26th BCLF 2018
Skopje • October 3 - 5, 2018

BALKAN JOURNAL OF CLINICAL LABORATORY

The 26th Meeting of the Balkan Clinical Laboratory Federation

The 6th National Congress of the Macedonian Association of Medical Biochemistry and Laboratory Medicine

03th - 05th October, 2018 Skopje, Macedonia

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The 26th Meeting of the Balkan Clinical Laboratory Federation

The 6th National Congress of the Macedonian Association of Medical Biochemistry and Laboratory Medicine are organized under the auspices of the:

International Federation of Clinical Chemistry and Laboratory Medicine

European Federation of Clinical Chemistry and Laboratory Medicine

Balkan Clinical Laboratory Federation

University Ss Cyril and Methodius in Skopje

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26th Meeting of Balkan Clinical Laboratory Federation

6th National Congress of the Macedonian Association of Medical Biochemistry and Laboratory Medicine

SCIENTIFIC PROGRAM

Aleksandar Palace Hotel
Skopje, Macedonia

03th-05th October, 2018
Skopje, Macedonia

President's Invitation

Dear colleagues and friends,

On behalf of the Macedonian Society for Medical Biochemistry and Laboratory Medicine, we would like to invite you to the 26th BCLF Meeting, and the 6th National Congress, which will be held from 3rd to 5th, October, 2018, in hotel Aleksandar Palace, Skopje.

It is our pleasure to inform you that we are organizing this meeting for the fourth time. The 26th BCLF Meeting is organized under the Auspices of International Federation of Clinical Chemistry (IFCC) and European Federation of Clinical Chemistry and Laboratory Medicine (EFLM).

We believe that the Meeting will offer rich content of scientific papers from colleagues from all Balkan countries and Europe. This event will be a great opportunity for an exchange of knowledge and experiences of experts in the laboratory field. The scientific program will include presentations, discussions, promotions and innovations in the field of clinical laboratory achievements.

Professional events are always a great opportunity to bring together experts in a certain field to present their research, results, and share their findings. Thus, we believe that the 26th Meeting of the Balkan Clinical Laboratory Federation (BCLF) in 2018 will bring new conclusions, findings and will significantly contribute to the progress of our medical branch.

Furthermore, there will be an exhibition and presentation of a large number of exhibitors of items, products and appliances and chemicals of a number of companies and laboratories related to the topic of clinical laboratory.

We assure you that besides the scientific meeting program, your stay will be enriched with the warm hospitality of the host, as well as the beauties of the city of Skopje, a city with a 2000-year-old tradition, and the birthplace of Mother Teresa; it will give the opportunity to see the beautiful quay of the Macedonian river "Vardar", the narrow streets of the Old Bazaar (the biggest bazaar preserved in the Balkans today), the "Kale" (1500 year-old fortress), the 2m underground submerged "Sveti Spas church with its impressive wooden iconostasis, the Daut Pasha hammam and many more historical and cultural monuments that are at the very center of the city easily accessed by foot, bus or car.

We hope that you will enjoy your stay in Skopje,

Best Regards,

Prof. dr. Danica Labudovic
MSMBLM President

Dear Friends & Colleagues

On behalf of Balkan Clinical Laboratory Federation I am most pleased to extend to you a warm invitation to attend 26th Meeting of the Balkan Clinical Laboratory Federation (BCLF) which will take place in Skopje, Macedonia from October 3-5, 2018.

The BCLF Meeting will provide wonderful forum for you to refresh your knowledge base and explore the innovations in Clinical Laboratory. The Meeting will strive to offer plenty of networking opportunities, providing you with opportunity to meet and interact with the scientists and researches, friends and colleagues as well as sponsors and exibitors.

The organisers have invited international and regional speakers who are experts in their field and wellknown for their good presentation skills. The BCLF Meeting 2018 will be vaulable and important platform for inspiring regional and interdisciplinary exchange of information and experiences in laboratory medicine.

In the land of the rising sun and great people I hope we will find new inspiration for the work which is ahead of us.

I wish you successful and fruitful 26th BCLF Meeting and pleasent stay in Skopje.

Jozo Coric
BCLF President

PLENARY LECTURES

THE CHALLENGES OF POC TESTING

Sverre Sandberg

The Norwegian Quality Improvement of Primary Care Laboratories (NOKLUS), University of Bergen, Bergen, Norway

POC instruments are increasingly used throughout the community and are the fastest growing part of the IVD industry. Instruments are used at GPs offices, pharmacies, nursing homes, departments in the hospitals and in the hands of patients. How can the quality of these instruments be ensured? It is the challenge of laboratory medicine to ensure that these instruments are used in the right clinical pathways and that they have enough good quality. There are relatively more errors of POC instruments in the analytical phase compared to central laboratory instruments. But, of course, errors in the pre-analytical and post-analytical phase are also frequent. First of all, politically it has to be decided that quality of POC instruments is the responsibility of the laboratory profession. It should be a goal for laboratory medicine to ensure the quality of equipment of POC instruments wherever they are situated. Most clinicians and patients do not know that POC results can be misleading and prone to errors. Therefore, an important aspect will be education of the users of the instruments, both in pre-analytical errors, in how to choose the right instrument for their use and how to run it and of course the post-analytical aspects, for e.g. how to report the results. We have to set sensible performance specifications for POC instruments and they can be different from the performance specifications used in the central hospital. As a laboratory profession we have critically to judge if, and how to use traditional internal quality control. External quality control for POC instruments have to be improved securing that we can get information on both participant performance as well as method performance. To be able to do this, improved quality control material has to be used and/or methods to improve the "commutability of the EQA schemes" have to be developed.

Sverre Sandberg is a MD, PhD and specialist in laboratory medicine. He is director of NOKLUS, a Norwegian organisation for quality improvement of laboratory activity (www.noklus.no) which serves about 80 hospital laboratories and about 3100 users of POC equipement outside hospitals (GP offices, nursing homes, oil platforms etc), chair of SKUP, Scandinavian Evaluation of Laboratory Equipment for Primary Health Care (ww.skup.nu) and director of the Norwegian Diabetes Registry. He is director of the Norwegian Porphyria Centre (NAPOS) (www.napos.no). He is professor at the Institute of Global Health and Primary Health Care at the University of Bergen. From 2002 – 2012 he was director of Laboratory of Clinical Biochemistry at Haukeland University Hospital in Bergen.

He was from 1996 – 2002 chair of the Committee on Evidence-Based Laboratory Medicine and from 2002 – 2008 chair of The Global Campaign of Diabetes Mellitus in IFCC (International Federation of Clinical chemistry and Laboratory Medicine). Since 2000 he has been a board member of EPNET (European Porphyria Network), a partly EU-funded project. From 2012-14 he was president of the European Organization for External Quality Assurance in Laboratory Medicine (EQALM). In 2009 – 2014 he was chair of the Scientific Committee in EFLM (European Federation of Clinical Chemistry and Laboratory Medicine). From 2014-15 he was vice president and from 2016-2018 president of EFLM. He is EFLM representative in EB of IFCC. He is chair or member of different working groups in EFLM and IFCC.

He has written peer reviewed papers and book chapters given international lectures in his fields of interests: evidence based laboratory medicine, quality improvement of point of care instruments, biological variation, performance specifications in laboratory medicine, quality assurance of the total testing process, laboratory aspects of diabetes, porphyria and photobiology. He likes the sound of raindrops and of the wind soughing through the threes, has supervised numerous PhD students and got some awards.

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HARMONIZATION OF THE PREANALYTICAL PHASE: THE STRATEGY OF THE EUROPEAN FEDERATION OF CLINICAL CHEMISTRY AND LABORATORY MEDICINE (EFLM)

Giuseppe Lippi

Section of Clinical Biochemistry, University of Verona, Verona, Italy

After decades of research in the total quality of laboratory diagnostics, it has now become rather clear that the preanalytical phase is the most vulnerable part of the total testing process, where errors are most likely to happen, thus impairing tests reliability and jeopardizing patient safety. The Working Group for the Preanalytical Phase (WG-PRE) has been officially founded by the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) in the year 2013. The main scope of this WG is to reduce the impact of preanalytical variability on quality of testing and improve harmonization in the still manually-intensive activities related to collection, handling, transportation, storage and preparation of biospecimens. Since its birth, the WG-PRE has finalized many valuable projects, encompassing a final definition of fasting status, as well as the harmonization of patient and blood tubes identification, color coding of blood collection tubes, sequence of blood tubes during collection, serum indices, but has also participated in the project of developing reliable quality indicators for the preanalytical phase. Additional projects of the WG-PRE include drafting European phlebotomy guidelines, producing indications on local validation of blood tubes and glucose stabilizers and organization of many European surveys and meetings.

Giuseppe Lippi was born in Padova (Italy) on October 4th, 1967. He has taken the degree in Medicine in 1992 and the specialization in Clinical Biochemistry and Laboratory Medicine in 1996. He currently serves as Full Professor of Clinical Biochemistry and Molecular Biology at the University of Verona (Italy) and Director of the Clinical Chemistry and Haematology laboratories of the University Hospital of Verona (Italy). He has published more than 1500 articles in peer-reviewed journals, his total Impact Factor is over 5500 and the Hirsch Index (H-index) is 80. He has participated to more than 500 national and international congresses and has given more than 250 lectures to national and international meetings. In 2017 he has been appointed as Secretary of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM). He has been awarded with the 2014 Management Sciences and Patient Safety Division Award of the American Association for Clinical Chemistry (AACC) for outstanding contributions in the field of patient safety in the clinical laboratory/healthcare industry, and with the 2015 Outstanding Speaker Award by the AACC. He has also received research grants from the European Community and from Regional Heath Care Services. Giuseppe Lippi is Editor in Chief of "Annals of Translational Medicine" and "Journal of Laboratory and Precision Medicine" and also serves as Associate Editor of the journals "Clinical Chemistry and Laboratory Medicine", "Seminars in Thrombosis and Hemostasis" and "Diagnosis", is National Representative of the Italian Society of Clinical Biochemistry and Laboratory Medicine (SIBioC) and member of the European Federation of Laboratory Medicine (EFLM) Working Group on Preanalytical Variability (WG-PRE). The main fields of research include pre-analytical variability, analytical and clinical validation of biomarkers, proteomics, diagnostics of the acute coronary syndrome, metabolism of lipoproteins and relevant assay methods, frailty, diagnosis and management of disorders of hemostasis.

