the presence of arterial hypertension, diabetes mellitus, smoking history, dyslipidemia, and ischemic heart disease were recorded.
Stroke severity on admission and at 72 hours was assessed with the National Institute of Health stroke scale (NIHSS). Functional outcome was measured on discharge, at 3-, 6- and 12-months after stroke, using the modified Rankin Scale (mRS). Poor outcome was defined by an mRS-score>4 or death and non-poor outcome was defined as an mRS-score<3. During the follow-up period a structured interview was conducted to assign grades on the mRS-score. Blood samples (serum and EDTA-plasma) were collected upon admission, at 24, 48, 72, 96 hours and the 7th day thereafter. Serum and plasma were aliquoted and stored at -80oC until tested. A cohort of 75 healthy adult individuals served as controls.
We will show the distribution of these biomarker values among healthy individuals, and also we will show in detail the kinetics of these biomarkers in acute stroke and their possible correlation with outcome. We will also show the ability of some of these biomarkers to discriminate early between haemorrhagic and ischaemic stroke.

EDUW 34 – SIEMENS – Wednesday 14 June, 14.30-15.30

NOVEL BIOMARKERS IN THE ASSESSMENT OF GLOMERULAR DAMAGE

M. Prof. Dr. Serteser [1], C. Prof. Dr. C.f. Albert [2]
[1]*Acibadem University, School of Medicine, Department of Medical Biochemistry, Istanbul, Turkey*
[2]*Universitätsklinik für Nieren- und Hochdruckkrankheiten, Diabetologie und Endokrinologie, Otto-von-Guericke Universität Magdeburg, Germany*

Novel biomarkers in the assessment of glomerular damage:
1. Beta trace protein as GFR marker in children – Can we establish a reference range?
2. Monitoring acute tubular damage associated with acute kidney failure with NGAL assay
As incidence of renal failure escalates among populations, there is a compelling need to understand the importance for early detection of acute tubular damage to allow early intervention for better clinical outcomes. The limitations of estimates of glomerular filtration rate (GFR) based only on serum creatinine measurements have spurred an interest in more sensitive markers of GFR, especially because the level depends on the body's muscle mass, and its concentration is insensitive to early changes of GFR. It appears that Schwartz-estimated GFR cannot be accurate in patients with low muscle mass. Beta-trace protein (BTP) is a low-molecular-weight glycoprotein freely filtered through the glomerular basement membrane and with minimal non-renal elimination. Recent findings suggest that beta-trace protein (BTP) is at least equal if not superior to serum creatinine as a marker of glomerular filtration rate (GFR), particularly since it is independent from height, gender, age, and muscle mass. Laboratory reference intervals are of particular importance in assessing pediatric patients where there may be marked changes in results at different ages due to physiological causes .The aim of this discussion is to review the establishment and verification of reliable pediatric reference intervals for use in clinical laboratory medicine that are necessary for pediatric clinical interpretation. (M.Serteser). Acute kidney injury (AKI) is a frequent and severe complication in intensive care patients, especially in connection with cardiac surgery. Globally >13 million acute kidney injury incidents occur each year. Serum creatinine is currently considered as 'gold standard' for AKI, but levels start to rise after 1-3 days when up to 50% of kidney functions might have already declined. The persisting high prevalence of morbidity and mortality due to AKI