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CAUSES OF INDIVIDUAL ANALYTICAL ERRORS AND MECHANISMS FOR THEIR DETECTION

Vera Lukic

Laboratory Department, Railway Health Care Institute, Belgrade, Serbia

Because of automation of laboratory testing and routine internal and external quality control procedures, it is assumed that nowadays analytical phase of laboratory testing is completely brought under control. Over the last years biochemists have been focused on the preanalytical and postanalytical phases which are considered a main source of errors in laboratory medicine. But, recently a novel concept of irregular or individual analytical errors has been introduced by Vogeser and Seger. Irregular error is defined as an inaccuracy of a test result that is so high that it cannot be explained by measurement uncertainty of the utilized routine assay operating within the accepted limitations of the associated process quality control measurements. This concept has been the focus of our attention on analytical errors in individual patient sample which cannot be detected by routine quality control procedures, but can be clinically significant. There are many possible causes for this type of error. It can be caused by different interfering substances such as heterophilic antibodies or biotin, by matrix effect, high dose hook effect, carryover on analyzers, errors during individual sample preparation or liquid handling volume, etc. The exact prevalence of irregular analytical errors is not known, but we should be aware of them in our everyday practice and take additional measures for their detection. Some of these measures can be: delta check, transversal and longitudinal data assessment and close communication between clinicians and laboratory for any result which is inconsistent with patient's clinical status.

Doctor, specialist in Clinical Biochemistry

PhD student of Medical Biochemistry at Faculty of Pharmacy at Belgrade University.

Head of Laboratory Department in Railway Healthcare Institute in Belgrade.

Mentor for practical training of doctors attending Specialization in Clinical Biochemistry at Faculty of Medicine at Belgrade University and of medical biochemistry students at Faculty of Pharmacy at Belgrade University.

Speaker at different national and regional conferences and symposia.

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STANDARDIZATION AND HARMONIZATION OF LABORATORY DIAGNOSTICS OF CHRONIC KIDNEY DISEASE IN CROATIA

Vanja Radišić Biljak

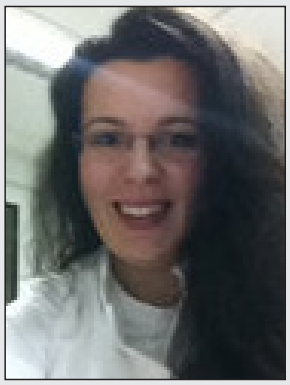
Department of Medical Laboratory Diagnostics, University Hospital "Sveti Duh", Zagreb, Croatia

Aim: In 2014, the Joint Croatian Working Group (JCWG) for laboratory diagnostics of CKD on behalf of the Croatian Society of Medical Biochemistry and Laboratory Medicine (CSMBLM) and Croatian Chamber of Medical Biochemists (CCMB) conducted a survey across Croatian medical-biochemistry laboratories to assess the current practice in this area of laboratory medicine. The results of the survey showed a large heterogeneity among Croatian laboratories, which set the background for the process of standardization and harmonization.

Methods: To ensure the tools for the standardization process, in 2015 JCWG issued the first national recommendations for laboratory diagnostics of CKD. The main goal was to give recommendations that can be easily applied. To assess the national recommendation implementation process, a slightly modified survey was repeated in December 2017.

Results: The survey results showed a substantial decrease in the number of laboratories which measure creatinine with non-standardized uncompensated Jaffé method, compared with the initial assessment conducted in 2014; 7% vs 40%, respectively. The number of the laboratories that do not report eGFR values decreased almost by half compared to the initial 2014 data (37.6% vs 74.4%). However, similar number of laboratories (54/98 vs 58/80) still do not measure urine albumin or protein.

Conclusions: The first Croatian recommendations for laboratory testing of CKD implementation process reached their first year which resulted in substantial improvement in the standardization of the serum creatinine measurement, as well as in reporting of eGFR. However, albuminuria or proteinuria assessment is still not implemented nationwide, mainly due to legislative reasons.



Vanja Radišić Biljak, PhD, born in Sisak, Croatia where she finished elementary and high school. She studied Medical Biochemistry at the Faculty of Pharmacy and Biochemistry, University of Zagreb, since 1999 and finished it 2004. 2005 she started postgraduate doctoral study in Medical Biochemistry and defended her doctoral thesis „Chronic obstructive pulmonary disease and glutathione cycle" in 2010, gaining her PhD degree. Since 2010 till 2017 she has been employed in Merkur University Hospital. She started her residency in Medical Biochemistry and Laboratory Medicine and finished it 2014 when she became Specialist in Laboratory Medicine. Her major interest shifted towards diabetes, nephrology and medical informatics. She is currently employed in Department of Medical Laboratory Diagnostics, University Hospital "Sveti Duh".

Scientific development, grants and awards

In April 2003 she was at Faculty of Pharmacy in Ljubljana in scope of a CEEPUS Project.

In 2010. she got a full scholarship for EASD Young Scientists Training Course "Reactive metabolites in late diabetic complications" (University Hospital Heidelberg, Dept. of Medicine I and Clinical Chemistry) in Heidelberg, Germany.

In 2011 she attended the postgraduate course „Statistical analysis of data in biomedical research" in organisation of Medical School, University of Rijeka.

In 2013 she received a travel grant for the EFLM Postgraduate Course in Clinical Chemistry and Laboratory Medicine „New Trends in Diagnosis and Monitoring using POC Instruments" which was held in Dubrovnik and organised by the Croatian Society of Medical Biochemistry and Laboratory Medicine, European Federation of Clinical Chemistry and Laboratory Medicine and Slovenian Association for Clinical Chemistry.

In 2015 she attended the EFLM Postgraduate Course in Clinical Chemistry and Laboratory Medicine "How to assess the quality of your method?" which was held in Zagreb and organised by the Croatian Society of Medical Biochemistry and Laboratory Medicine, European Federation of Clinical Chemistry and Laboratory Medicine and Slovenian Association for Clinical Chemistry.

In 2016 she was awarded as a best young scientist for 2015. The award was presented from the Croatian Society for Medical Biochemistry and Laboratory Medicine.

Projects

In 2012 she was IT assistant in implementing new software for mandatory national scheme for external quality control (CROQALM).

In 2013 she was elected a Corresponding Member of the IFCC-WASPaLM Task Force on Chronic Kidney Disease (TF-CKD). In 2017 she became a Full Member of the TF-CKD for a three year period (2017 – 2019).

Since 2014. she is a Chair of the national Working group for laboratory diagnostics in CKD.

In period from 2015 by the end of 2016 she was a Secretary of Croatian Society of Medical Biochemistry and Laboratory Medicine.

She was Assistant Editor in Biochemia Medica Journal in 2015 and 2016.

In 2017 she was a guest Editor on a special issue of eJIFCC dedicated to the laboratory diagnostics of Chronic Kidney Disease.

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SIX SIGMA QC DESIGN AND RISK ASSESSMENT FOR QC FREQUENCY

Sten Westgard

Westgard, Madison Wisconsin, USA

For more than 50 years, QC Frequency has been guided by compliance to regulation and accreditation. It has been policy and "planet-based", often determined by the rotational speed of the earth (once per 24 hours) or the changing shifts of personnel (once per shift). It is long overdue that change and adapt our QC frequency to be Patient-based - run to ensure that

the needs of the patient for an accurate result are met by the observed performance of the system. In the last few years, a graphic tool - A Six Sigma QC Frequency Nomogram - has emerged that easily allows laboratory to scientifically determine how often to run QC minimizing the risk to the patient.

The risk assessment concepts were introduced by ISO and US CLIA regulations, as well as CLSI's EP23[tm] guideline on QC Frequency, but with the introduction in 2016 of the Individualized Quality Control Plan (IQCP), it became mandatory for laboratories wishing to customize their QC frequency that they perform Risk Assessment. The EP23 and IQCP, while

created for US laboratories, became an international standard through the global influence of CAP accreditation. Unfortunately, EP23 and IQCP only provide vague guidance and very few scientific, reproducible tools to plan QC frequency. Only through the Parvin model of Max(Enuf), introduced more than a decade ago, has an evidence-based, data-driven method of determining QC frequency been created. Parvin's model, however, was so complex that few labs could implement it. Only through recent graphic tools in the form of nomograms has this risk assessment process been transformed into something practical and achievable for routine laboratory operation.

Through the determination of an analytical Six Sigma metric, laboratories can not only assess the acceptability of the method, they can now optimize QC rules, numbers of control measurement, and frequency, and in cases where world class performance is determined, significant savings can be realized, bu reduced consumption of supplies, reagent, controls, calibrators, as well as less staff time wasted on unnecessary trouble-shooting.

Sten Westgard, MS, is the Director of Client Services and Technology for Westgard Quality Control. Mr. Westgard earned his MS degree in Computer Science from Pace University (New York, New York).

For more than 20 years, Sten has managed the Westgard website, course portal, and blog, creating and administering online training, as well as editing and writing hundreds of reports, essays, and applications on quality control, method validation, Six Sigma Risk Management and other laboratory management topics.

He has edited and contributed to numerous books on quality, including Basic QC Practices, Basic Method Validation, Basic Quality Management Systems, Six Sigma QC Design and Control, Six Sigma Risk Analysis, CLIA Final Rules, Assuring the Right Quality Right, The Poor Lab's Guide to the Regulations and Nothing but the Truth about Quality.

Sten is also an adjunct faculty member of the Mayo Clinic School of Health Sciences in Rochester, Minnesota; an adjunct faculty member of the University of Alexandria, Egypt; an adjunct visiting faculty member of Manipal University in Mangalore, India; and an honorary visiting professor at Jiao Tong University, Shanghai.

CARBAMYLATION OF PROTEINS: PATHOPHYSIOLOGY AND BIOMARKERS

Philippe Gillery

IFCC Scientific Division Chair

Laboratory of Biochemistry-Pharmacology-Toxicology, University Hospital of Reims, France

Carbamylation belongs to a group of nonenzymatic post-translational modifications responsible for protein molecular aging. This reaction is due to the binding to amino groups of isocyanic acid, formed in vivo either by spontaneous dissociation of urea or by the action of myeloperoxidase on thiocyanate, and generates carbamylation-derived products (CDPs), the most characteristic one being homocitrulline. Proteins with a long half-life, like collagens and elastin in the extracellular matrix, are preferential targets of carbamylation.

Carbamylation leads to alterations of structural characteristics, biological properties or bioavailability of proteins. For example, carbamylation inhibits inflammatory processes and alters arterial wall remodelling. Carbamylation rate is increased during pathological contexts and is correlated to morbidity and mortality in patients with cardiovascular and renal disorders. Besides, tissue carbamylation appears to be a hallmark of aging due to the progressive accumulation of CDPs in tissues.

Different markers have been proposed for evaluating protein carbamylation in clinical practice, using immunoassays, HPLC, or LC-MS/MS. Carbamylated hemoglobin (cHb), classically described as an interference on HbA1c assays, has been proposed as a marker of "uremic memory" in patients with chronic renal failure (CRF), cHb rate being correlated with uremia and duration of exposure to urea. However, as many factors interfere with red blood cell metabolism in patients with CRF, the use of other markers such as plasma homocitrulline or carbamylated albumin (cAlb) constitutes a valuable alternative, for example for discriminating between acute renal failure and CRF. More generally, their concentrations seem to be related to atherosclerosis progression and cardiovascular complications in various pathological conditions.

Thus, carbamylation is an important pathophysiological process involved in several human diseases, and could constitute a target for new therapeutic strategies. Besides, CDPs are potential new biomarkers of cardiovascular complications in chronic diseases.

Prof. Philippe Gillery, MD, PhD, is Professor of Biochemistry and Molecular Biology at the Faculty of Medicine of Reims, University of Reims Champagne-Ardenne, France. He is the chair of the Laboratory of Paediatric Biology and Research and of the Biology and Pathology Department of the University Hospital of Reims, France.

He is currently appointed as Chair of the Scientific Division of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC), and is Associate Editor of the Clinical Chemistry and Laboratory Medicine Journal.

His research interests are related to the effects of nonenzymatic post-translational modifications on protein structure and functions, and to their involvement in the pathophysiology of diabetes mellitus and other chronic diseases. He has published more than 210 articles in peer-reviewed journals.

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BIOMARKERS IN AGE-RELATED MACULAR DEGENERATION (AMD)

Christos Kroupis

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Age-related macular degeneration is a late-onset disease of the eye macula that can result in blindness and in a significant deterioration of quality of life. Genes and oxidative stress from light exposure and smoking are major risk factors.

AMD can be considered a multifactorial dysfunction of the retinal photoreceptor cells and their support system, which includes the retinal pigment epithelium (RPE), Bruch's membrane (BrM), and the choroidal vasculature. The fundamental cause of vision loss in AMD is the progressive damage to photoreceptors, which can be triggered by RPE dysfunction and atrophy, impaired transport of oxygen, nutrients and metabolites between vessels and outer retinal cells and leakage from choroidal capillaries that invade the retina through the RPE.

There are two AMD forms: dry (in 90% of patients) and wet (in 10%). In the dry form of AMD, apoptosis of RPE, neuroretina and choriocapillaris is slowly progressing and causes permanent central vision loss. Initially, the BrM exhibits increased deposition of cholesterol and calcium with age. Drusen genesis is a sign of AMD progression. Drusen are amorphic extracellular deposits of lipids, proteins, inflammatory molecules in the space between RPE and BrM. In the advanced dry form of AMD, geographic atrophy (GA) develops from large, confluent drusen that proceeds to hyperpigmentation and then, to cell apoptosis. At present, there is no effective treatment of the dry form. In the wet form, the cause of potential central vision drop is a choroidal neovascularization (CNV). An inflammatory reaction initiates pathological angiogenesis that penetrates through defects in the BrM and the RPE layers to the subretinal space, where exudation and bleeding destroy photoreceptors. Commonly used anti-VEGF factors given in repeated intravitreal injections inhibit neovascularization and can stabilize vision acuity in most wet AMD patients.

Genetic biomarkers in AMD. Linkage of AMD families to the complement factor H (CFH) gene by many groups in 2005, led to the identification of the first common genome-wide significant risk variant, Y402H (rs1061170, g.43097C>T) with variable frequencies across various populations. This SNP (single nucleotide polymorphism) results in an impaired alternative complement pathway inactivation. Another major non-complement pathway AMD-associated locus (LOC387715) is the ARMS2 A69S SNP (rs10490924, g.5270G>T). These initial promising findings prompted world-wide efforts and culminated in the AMD Gene consortium 2013 study where 19 common variants were associated with the disease in a large number of patients with the use of SNP microarrays; still the two aforementioned SNPs possessed the highest odds ratios (OR) for AMD development (between 2.4-2.7) with some differences in their effect according to their different allele frequencies in various populations. It was estimated that these 19 variants can explain ~45% of the genetic heterogeneity in AMD patients above 85 years old; the two main AMD associations with CFH and ARMS2 genes account for a significant 25% of the total cases. Therefore, we and other groups have developed fast, high-throughput robust and accurate assays for their accurate detection. Homozygosity for both CFH and ARMS2 risk alleles increases the progression to advanced AMD stages (GA or CNV) to 48% compared to 5% for those carrying wild-type alleles in both genes. Models incorporating these alleles and/or an expanded variant panel along with smoking and body mass index have been the basis for various commercial tests estimating AMD risk. Potential nutrigenetic antioxidant interventions have been proposed based on CFH and ARMS2 genotypes.

Plasma epigenetic biomarkers in AMD. Small, non-coding RNA (18-24 nt) which are called microRNAs (miRNA) have proved relevant to AMD and are detected as circulating nucleic acids in human plasma. Recent studies have identified plasma miRNA expression profiles that are specific for AMD patients compared to healthy controls and that can also discriminate between dry and wet AMD patients.

Christos Kroupis, MSc, PhD, EuSpLM

Dr. Christos Kroupis obtained a MSc degree from Cornell University in Ithaca, NY, USA for his work on T. fuscamutants and a PhD degree from University of Athens, Greece for molecular studies in BRCA genes. Before becoming a Lecturer of Clinical Biochemistry and Molecular Diagnostics in Attikon University Hospital, University of Athens Medical School in 2006 and then an Assistant Professor in 2011, he has worked as a researcher for Hoffmann-La Roche, NJ, USA (basic cardiovascular research) and as a staff Clinical Chemist and Molecular Biologist for labs at Onassis Cardiac Center and Mitera Surgical Center in Athens, Greece for over 12 years.

He serves also as a Lead Assessor in the National Accreditation System of Greece (E.SY.D.) and as a National Representative in European Federation of Clinical Chemistry and Laboratory Medicine (EFLM). Christos Kroupis is an Asst. Prof. of Clinical Biochemistry and Molecular Diagnostics in Attikon University General Hospital in Athens, Greece.

He has authored or co-authored 60 papers that have obtained over 1200 citations (h-index 18).

His current research interests are: Biomarkers for cervical neoplasia, Cancer, glaucoma and macular degeneration genetics.

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ST2 AS A NOVEL PROGNOSTIC MARKER IN END-STAGE RENAL DISEASE PATIENTS ON HEMODIAFILTRATION

Evgenija Homšak

University Clinical Centre Maribor, Department of Laboratory Diagnostics, Maribor, Slovenia

Background: Patients with end-stage renal disease (ESRD) are prone to severe heart failure (HF) and to several life-threatening events. Therefore, the ability to assess disease prognosis and the risk of short-term events or death is of great importance. ST2 (growth STimulation expressed gene 2) is a member of the interleukin-1 receptor family that is expressed as a transmembrane (ST2L) and soluble isoform (sST2). Plasma sST2 is expressed by fibroblasts in the heart and elevated in response to heart failure (HF) disease or injury, and it is a direct participant in the fibrosis or cardiac remodeling process. sST2 is a novel prognostic biomarker of HF risk assessment with growing importance in the prediction of cardiovascular events. The role of sST2 as a potential new prognostic marker in ESRD patients is not yet known. The aim of our study was to assess the prognostic value of sST2 in ESRD patients on hemodiafiltration (HDF) and compare it with NT-proBNP, an established prognostic marker for HF and renal disease.

Methods: A total of 123 ESRD patients on HDF were prospectively followed up from the date of the sST2/NT-proBNP measurement until their death or maximally up to 829 days. Blood was sampled by venepuncture before HDF. sST2 concentrations were measured using a manual ELISA method. Primary endpoint was the composite of all-cause death. Patients were divided into a low sST2 group (<35 ng/mL) or a high sST2 group (<35 ng/mL) according to their measured sST2 concentration at the start of the study. Kaplan-Meier survival curves, Cox regression model and ROC analyses were used in statistical analysis.

Results: During follow-up 32 (26.0%) patients died (all cause mortality). Median (IQR) sST2 serum concentrations of survivors and deceased were 26 (24-29) and 36 (28-59) ng/mL, respectively. The Kaplan-Meier survival analysis showed that survival rate of the high sST2 group was statistically significantly lower than of the low sST2 group (P<0.01). Cox regression model for sST2, using a dichotomized (cut-off = 35 ng/mL, hazard ratio (HR) (95%CI) = 2.72 (1.50-4.90), P=0.001) and continuous approach with log-transformed values in univariate (HR (95%CI) = 17.35 (4.84-62.22), P<0.001) and multivariate analysis (HR (95%CI) = 7.19 (1.89-27.38), P=0.004) showed that sST2 alone and in combination with NT-proBNP can predict all cause mortality.

Conclusions: sST2 has confirmed prognostic value and is independent of renal function and of HDF treatment. It could be a useful independent prognostic marker for stratifying ESRD patients on HDF at high risk for life-threatening events, hospitalisation and death, especialy in combination with NT-proBNP.

Evgenija Homšak, MPharm, Ph.M.

EuSpLM has graduated at the Faculty of Pharmacy, University of Ljubljana, completed a specialization in the field of medical biochemistry (Medical biochemistry specialist) and finished masters postgraduate study (Ph.M.) at the Faculty of Pharmacy, University Ljubljana. Since 2007 she is registered as European Specialist of Clinical Chemistry and Laboratory Medicine (EuSpLM).