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calls for novel, early and efficient biomarkers to identify early tubular injury before non-reversible damage develops. Acute tubular damage biomarkers such as neutrophil gelatinase–associated lipocalin (NGAL) has been shown to precede functional AKI and has emerged as a promising noninvasive biomarker to identify very early tubular damage. The aim of this discussion is to review the current available evidence on NGAL applicability in adult cardiac surgery patients. (C. Albert). Beta-trace protein (BTP), also known as prostaglandin D synthase, is a low-molecular-mass protein which belongs to the lipocalin protein family. It was found to be increased in the serum of patients with renal diseases. We have had a unique opportunity to collect reference interval data on an unequivocally healthy cohort of normal children (>1 year through <16 years of age). We conducted a prospective observational study to establish pediatric reference range intervals by detecting GFR with Beta-trace protein as compared to the traditional biomarkers Cystatin C, ß-2-Microglobulin and Creatinine. (M. Serteser). NGAL, a small protein of the lipocalin family is primarily expressed by neutrophils and renal proximal tubules. NGAL is one of the earliest and most rapidly increasing proteins in plasma and urine in response to ischemic or nephrotoxic kidney injury. A scoring system based on plasma or urine NGAL levels helps in identification of cardiac-surgery associated tubular damage with the potential to enable intervention and therapy earlier to reduce the incidence of cardiac surgery-associated AKI. However, with accumulating evidence, conflicting observations raise concern about the robustness of NGAL as a biomarker. To address this issue, we performed a systematic review and meta-analysis of observational studies to estimate the diagnostic and prognostic accuracy of NGAL and to identify potential confounders or effective modifiers of its value in AKI. We hypothesized that NGAL level is of diagnostic and prognostic value both overall and across a range of subgroups developing AKI, urine and plasma/ serum NGAL levels are both valuable for the early diagnosis of AKI, NGAL performs better in children and that there might be an advantage for standardized measurement of NGAL with clinical laboratory platforms. (M. Albert)
BTP measurement in serum, plasma and/or urine can be used as an aid in diagnosis and monitoring of kidney disease. Increased concentrations in serum, plasma or urine are associated with glomerular or tubular disease. The results of our pediatric reference interval study suggest that BTP may be a useful and reliable urinary marker of renal dysfunction and may have a place as an alternative marker for tubular damage and the magnitude of renal impairment in pediatric patients with chronic kidney disease. Laboratory reference intervals are of particular importance in assessing pediatric patients where there may be marked changes in results at different ages due to physiological causes. The availability of reference intervals is essential for the practice of modern medicine—only by having a feel for what is "normal" can a physician judge how "abnormal" a laboratory result is. (M. Serteser). Acute tubular damage without functional AKI (i.e., subclinical AKI) affects hard outcome measures, and the recognition of its presence has the potential to facilitate the earlier implementation of interventions or precautions to prevent further damage and/or progression to functional AKI. We found NGAL level to be a useful early predictor of AKI, both overall and across a range of clinical settings. NGAL level had prognostic value for clinical outcomes. Early detection of AKI could permit timely renal salvage therapies, which, with associated monitoring of response to therapy, may result in preserved renal function and avoidance of renal replacement therapy (RRT) requirement and perhaps translate into improved patient morbidity and mortality. In conclusion, we have constructed a bridge between science and a possible clinical application for NGAL. It is time to recognize that for a defined patient population at high risk for procedure-related functional AKI, acute tubular damage may occur before dysfunction becomes apparent. (M. Albert). Diagnostic testing continues to evolve improving quality and consistency in results. In order to best assist physicians in the diagnosis and management of patients with acute tubular damage, it is important that clinicans and the laboratory are well-versed in innovative biomarkers essential to achieve effective renal disease management and improved outcomes.

EDUW 35 – SIEMENS – Wednesday 14 June, 15.45-16.45

CLINICAL USEFULNESS OF MEASURING ACTIVE-B12 (HOLOTRANSCOBALAMIN)

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[1]*Siemens Healthineers*

Vitamin B12 (cobalamin) plays an important role in DNA synthesis and neurologic function. Deficiency can lead to a wide spectrum of hematologic and neuropsychiatric disorders that can often be reversed by early diagnosis and prompt treatment. Vitamin B12 deficiency is an increasing global health concern. World Health Organization (WHO) estimates B12 deficiency affects millions of individuals across all ages. Estimation of prevalence is may be as high as 10-15% in those over age 60. The primary analysis of vitamin B12 deficiency is the measurement of serum cobalamin (vitamin B12). These commonly used tests measure total vitamin B12, which is found in blood bound to two carrier proteins: haptocorrin and transcobalamin (holoTC). Only B12 in

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this form is available to other tissues for physiologic use. Holotranscobalamin (holoTC) is considered the earliest marker that declines when vitamin B12 depletion starts. The diagnostic challenge with patients that are vVitamin B12 deficient is that often they have no clear signs or symptoms or obvious anemia. It is difficult to diagnose these patients but important to do so since treatment can be readily administered, safe and effective and neurological impairment may be irreversible if treatment is initiated too late. Active-B12, which appears to be an early marker of B12 depletion, can provide a solution.
Traditionally, anemia testing is comprised of vVitamin B12, Folate, and Ferritin. Active-B12 is an innovative new marker for assessing vitamin B12 deficiency that can be used to complement current vitamin B12 testing due to its increased sensitivity and specificity. Studies will be presented reviewing the current practices of testing for vitamin B12 deficiency and how Active-B12 can be incorporated into testing algorithms. These studies will demonstrate the clinical utility of Active-B12 (Holotranscobalamin) and how it offers a more reliable assessment of vitamin B12 status.
Identification of B12 deficiency needs to be accurate and its needs to happen early in the progression of deficiency. Active-B12 (Holotranscobalamin) is a novel and highly accurate way to assess vitamin B12 status.