She is the head of the laboratory for hormone and autoimmune disease diagnostics at the Department of Laboratory Diagnostics in University Clinical Centre Maribor, Slovenia.

She is an associate researcher at University Clinical Centre Maribor and has been / is active involved in several research projects, participated in many professional national and international meetings and congresses, as a lecturer and as a member/president of organizing and scientific committees as well. Her main research interests are in the field of

autoimmunity, biomarkers and hormone diagnostics. She published several abstracts and articles in national and international journals. As the assistant for the field of Clinical Biochemistry, she is actively involved in education process at the Medical Faculty, University Maribor.

From 2007-2011 she was the secretary and from 2011-2017 she was the president of the Slovenian Association for Clinical Chemistry and Laboratory Medicine (SZKKLM). Since 2017 she is the past president of Slovenian Association for Clinical Chemistry and Laboratory Medicine and national representative of IFCC.

She is also active in European Federation for Clinical Chemistry and Laboratory Medicine (EFLM). From 2011-2017 she was the national representative and was the member of the Scientific and Organizing Committee for the organization EFLM post-graduate education (EFLM Postgraduate Courses in Clinical Chemistry and Laboratory Medicine). Since 2015 she has been a member and since 2016 she is the chair of EFLM working group for continuing postgraduate education and congresses (WG-CPE) at EFLM Committee of Education and Training. She is also the member of the Commission for specialization at the Chamber of Laboratory Medicine Slovenia.

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LIQUID BIOPSY: PAST, PRESENT AND FUTURE

Prof. Dr Tomris Ozben

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Board of Directors, IFCC Foundation for Emerging Nations (FEN)
Akdeniz University, Medical Faculty, Department of Clinical Biochemistry Antalya, Turkey

Recent technological advances have made it possible to use blood and plasma as a "liquid biopsy". Nucleic acids are shed from several organs and tissues into circulation. Intensive research is ongoing to investigate circulating cell free DNA (cfDNA) as a diagnostic and prognostic biomarker in several disease conditions. Analysis of cfDNA can be used for prenatal testing, as an early marker for organ rejection, in oncology and as an indicator of pathogen infections, neurodegenerative, autoimmune and cardiovascular diseases. Analysis of cell-free fetal DNA released from the fetus into maternal blood is an established method for non-invasive prenatal testing (NIPT). Examination of fetal DNA can uncover point mutations and aneuploidy responsible for genetic disorders as early as seven weeks following conception. The genomic profiles of cancer patients are highly variable which dramatically influence the development of the disease and the efficacy of potential treatments. Personalized healthcare employs molecular diagnostics to test each patient's genomic variants as a guide for best treatment. Analysis of circulating tumour DNA (ctDNA) and circulating tumor cells (CTC) has made a revolution in molecular diagnostic and prognostic biomarkers in cancer. Clinical implications of ctDNA and CTC are recent and rapidly developing research topics. Several studies have shown the potential role of ctDNA and CTC levels shed by tumors into the plasma of cancer patients in the assessment of different malignancies as a prognostic and predictive tool for early diagnosis and early intervention, clinical management and follow-up of cancer patients identifying specific genomic alterations to guide therapeutic selection, monitoring therapeutic responses, and detecting recurrence. Blood is a readily obtained, repeatable clinical sample; whereas serial tumor biopsy is often challenging, more expensive and not without risk. Instead of extensive imaging and invasive tissue biopsies, liquid biopsies can be used for screening of tumors that are not yet visible on imaging and before symptoms arise and to guide cancer treatment to detect disease progression or treatment resistance. I will present an overview of the exciting developments in this area.

Prof. Dr Tomris Ozben, Lab. Specialist, Ph.D., D.Sc. is a full professor at the Dept. of Clinical Chemistry, Faculty of Medicine, Akdeniz University, Antalya, Turkey. She is the current Treasurer of IFCC and member of the Board of Directors of IFCC Foundation for Emerging Nations (FEN) and past-President of the Balkan Clinical Laboratory Federation (BCLF). Over her tenure at Akdeniz University, she has been the Director of Central Laboratory, Akdeniz University Hospital, Vice Rector and Head of the Dept. of Clinical Biochemistry. Her research interests include identification of early biomarkers for diagnosis and prognosis of cancer, and cardiovascular diseases. In 2003, she received the "Outstanding Service" award and 2006 "Science" award of Akdeniz University. In 2002, she received American Association of Clinical Chemistry (AACC) Van Slyke Society and in 2005 AACC TDM/Toxicology Division awards. In 2016, she received "Distinguished Abstract for Scientific Excellence" award of AACC's National Academy of Clinical Biochemistry (NACB) presented as a hot topic lecture in Clinical Chemistry. She has been Chair or Member in many Scientific Organizations. She has been member of the Editorial Boards of several Scientific Journals. She has published over 160 papers, 10 book chapters, edited several books and invited to speak at more than 200 international conferences. She took part in the organization of several international congresses, conferences, courses and workshops such as WorldLabs, EuroMedLabs, IFCC General Conferences, FEBS-IUBMB Advanced Courses and Workshops.

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LANDSCAPE OF BREAST CANCER GENES

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Breast cancer (BC) is the most prevalent malignancy and the second leading cause of death in women. The etiology behind developing BC is multifactorial with many risk factors, one of the most important being a positive family history and a genetic predisposition. It is estimated that around 10% of BCs are hereditary due to mutations in autosomal dominant genes and up to 25% are familial with more BC cases in a family than expected, but with no specific pattern of inheritance. Several high and moderate-penetrance genes have been associated with BC risk, the two key players being BRCA1 and BRCA2 genes. Still, around 50% of cases associated with a family history for BC remain unexplained.

Over the last decade, efforts to explain the missing heritability of BC have been focused on discovery of other moderate and high-risk genes using the next generation sequencing (NGS), as well as identification of common low-risk genetic variants using genome-wide association studies (GWAS). Currently, a number of novel moderate-risk genes have been suggested to play a role in BC development. Many common genetic variants have also been identified that explain up to 18% of BC heritability, suggesting that BC is a complex, polygenic disease.

The presentation will summarize the well-known and novel high and moderate-penetrance BC genes, as well as low-risk genetic variants associated with BC. The Macedonian BC association study will also be presented, including the NGS results, obtained using a panel of 94 cancer genes among more than 400 BC patients.

Prof Dijana Plaseska-Karanfilska has received her MD degree from the Medical Faculty in Skopje and PhD from the Medical Faculty in Maastricht, the Netherlands. She is employed at the Research Centre for Genetic Engineering and Biotechnology "Georgi D Efremov", Macedonian Academy of Sciences and Arts, Skopje, R. Macedonia where she holds a position of Full Professor and Head of laboratories for Genomics and Molecular Diagnostics. She is also elected professor at the University "Ss. Cyril and Methodius", Skopje and participates in lecturing of biomolecular subjects within the undergraduate, Master's, PhD studies and specialization in Clinical Laboratory Genetics. She has successfully mentored six PhD and ten MSc students.

She has been engaged in the molecular diagnostics of inherited, malignant and infectious diseases and has contributed to the molecular characterization of different monogenic diseases in the Republic of Macedonia and translation of a number of molecular genetic tests to clinical practice. Her recent research interest focuses in the fields of rare diseases, breast cancer and reproductive genetics.

She has coordinated several international and national scientific projects, including the EU FP7 REGPOT project that has strengthened the national research capacities in the fields of genomics and proteomics. She has published more than 100 papers in peer-reviewed journals, several book chapters and has participated with more than 160 presentations on different scientific events.

She is editor of the Balkan Journal of Medical Genetics, president of the Macedonian Society of Medical Genetics, member of the Board of the European Society of Human Genetics, member of the COST Scientific Committee and a coordinator for Macedonia in the European Biotechnology Thematic Network Association.

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CLINICAL MANIFESTATIONS AND LABORATORY DISORDERS IN EARLY DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Introduction: Systemic lupus erythematosus (SLE) is a chronic, multifaceted autoimmune inflammatory disease that can affect any part of the body. The Systemic Lupus International Collaborating Clinics (SLICC) group revised and validated the American College of Rheumatology (ACR) classification criteria in order to improve clinical relevance and incorporate new knowledge regarding the immunology of SLE.

The aim of this study was to examine the symptoms, clinical manifestations, laboratory disorders and fulfillment of the SLICC criteria in early diagnosis of SLE.

Methods: One hundred patients with diagnosis of SLE were enrolled in the study. We analyzed the general conditions, initial symptoms, clinical manifestations and specific and non-specific laboratory parameters at the time of diagnosis of SLE, as well as the presentation of each ACR criteria and the fulfillment of new SLICC criteria.

Results: There were 91 females and 9 males. The average time from the onset of the disease to the diagnosis was 10 months. The most frequent presenting signs and symptoms were fatigue (67%), fever (54%), and exhaustion (77%). The most frequent clinical manifestations were photosensitivity (55%), malar rash (48%), arthropathy (83%), leucopenia (47%). Antinuclear antibodies (ANA) were detected in 99% of the patients and were associated significantly with most clinical presentations. New SLICC criteria were met in all patients.

Conclusion: Our results confirm that the SLICC criteria are useful and reliable criteria for the diagnosis of SLE and they can help in early diagnosis of SLE which is a crucial step for better outcome.

Nevena Terzić Stanić was born in Pljevlja, Montenegro, in 1975. She graduated in Medicine in 2001, specialized in Clinical Biochemistry in 2008 and in Clinical Biochemical Rheumatology in 2015 at the University of Belgrade. Since 2011, she has worked at the Department of Clinical Biochemistry of the Clinical Center for Laboratory Diagnostic, Clinical Center of Montenegro, Podgorica, Montenegro. She is a Head of the Department of Laboratory Diagnostic of the Emergency Center, Clinical Center of Montenegro. She has actively participated in many national and international congresses in laboratory medicine. She is the author and co-author of several articles focused on oxidative stress, diagnostics of rheumatology diseases and preanalytical phase of laboratory processes.

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ENHANCING PRECISION MEDICINE THROUGH CLINICAL MASS SPECTROMETRY PLATFORM

Dobrin Svinarov

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Mass spectrometry (MS) could be viewed as one of the major tools that promote the development of precision medicine. Precision medicine (also referred to as personalized medicine), employs patient's genotype and phenotype investigation to establish individually tailored drug treatment. While genetic testing allows the physician to choose appropriate medicine, MS assays provide patient's actual phenotype, with all of the environmental, pharmacological and pathological variables. Therefore, MS is essentially important technology for personalized patient management. LC-MS/MS is today's most utilized analytical platform, but high-resolution MS systems are also employed to resolve challenging demands. The ability of LC-MS/MS to perform panel profiling with simultaneous measurement of bioactive compounds, their precursors and metabolites in a single sample, enormously amplifies the informative value of results, with ultimate improvement of patient care. With over 13 years of experience, our laboratory exemplifies the entrance of LC-MS/MS in medical laboratory with analysis of immunosuppressive drugs, vitamin D status, steroids, anticonvulsants etc. It should be specially emphasized that clinical MS meets chemical and anatomical pathology: MS imaging and I-knife-MS guidance in surgery, although still in research phase, open new horizons for personalized treatment and individualized care. So far MS is the preferred technique in laboratories, where the expertise and larger sample workload provide cost-effectiveness and reliability of results. At the same time, MS platforms, as convenient as routine clinical chemistry analyzers appear on the scene and that will promote much wider application of MS techniques in clinical laboratories in the near future.

Professor Dr. Med. Dr h.c. Dobrin Svinarov is a specialist of clinical laboratory medicine and clinical pharmacology, Head of Clinical Laboratory and Clinical Pharmacology at Alexandrovska University Hospital, Chairman of the Department of Clinical Laboratory and Clinical Immunology at the Faculty of Medicine, Medical University of Sofia, and President of the Bulgarian Society of Clinical laboratory. He is academician of the Bulgarian Academy of Sciences and Arts, and President of its General Assembly. Professor Svinarov has more than 30 years of experience in the measurement of drugs as a guide to therapy, and has been responsible for the development of wide range of chromatographic and LC-MS/MS assays to monitor variety of therapeutic agents. In 1987 he specialized therapeutic drug monitoring at National Institutes of Health, Bethesda MD, and at Cleveland Clinic Foundation, Cleveland OH, USA. In 1990 he became one of the co-founders of IATDMCT, and in 1997-1999, served as Councilor of the Executive Board of the Association. In 1999-2000 professor Svinarov was granted a one year Stecker Scholar Stipend and performed the duties of visiting professor of pediatric clinical pharmacology at Columbus Children' Hospital, Ohio State University, OH, USA. After his return in Bulgaria he was involved in definitive clinical trials and pharmacokinetic studies of a broad range of new drugs and established the first General Clinical Research Center for the Medical University of Sofia. Since 1997 now professor Svinarov serves as National Referee and Consultant for Clinical Laboratory Medicine at the Ministry of Health. His research interests are in the field of laboratory medicine, therapeutic drug monitoring and clinical pharmacology, and include the development of mass-spectrometric assays for the measurement of therapeutic drugs and endogenous markers of organ damage and dysfunction, proteomic research, pharmacodynamic biomarkers, and personalized medicine. Professor Svinarov and his colleagues received continuous funding from sponsors such as the National Research Foundation of the Bulgarian Ministry of Education Science, Medical University of Sofia, Volkswagen Foundation, and Industry. He and his collaborators authored over 350 scientific works, including books and book chapters, publications in peer reviewed journals and invited lectures all over the world. He is an active member of several national and international scientific societies, and serves as reviewer and Editorial Board member of several peer reviewed journals, including Therapeutic Drug Monitoring. Professor Svinarov performed the duties of Bureau member of WASPaLM for the period 2013-2017 year.

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PHARMACOGENETICS IN CARDIOVASCULAR DISEASE: WHERE DO WE STAND?

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In the era of personalized medicine, with the increasing understanding of the molecular mechanisms behind inter- and intraindividual variability in drug exposure and drug effects, great expectations have been posed on pharmacogenetics as a tool for individualized pharmacotherapy. Over the past decade, a significant progress has been made in the field of cardiovascular pharmacogenetics. The use of genomic markers for optimally individualizing pharmacotherapy has a huge potential to improve healthcare by maximizing effective therapy, predicting and avoiding adverse drug effects. This presentation will try to summarize current knowledge about well-documented associations between key genetic polymorphisms and variability in pharmacokinetics, response to treatment, toxicity of major cardiovascular medications such as antiplatelet agents, oral anticoagulants, statins, beta-blockers, etc. Clopidogrel, commonly prescribed antiplatelet drug, is a good example of the development and potential application of pharmacogenetics in clinical medicine. The pharmacogenetics of clopidogrel used in cardiology practice will be discussed in more detail, with focus on additive value of clopidogrel-pathway gene polymorphisms to clinical risk-stratification of patients with ST-segment elevation of myocardial infarction undergoing primary percutaneous coronary intervention assessed in prospective single-center study in our institution. With the knowledge and tools available today, we can personalize drug therapy and achieve this at reasonable costs. Following the growing and widespread interest in the cardiovascular pharmacogenetics field, laboratory medicine can play an important role in providing this service for health care professionals and patients.

Sanja Stankovic is the Director of Center for Medical Biochemistry in Clinical Center of Serbia. She obtained her BSc, MSc, specialization in medical biochemistry, subspecialisation in clinical enzymology, specialization in pharmacoeconomics and pharmaceutical legislation and Ph.D. from Faculty of Pharmacy University of Belgrade in Belgrade. She was employed at the Faculty of Pharmacy University of Belgrade for 17 years. She is assistant professor in the Faculty of Pharmacy, Novi Sad and Senior Research Associate at Faculty of Medicine University of Belgrade in Belgrade. She is the President of Serbian Committee for Biochemistry-Republic of Serbia Ministry of Health, President of the Commission for taking the state exam for graduate pharmacists-medical biochemists, member of Committee for assessment of new health technologies etc. and President of the Assembly of Serbian Chamber of Biochemists. She is the General Secretary and Board Member of European Society of Pharmacogenetics and Personalized Therapy (ESPT), eJIFCC journal Editorial Board Member and EFLM Task Group Cardiac Markers Member. She has been serving as Balkan Clinical Laboratory Federation Secretary and corresponding member of EFLM WG of Cardiac Markers, President of the Committee for Cooperation with IFCC, EFLM, BCLF and related national organizations, Member of Scientific Committee and Member of Congresses and Conferences Committee in Society of Medical Biochemists of Serbia. She is founder and President of Serbian Society for Clinical Laboratory Medicine and Science (SCLM), President of Serbian Biomarker Society (SERBIS) and President of Serbian Society of Pharmacogenetics and Personalized Therapy (SSPT). She is accreditation assessor in the Accreditation Board of Serbia and in Agency for accreditation of health care institutions of Serbia. She is founder and director of international symposium SERBIS (Serbian Biomarker Symposium), and international conference CLAQ (Conference on Medical Laboratory Accreditation and Quality Systems: European Answers). She actively participated in more than 30 scientific and organizational committees of international congresses and conferences, and with ESPT organized European Summer School of Pharmacogenetics and Personalized Therapy in Belgrade. She is actively included in domestic project supported by the Ministry of Education, Science and Technological Development of Serbia "An integral study to identify the regional genetic and environmental risk factor for the common noncommunicable diseases in the human population of Serbia (INGEMA_S), clinical studies and international projects. She has published 70 peer reviewed articles (h-index 12, total citations 456).

ORAL PRESENTATIONS

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ACCREDITATION OF MEDICAL LABORATORIES: ISO STANDARD 15189-BENEFITS

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One and the most important of the priorities in laboratory medicine is improvement of quality management system for patient safety. The laboratory accreditation system is important for the acceptance of test results nationally and internationally. The strategic plans of IFCC and EFLM include focusing on accreditation of labs based on ISO standards and cooperation with European Accreditation and national accreditation bodies. IFCC and EFLM recognized that ISO 15189:2012 encompasses all of the assessment criteria specified in the policy of quality.

According to the EC REGULATION No 765/2008 "The particular value of accreditation lies in the fact that it provides an authoritative statement of the technical competence of bodies whose task is to ensure conformity with the applicable requirements". To ensure continued compliance, accredited laboratories are regularly reassessed to check that they are maintaining their standards of technical expertise. These laboratories will also be required to participate in regular proficiency testing programs (known as external quality assurance programs or EQAS) as an on-going demonstration of their competence. The need to drive up the quality of care for patients, whilst delivering efficiency and productivity, is a key principle for regulators of healthcare services. Accreditation can be used as a tool to support the commissioning or specification of medical laboratory services that are technically competent, safe and reliable, and that continually improve the experience for patients by providing an independent assurance of quality and safety that supports world-class decisions on how to deliver better care and value for patients, providing a mechanism for measuring quality improvement, supporting consistency in the quality of care and encouraging innovation. Accreditation requires that the laboratory assesses the value and relevance of the testing in relation to patient's clinical management. It demonstrates that medical laboratories comply with an international standard, confirming that: there is consistency in the quality of care; comparability of tests results; the service has up-to-date-technologies and its procedures and techniques reflect current best practice; and staff providing the service are competent to undertake the tasks they perform. Accreditation provides proof that a laboratory complies with the best practice. It also offers authoritative assurance of the technical competence of a laboratory to undertake specified analysis or measurements according to validated methods. Accreditation provides an opportunity for external perspectives on laboratory practice. Additionally, it can prevent the unnecessary duplication of information gathering on performance often required by regulatory bodies, encourages the sharing of best practice, stimulates innovation, reduces risk and provides international recognition. Laboratory services will be the centre of attention regarding quality due to their wide-ranging impact on the care for patients.

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CLINICAL CHEMISTRY IN THE REPUBLIC OF MACEDONIA: WHERE DO WE STAND?

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Laboratory medicine practice varies across the European Union member states. Clinical chemistry (medical biochemistry) practice in the Republic of Macedonia (still not a member state) is regulated by the Ministry of Health according to the Law on Health Protection of the Republic of Macedonia.