EDUW 37 – A. MENARINI – Wednesday 14 June, 15.45-16.45

A NEW FULLY AUTOMATED ANALYSER FOR THE DETERMINATION OF ANTINUCLEAR ANTIBODIES (ANA) ON HEP-2 CELLS

M. Berth [1]
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The introduction of automated methods for indirect immunofluorescence (IF) slide processing and slide reading in clinical laboratories the last two decades have improved not only the quality of the antinuclear antibody (ANA) results, but also decreased the hands-on time of this labour-intensive laboratory assay. Further automation by combining the IF slide processing and reading into one analyser is the next step in this evolution. In this presentation we will show and discuss the first analytical results obtained with a new and fully automated IF analyser (Zenit-PRO, Menarini) using HEp-2 slides, and give a first impression on its practical advantages and disadvantages for clinical laboratories.

EDUW 37 – A. MENARINI – Wednesday 14 June, 15.45-16.45AN ALL-IN-ONE WORKSTATION FOR IIF AUTOMATED PROCEDURE

D. Picchioni [1]
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The presentation aims to describe a novel high-performance automated system for IFA screening.
The platform provides the laboratory with an all-in-one solution that integrates automated IIF slide preparation with coverslipping, whole-well slide scanning, image analysis, reporting and data sharing. The new automated system aims to standardize each critical step of the biological protocol, eliminating the inconsistency of human intervention and maximizing the accuracy of the overall IIF process.

EDUW 36 – DIASORIN – Wednesday 14 June, 17.00-18.00

THE THREE MAIN RENAL BIOMARKERS (FGF 23, 1,25 VIT D, 1-84 PTH) IN FULL AUTOMATION TO SUPPORT THE CLINICAL OUTCOME

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Fibroblast growth factor 23 (FGF23) has emerged as an important regulator of phosphate and vitamin D homeostasis. The mineral homeostasis is regulated by three main biomarkers: FGF 23, parathyroid hormone (PTH) and Vitamin D. Basically for the clinicians it is important to understand how FGF23 interacts with vitamin D (in particular the 1,25 dihydroxy vitamin D) and PTH in a FGF23-Vitamin D-PTH axis to manage

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at best patient's clinical status and follow-up. Fibroblast growth factor 23 (FGF23), is a hypophosphatemic hormone produced by the osteocytes, that also decreases 1,25-(OH)2D levels. FGF23 increases early during the course of CKD. Increased FGF23 levels are associated with increased mortality in patients entering dialysis. Active FGF23 peptide is cleaved in the circulation and assays available on the market either measure the "intact" peptide or the "C-terminal" peptide.
In this workshop the presentations will address the clinical influence of these three biomarkers, their key analytical issues, the current recommendations for the diagnostic use and recent scientific highlights.
More details will be addressed to the analytical importance of the determination of those biomarkers in regards of the definition of reference ranges, evaluations of the concentrations analyzed versus a healthy population group and patient with different CKD stages using the DiaSorin's chemiluminescent immunoassays.
The LIAISON 1-84 PTH immunoassay, third generation, is specific for the determination of the whole molecule 1-84 PTH allowing a better discrimination within the pathologic patient group without missing any fragment. Great feature that always implement the clinical support and decision.
The LIAISON 1,25 Vit D is already recognized to be important in the CKD diagnosis and there finds its best positioning. With the new availability of the LIAISON FGF 23 assay it I now possible to study more in depth the FGF23-Vitamin D-PTH axis and getting better overview for the clinical status.

EDUW 29 – MINDRAY – Wednesday 14 June, 15.45-16.45

CIRCULATING TUMOR DNA: A PROMISING BIOMARKER IN THE LIQUID BIOPSY OF CANCER

M. Ferrari [1]
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Advanced genetic diagnostics based on circulating molecular markers requires innovative methods for the detection of minority mutant alleles. This is particularly true in the case of mixed samples, where mutations are present at a low concentration among a background of wild-type sequences. Most of the molecular alterations found in cfDNA circulating in plasma reflect the genetic and epigenetic changes found in primary tumors and, thus, the analysis of such tumor cfDNA might be valuable for tumor diagnosis and monitoring. Highly sensitive methods are required to detect those alterations among larger quantities of non-altered cfDNA molecules. The molecular analysis of genetic biomarkers in plasma has also a huge significance from a cancer therapeutic perspective. The analysis of cell free tumor DNA in the plasma of cancer patients allow the potential opportunity to perform mutation testing without a biopsy specimen. It has also been argued that analysis of cell free DNA, compared to the analysis of tumor tissue DNA, might yield real-time information about all subclones within the tumor and about the presence of any genotypic changes responsible for development of drug resistance. The clinical value of cfNAs circulating in plasma is already more than a theoretical idea, since the characterization and the quantitation of such nucleic acids (NAs) have been shown to be complementary tools. It is therefore expected that in the coming years, an improved understanding of the relationship between CNAPS and the molecular biology of cancer will lead to better diagnosis, management, and treatment.