The four year specialization syllabus was made by the Department of Biochemistry, Medical Faculty Skopje in 2008, according to the EU4 Directive and is still in force. Eligible to enter the specialization program are medical doctors and pharmacists. Completing the specialization program and the final exam are requirements for issuing the license for independent clinical chemistry practice by the Macedonian Doctor's Chamber. The common training meets the requirements for the perspective professional movements across EU borders for the medical doctors. In the era of the new analytical techniques, use of statistics, it will be of great importance to update the present syllabus according to the fifth version of the European Syllabus for postgraduate training for specialists in Laboratory Medicine and the needs of our country. The revised training program should call attention towards the structure of the program, as well as towards the expected responsibilities of trainees and trainers. The Medical Faculties providing the training in medical biochemistry in the Republic of Macedonia should be included in updating the syllabus in order to have equally trained professionals who can face the new requirements in laboratory medicine in the Republic, but also qualified specialists prepared for the free movement across the European Union borders in the future.

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ASSOCIATION OF RESISTIN AND ITS RECEPTOR ADENYLATE CYCLASE-ASSOCIATED PROTEIN 1 WITH CHRONIC KIDNEY DISEASE

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Aim: Human resistin is a proinflammatory cytokine, which exerts important proatherogenic effects. Patients with chronic kidney disease (CKD) have extremely elevated risk of cardiovascular disease (CVD) development. CAP1 (adenylate cyclase-associated protein 1) is a newly identified receptor for human resistin, but CAP1 has never been previously evaluated in patients with CKD. Therefore, the aim of this study was to determine peripheral blood mononuclear cells (PBMCs) resistin and CAP1 gene expression as well as resistin plasma concentrations and to evaluate their implication in CKD.

Methods: This study included 27 healthy subjects (CG) and 33 patients with CKD on hemodialysis. PBMCs CAP1 and resistin gene expression levels were determined by real-time PCR, while circulating resistin was measured by ELISA.

Results: Resistin gene expression was not different between CKD patients and CG. CAP1 gene expression was significantly higher in CKD patients compared to CG (P<0.001). Plasma resistin was significantly higher in CKD patients compared to CG (P<0.001). CAP1 gene expression positively correlated with intima media thickness in patients (P=0.008, ρ=0.453). CAP1 gene expression was upregulated in CKD patients with increased IMT compared to patients with normal IMT (P=0.043).

Conclusions: A significant upregulation of CAP1 gene expression was observed in CKD patients, as well as its association with IMT in these patients, indicating its implication in atherosclerosis development. Furthermore, elevated resistin could exert its proatherogenic effect stronger, and thus contribute to increased risk for cardiovascular complications in CKD patients.

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URINARY NEPHRIN - BIOMARKER FOR EARLY DETECTION OF DIABETIC NEPHROPATHY

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Aim: Diabetic nephropathy (DN) is a common cause of end-stage renal failure. Podocyte specific proteins are deregulated in DN, thus urinary nephrin may be elevated in diabetic patients even before the appearance of microalbuminuria. The aim of this study was to test the significance of nephrinuria in early detection of DN.

Methods: Our study included 90 patients with type 2 diabetes mellitus (T2DM), (n=30 with diagnosed diabetic nephropathy, n=60 without diagnosed nephropathy) and 30 healthy subjects as a control group. According to urinary microalbumin/creatinine ratio,all patients were divided into three groups: normoalbuminuric, microalbuminuric and macroalbuminuric patients. The concentration of nephrin in urine was measured by an immunoenzyme assay, microalbumin with turbidimetric and creatinine with photometric method. Also, we performed an electrophoretic separation of urinary proteins by polyacrylamide gel. In blood sera, we measured a few standard biochemical parameters.

Results: Nephrinuria was found in 100% of diabetic patients with macroalbuminuria, 88% with microalbuminuria, and 82% of patients with normoalbuminuria. A concentration of urinary nephrin was significantly increased in all groups of subjects with T2DM compared to the control group (p<0.05). Nephrinuria correlated statistically negatively with eGFR (r=-0.54, p<0.05). ROC analysis showed that nephrin has high discriminatory power among patients with DN and healthy subjects. The most common type of proteinuria in diabetic patient with macroalbuminuria was tubular proteinuria, while in patients with microalbuminuria was mixed type of proteinuria.

Conclusions: Urinary nephrin is a useful biomarker in the early and non-invasive detection of DN.

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INVESTIGATION OF NECROTIC GENES OF SODIUM FLUORIDE (NAF) IN RENAL CELL LINE

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Aim: Kidneys are the organs that play an important role in fluorine metabolism. This study was planned to investigate the possible role of NaF administration in the NRK-52 kidney line, which causes certain levels of cytotoxicity.

Methods: Rat renal epitelial NRK-52E (ATCC® CRL-1571™) cell line was cultured in standard cell culture conditions. NaF concentrations were prepared in the medium (50, 100, 250, 500, 1000, 2000, 5000, 7500, 10000 and 20000 µM). MTT assay was performed to detect the cytotoxic effect of NaF in NRK-52E cells. The cells treated with NaF at IC50 value dose were divided into 3 groups on time (3, 12 and 24th hours). Then, total RNA isolation followed by cDNA isolation was performed. Expressions of the necrotic genes (RIP 1 and RIP 3) were determined by RealTime-PCR.

Results: Ripk1 gene was decreased at 3 and 12 hours and increased at 24 hours. A significant difference was detected between groups in terms of gene expression pattern. Ripk3 was decreased at 3 hours and increased at 12 and 24 hours. The change in the 24 hours was significantly higher than in the other groups.

Conclusions: In conclusion, this study was conducted to elucidate the cause of NaF-induced cell death in renal epithelial cells (NRK-52E). It has been suggested that genes involved in necrotic mechanisms are gradually up-regulated and necrotic genes become more active.

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DETERMINATION OF METHYLGLYOXAL LEVELS VIA ULTRA-PERFORMANCE LIQUID CHROMATOGRAPHY

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Aim: Methylglyoxal (MG), an alpha-oxoaldehyde, is mainly formed from intermediates of glycolysis such as dihydroxyacetone phosphate (DHAP) and glyceraldehyde-3-phosphate (G3P). As a highly reactive electrophilic compound, MG is a major precursor of advanced glycation endproducts (AGEs). Oxidative stress and glycation reactions play a major role in the development of chronic degenerative diseases and in aging processes. The aim of this study was to present a simple, reliable and rapid method for determination of methylglyoxal levels via chromatography.

Methods: Methlglyoxal levels were detected by chromatographic separation on a C18 column with a mobile phase consisting of acetonitrile:water (4:1, V: V) using isocratic elution at a flow rate of 2 ml/min. For sample preparation, 100 µL of perchloric acid was added to 200 µL of the sample and vortexed for 5 sec-

onds. 250 µL of orto-phenylenediamine was added to this mixture and vortexed again. 200 µL of internal standard (5-methylquinoxaline) was added. The mixture was incubated at room temperature for 24 hours in the dark. At the end of incubation, the sample was centrifuged at 4°C for 12 minutes at 12.000 rpm and 100 µL of the supernatant was injected into the system.

Results: Total run time was 10 minutes at 315 nm UV wavelength. The detection limit was 1 µmol/L.

Conclusions: The short analysis time, high sample throughput and the small amount of sample required make this method very suitable for routine analysis in the clinical setting. This method may be routinely used for determining the methylglyoxal levels.

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LUTEIN AND VITAMIN E LOADED PLGA NANOPARTICLES - A PROMISING ANTIOXIDANT DEFENSE

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Aim: Currently, poly (lactic-co-glycolic acid) (PLGA) is one of the most effective biodegradable polymeric nanoparticles (NPs) approved by the US FDA as delivery system for many drugs in the treatment of cancer, osteoporosis, cardiovascular and neurodegenerative diseases. The aim of our study was to evaluate the antioxidant effect of PLGA NPs loaded lutein and vitamin E in Wistar male rats that received hypercaloric diet during 21 days.

Methods: PLGA NPs were prepared by emulsion-solvent evaporation method. Fifteen Wistar male rats were divided into 3 groups, each containing 5 rats that received daily hypercaloric diet (group C), hypercaloric diet with PLGA-vitamin E (group E) and hypercaloric diet with PLGA-lutein (group L) (daily 50 mg/kg body weight). Oxidative stress biomarkers such as glutathione (GSH), malondialdehyde (MDA), total antioxidant capacity (TAC) advanced human oxidation protein products (AOPP) and vitamin E were analyzed in liver tissue homogenates using ELISA and spectrophotometric methods.

Results: Our results showed important modifications in redox status in liver revealed by statistically significant lower values for MDA and AOPP and higher values for GSH and TAC in groups L and E versus group C ($p<0.01$). Results of our study revealed statistically significantly increased levels of vitamin E in group E versus group C ($p<0.01$).

Conclusions: The PLGA NPs loaded lutein and vitamin E may be considered as a promising approach to enhance the antioxidant defense system in treatment of many diseases with high efficacy and few side effects.

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MATERNAL THROMBOCYTOPENIA IN PREGNANCY: AN INTERDISCIPLINARY CHALLENGE

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Thrombocytopenia is the second (after anemia) most common abnormality of the complete blood count in pregnancy among European women. The incidence is 6.6% to 11.2%, with gestational thrombocytopenia being the most leading cause accounting for 75% of all cases. Thrombocytopenia is most pronounced in the third trimester, where the platelet count usually remains above 110×109/L in otherwise healthy pregnant cases. The differential diagnosis of thrombocytopenia is highly important, as the risk of bleeding for both mother and child and the risk of severe maternal complications vary from one underlying disease to another, as does the required treatment. Women with low platelet counts in pregnancy are generally less symptomatic due to the procoagulant state induced by increased levels of fibrinogen, f. VIII and von Willebrand Factor (VWF), suppressed fibrinolysis and reduced protein S activity. Diagnostic assessment of thrombocytopenia in pregnancy is needed in cases with antenatal thrombocytopenia, unusual appearance in the first or second trimester, the platelet count less than 80×109/l at any time in pregnancy or a bleeding tendency. In the first and second trimesters, low platelet counts are most likely due to an immune process or a platelet production defect. Disseminated intravascular coagulation (DIC) and HELLP (hemolysis, elevated liver enzymes and low platelet counts) are one of the most serious complications that occur in pregnancy. A diagnostic approach and management of thrombocytopenia during pregnancy are summarized in this presentation. Non-pregnancy specific causes will only be discussed with respect to specific pregnancy-related differences in management.

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THYROID FUNCTION TESTS DURING PREGNANCY: THE IMPORTANCE OF SPECIFIC REFERENCE RANGE ESTABLISHMENT

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Aim: The proper function of the thyroid gland during pregnancy is important not only for the pregnant woman, but also for the normal fetus development. For an adequate interpretation of test results, reliable reference intervals should be established and re-evaluated periodically. As we have changed the immunoassay method, our purpose was to validate the manufacturer's reference range for TSH and FT4, as first –line tests, and to compare the results with the working, reference interval for pregnant women.

Materials and methods: The reference population was selected from pregnant women without history of thyroid pathology. For validation of the manufacturer's reference interval in pregnancy, we followed the CLSI (C-28-A3) protocol. TSH and FT were assessed by IMMULITE 2000 chemiluminescent immunoassay system. The values for each analyte were expressed as median. To compare the differences between trimesters, Mann-Whitney U test was used. The reference values were obtained by nonparametric method.

Results: For TSH we did not find significant trimester differences (p=0.797). Our median was higher in comparison with manufacturer's (1,9 mIU/L vs. 1,1 mIU/L), and we found 4 values outside the proposed reference interval. For FT4 our findings indicated significant differences between the first and second and third trimester (p=0,002) and lower medians (11.6 pmol/L vs. 16.1 pmol/L and 10.3 pmol/L vs. 13.9 pmol/L).

Conclusion: Following the C-28-A3 protocol, we did not verify the reference range proposed by the manufacturer. Further activities towards establishment of own TSH and FT4 trimester specific reference values, with appropriate number of samples should be undertaken.

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CALCIUM, PARATHYROID HORMONE, AND BONE MINERAL DENSITY IN PRIMARY AND SECONDARY HYPERPARATHYROIDISM

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This study covered 94 patients (average age 63.73±10.5) from Osteoporosis Cabinet of Institute for Physical Medicine and Rehabilitation "Dr Miroslav Zotović". The patients had a higher blood values of the parathyroid hormone in the period from 2012 to 2016. Based on the ionized calcium (Ca++) levels and total serum calcium levels (total CaS), preliminary diagnosis of the primary hyperparathyroidism was established in 47.87% of the patients (Ca++=1.45±0.10 mmol/L, total CaS = 2.72±0.04 mmol/L; PTH = 156.45±124.00 pg/mL), and secondary hyperparathyroidism in 52.13% ones (Ca++ = 1.27±0.04 mmol/L, total CaS = 2.33±0.12 mmol/L; PTH = 87.36±30.06 pg/mL). There was a statistically significant difference among the examined parameters of these two groups of patients: Ca++ - $t(92) = 12.06$, $p < .01$; total CaS - $t(92) = 10.80$, $p < .01$; PTH - $t(92) = 3.80$, $p < .01$. The PTH values did not show significant correlations with Ca++ and total CaS levels in patients with primary and secondary hyperparathyroidism, respectively. Primary hyperparathyroidism was commonly established in patients with osteoporosis (28.72%), and then in ones with osteopenia (15.96%). Unlike that, secondary hyperparathyroidism was commonly established in patients with osteopenia (22.34%), and then in ones with osteoporosis (21.28%). Statistically significant correlation was shown between PTH and Ca++ ($p < .01$) in patients with normal DXA medical report and osteopenia, and with CaS in patients with osteopenia ($p < .05$).

Conclusions. The values of PTH, Ca++, and CaS are higher in patients with primary hyperparathyroidism and the percentage of those patients was more in the zone of osteoporosis.

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ASSOCIATION OF SERUM LEVELS OF ADIPOKINES AND INSULIN RESISTANCE IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Objective. With the many recent advances in the medical world, vast changes are taking place in our growing knowledge of the physiological aspects of almost all the tissues and organs of the human body. One of the most prevalent topics of discussion is the question of obesity and its effect on the metabolic changes in the human body. The original classical role of adipose tissue as an energy storage organ has been greatly modified. We now know that it is an endocrine organ, producing adipokines which modulate metabolic processes in the body. Further, these adipokines may interact with long term energy modulators like insulin. Polycystic ovary syndrome (PCOS) is the most common endocrinopathy associated with infertility and metabolic disorder in women of reproductive age. PCOS is often connected with obesity and insulin resistance.

Aim. The purpose of this study was to evaluate whether the levels of adipocytokines (adiponectin, and leptin) are different between women with PCOS and healthy group of women. Furthermore, we evaluate correlations with other metabolic parameters, such as anthropometric measures, indexes of insulin resistance and lipid markers.

Material and Methods. The study included 89 women diagnosed with PCOS set by the Rotterdam criteria and 60 healthy women. Serum levels of adiponectin and leptin had been taken in all woman involved in this study. Obesity measurements (weight, waist and hip circumference) were also evaluated.

Results. We found statistically significant differences among adiponectin and leptin levels between PCOS women and healthy controls ($p<0.001$). Women with PCOS presented higher, triglyceride, and LDL levels than women without PCOS ($p<0.001$). A significant negative correlation for adiponectin, and significant positive correlation for leptin was found with BMI, and waist circumference ($p<0.001$). A significant positive correlation for leptin was found with indexes of insulin resistance ($p<0.001$).

Conclusion. Given the abnormal adipokine profile in women with PCOS irrespective of the presence or absence of obesity, PCOS may reciprocally influence the secretion of adipokines. Adipokines may thus serve as an endocrine link between obesity and PCOS. Identification of women with altered adipokine expression as putative markers of possible metabolic and cardiovascular complications would be useful for setting up preventive strategies by life-style changes and/or use of insulin- sensitizing agents.

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ASSOCIATION ANALYSIS OF GENETIC VARIANTS WITH TYPE 2 DIABETES RISK AND RELATED TRAITS

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Background. Type 2 diabetes (T2D) is a polygenic disease, and numerous studies have identified about 120 genetic loci involved in the pathophysiology of this disease. This is the first study that investigated the impact of genes that literature proposed as a candidate for T2D in the populations from Bosnia and Herzegovina and Kosovo. Selected variants of candidate genes that we analyzed in our study, are associated with dysfunction and reduction of β cell mass, while some variants are associated with obesity.

Aim. In the present study, we examined the impact of selected candidate gene polymorphisms on the risk of developing T2D, and their association with clinical and biochemical indicators of disease.

Matherial and methods.The study included 638 patients with T2D and prediabetes and 360 healthy subjects as a control group recruited at the Clinical Centre University of Sarajevo, University Hospital of Clinical Centre in Banja Luka, General Hospital in Tešanj and Health Centre in Prizren, from both sexes, aged from 40 to 65 years. Genotyping of analyzed polymorphisms was performed by MassArray Sequenom iPlex

platform in cooperation with Diabetes Centre in Lund University (Malmo, Sweden), and RT-PCR method in cooperation with the Department of Clinical Chemistry, F aculty of Pharmacy, University of Ljubljana (Ljubljana, Slovenia) and Clinical Centre of Charles University (Hradec Kralove, Czech Republic).

Results. of the study confirmed the correlation of analyzed gene polymorphisms with the most significant clinical and biochemical indicators of T2D, especially with glycemic control markers, markers of insulin resistance and status of pancreatic β-cell, and also with markers of inflammation and obesity.

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ELEVATED SERUM ISCHEMIA MODIFIED ALBUMIN LEVELS IN PATIENTS WITH BREAST CANCER

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Aim: Worldwide breast cancer is the most common invasive cancer in women. The incidence of breast cancer is very high in western countries. Ischemia-modified albumin (IMA) is produced by human serum albumin (HSA) which local structure differs when it passes through ischemic tissues. Local tissues can produce oxidative stress products when myocardial ischemia exists, and the N-terminal amino acid sequence of albumin is oxidatively modified, which results in IMA production. The aim of this study was to investigate serum ischemia modified albumin levels in patients with breast cancer.

Methods: A total of 93 healthy controls and 130 patients with breast cancer were enrolled in the study. 50 µL of cobalt dichloride reagent was added to 200 µL of serum and incubated for 10 minutes. During the incubation period, cobalt bound to N-terminal of the unmodified albumin. Fifty microliters of dithiothreitol (DTT), at a concentration of 1.5 mg/mL, was added as a colorizing agent, and the reaction was stopped 2 minutes later by adding 1.0 mL of 0.9% NaCl. The colored product was measured at 470 nm and compared to a serum-cobalt blank without DTT and reported in absorbance units.

Results: Serum IMA levels were significantly higher in breast cancer patients - 0.66 (0.31-3.30) compared to healthy controls - 0.62 (0.19-1.31) (p=0.031).

Conclusions: Cancer attributes to oxidative stress in cells and serum ischemia modified albumin levels might be considered as an oxidative stress biomarker for patients with breast cancer.

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TELOMERASE TARGETED THERAPIES IN CANCER AND AGING

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Telomerase plays a primary role in the maintenance of telomeres in immortal, germ, and tumor cells in humans, but is lacking in most somatic cells and tissues. Hence, telomeric ends shorten with time and stress, contributing to aging and age-related diseases. On the other hand, overexpression of telomerase confers limitless replicative potential to tumor cells. Telomerase is expressed in more than 85% of human tumors and the level of its activity is higher in advanced and metastatic tumors, making it highly attractive therapeutic target.

6-thio-2'-deoxyguanosine, a nucleoside analogue modified from 6-thioguanine is recognized by telomerase and incorporated into telomeric ends, making an immediate change in telomere structure. This disruption leads to telomeric DNA-damage due to telomere uncapping as shown by telomere dysfunction-induced foci (TIFs) formation. 6-thio-dG does not inhibit telomerase but reduces the lag phase by leading to massive and fast cancer cell death. Telomere uncapping agent 6-thio-dG results in rapid and progressive telomere shortening in cancer cells, but has minimal effects on normal human telomerase-silent cells. In vivo studies have shown 6-thio-dG reduced tumor growth rate compared to control and 6-thioguanine treated mice. It does not cause significant toxicity in liver, kidney or gastrointestinal system; besides weight lost and hematological toxicities were not observed in mice during 6-thio-dG treatment. 6-thio-dG represents an attractive chemotherapeutic approach targeting only telomerase expressing cancer cells, sparing normal cells.

Imetelstat (GRN163L) is 13-mer oligonucleotide N3'→P5' thio-phosphoramidate, a direct telomerase inhibitor targeting hTR subunit. Imetelstat has inhibited telomerase activity in multiple cancer cell lines, as well as in vivo xenograft mouse models inducing telomere shortening. The long lag period observed by GRN163L was dependent on initial cancer cell telomere lengths. Patients with relatively long telomeres would require longer treatment periods causing side effects such as thrombocytopenia, as evidenced in some clinical trials.

Maintaining telomere length and integrity is important during tissue regeneration. TA-65 is a telomerase activator extracted from Astragalus membranaceus that can upregulate telomerase activity and lengthen telomeres, therefore is proposed as a treatment for age-related diseases and tissue regeneration. TA-65 has shown to increase both median and short TLs in a statistically significant manner. Pharmacological research also indicates that it has antioxidant, anti-inflammatory, immunoregulatory, anticancer, hypolipidemic, antihyperglycemic, hepatoprotective effects. The strong genetic heritability of telomeres could promote the discovery of telomerase targeted novel therapeutics for personalized medicine.

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ACTIVITIES OF LECITHIN: CHOLESTEROL ACYLTRANSFERASE, CHOLESTERYL ESTER TRANSFER PROTEIN AND PARAOXONASE-1 IN COLORECTAL CANCER

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Aim: As previous studies yielded conflicting results concerning associations between lipid status and colorectal carcinoma (CRC), our goal was to investigate activities of lipid transfer proteins LCAT and CETP as well as PON-1, in attempt to elucidate the role of structural and functional alterations of HDL particles in the onset and progression of CRC. Also, we sought to explore the abilities of these parameters as risk predictors for CRC.

Materials and methods: Our study included 99 patients with CRC and 101 heathy individual. CETP and LCAT activity were measured as previously described by Asztalos. PON-1 activity was assessed kinetically, while parameters of routine lipid status were determined by standard laboratoratory methods.

Results: Lower values of TC ($p<0.001$), HDL-C ($p<0.001$) and LDL-C ($p<0.001$) were observed in patients, including decreased LCAT ($p<0.050$) and increased CETP activity ($p<0.050$). PON-1 activity was diminished in CRC ($p<0.050$). Univariate logistic regression singled out HDL-C (OR =0.218, $p<0.001$) as well as CETP activity (OR =1.010, $p<0.01$) as significant predictors of increased risk for CRC onset. In multivariate logistic analysis they maintained predictive significance (respectively OR=0.145, $p<0.001$; OR=1.010, $p<0.050$) after adjustment for age (OR =1.123, $p<0.001$), gender, LDL-C (OR =0.426, $p<0.001$) and TG levels.

Conclusion: HDL lipoprotein particles could be placed in the center of complex interaction of dyslipidemia, oxidative stress and inflammation during CRC development. Consequently, structural and functional analysis of this lipoprotein might provide important data regarding individual propensity towards CRC development, as well as the disease prognosis and treatment.

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HOW BENEFICIAL ARE MULTI-MARKER PANELS FOR OVARIAN CANCER DIAGNOSIS?

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Introduction. Ovarian cancer is the leading cause of death related to onco-gynecological diseases in women in developed countries. According to the current international guidelines the golden standard for managing this diagnosis is tumor marker CA 125. However, its insufficient specificity and the lack of expression in some histology types have challenged researchers to seek intensively new biomarkers or biomarkers combinations that will improve the early and reliable diagnosis of this disease group.

Aim: To compare the diagnostic sensitivity and specificity of the ROMA algorithm (Risk of Ovary Malignancy Algorithm) with the single use of CA 125 and HE4 in patients with a pelvic mass.

Methods: A total of 1279 women were included in the study: 246 healthy controls; 900 patients with benign ovarian cysts and 133 with histologically proven ovarian cancer. In all women the serum concentration of CA 125 and HE4 was tested via the CMIA method (Architect i2000 system Abbott Diagnostics), and ROMA index was calculated according to their menopausal status. Diagnostic specificity and sensitivity of the markers were calculated using ROC curves, as well as the negative and positive predictive value together with the measured area under the curves (AUC).

Results: When comparing the results of the patients in ovarian cancer group to healthy controls, the diagnostic specificity and sensitivity of the markers were found to be very close for CA125 (specificity 99.1% / sensitivity 93.2%) and ROMA (99.1% / 92.8%) versus 98.8% and 86.4% for HE4. These results did not differ significantly in the subgroups of pre- and postmenopausal women. The comparison of the results in menopausal women with a benign pelvis mass with the ovarian cancer group showed that ROMA was superior to the standalone testing of CA125 and HE4 with AUC= 0.982 and PPV= 100%. The highest NPV was found for CA125= 96.1%. In pre-menopausal patients the largest AUC=0.914 was calculated for CA125, the best specificity for HE4 – 98.5% and best NPV= 100% for ROMA.

Conclusions: The multi-marker approach in the management of patients with pelvic mass improves the diagnostic specificity of the markers and enhances differential diagnosis.

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DEXA AND BONE BIOMARKERS IN THE EVALUATION OF BONE DISEASES IN THALASSEMIA AND HEMOGLOBINOPATHY PATIENTS

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Introduction Osteoporosis in thalassaemia major (TM) represents a prominent cause of morbidity. The mechanism of pathogenesis of bone disease in TM is multifactorial and complicated. Currently bone mineral density (BMD) is the WHO standard for diagnosis of osteoporosis. Bone turnover markers may give information on bone formation and resorption, risk of fracture and response to treatments. Two cytokines, osteoprotegerin (OPG) and receptor activator of nuclear factor kappa B ligand (RANKL), have been identified as important mediators in the pathogenesis of osteoporosis in patients with β-thalassemia major (β-TM).

Aim of the study was to evaluate the level of RANKL and OPG in thalassemia patients and to examine the relation between these parameters and BMD.

Materials and Methods: Serum OPG and RANKLs were measured in 43 thalassemia patients, and 20 healthy age- and sex-matched control subjects, using ELISA methods. BMD was assessed using dual-energy X-ray absorptiometry (DEXA).

Results: In our study, thalassemia major patients showed significantly higher serum level of RANKL (0.26 ± 0.17 vs 0.11 ± 0.09 pmol/l; p = 0.015), lower serum level of OPG (3.24 ± 1.48 vs 10.2 ± 7.5 pmol/l; p = 0.000) than control group. A consequent significantly lower OPG/RANKL ratio was observed in thalassemia major patients. A significant correlation between OPG/RANKL ratio and BMD was also found in our study (OPG vs. T score: r = 0.729; p = 0.000 and RANKL vs. T score: r = - 409; p = 0.000).

Conclusion: This study shows the utility of the laboratory evaluation of RANKL and OPG in detecting bone loss in thalassemia patients.

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EVALUATION OF SERUM LUNG SURFACTANT PROTEIN A (SP-A) AND D (SP-D) AS BIOMARKERS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction. COPD is characterized by progressive loss of lung function. The usage of biomarkers could help in evaluating and preventing COPD severity and prognosis.

Aim. Evaluation of lung SP-A and SP-D, IL6, CRP and some other biomarkers in COPD.

Method. We studied 119 COPD patients (114 males, mean age 69±9 y and 5 females, mean age 70±9 y), 97 smokers (S) and 22 nonsmokers (NS). Emphysema (Emp) was present in 28cases, and respiratory failure (RF) in 87 cases. Clinical chemistry tests, fibrinogen, CRP and Il6 were performed.

Results. Controls' group mean levels of SPA were 22.97±16.28 ng/ml, and of SPD 90 ± 36.8 ng/ml. COPD patients had mean level of IL6 was 31±48ng/ml, of CRP 60±76 mg/L, SPA 47 ± 35ng/ml and of SPD 176±98.6ng/ml all p=0.000. SPA and SPD significantly discriminated S from NS groups. SPA in NS: 31±20 vs. 45± 36ng/ml p 0.017 in S. SPD in NS: 120±73ng/ml vs in S: 170±99ng/ml, p0.002. FEV1, CRP, IL6 and SPA significantly evaluated the presence of RF. SPD showed a negative correlation for presence of Emp in COPD cases (r=-.282, p=0.054). SPA had significant positive correlations with IL6, CRP, fibrinogen, WBC, pCO2, pack of cigarettes, and Sa O2 (r=0.247; r=0.309; r=0.401; r=0.429; r=0.321 and r=0.217, r=-0.274, respectively all p<0.05). SPD significantly correlated with pCO2 and COPD stages, pO2 and SaO2 (r=0.242, r=0.382, r= -0.240 and r= -0.223, respectively, with p<0.05.

Conclusion: Both SPA and SPD were increased in COPD patients. SPA reflects better the inflammatory status and severity of COPD. SPD reflects better the smoking status and the bad prognosis related to presence of emphysema in COPD patients.

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BLOOD PROFICIENCY TESTING STUDY-OUR EXPERIENCE

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Background. Blood proficiency testing studies (B-PTS) are specially designated for use in blood transfusion laboratories as a method for external quality assessment.

Aim. To assess the overall performance of the transfusion-transmisible infection testing based on inter-laboratory comparison of the results obtained from the B-PTS.

Material and method. The B-PTS study was designed, organized and conducted by European directorate

for the quality of medicines (EDQM). Blood testing laboratories in Skopje, Bitola and Stip tested the B-PTS samples and reported the results on the online result data sheet. Each set of B-PTS-samples contained 4 panels: anti-HCV, anti-HIV/p24, anti-Treponema and HBsAg panel. The samples were subjected to serological testing with two assays: enzyme immunoassay with Enzygnost system, Siemens using BEP2000 and chemiluminescent microparticle immunoassay with Architect system, Abbott using Architect i2000.

Results. The laboratories were classified as "satisfactory" for B-PTS: anti-HCV, B-PTS: anti-Treponema and for B-PTS: HIV/p24. Concerning B-PTS:HBsAg testing, laboratories were classified as "unsatisfactory" because two laboratories reported the reactive sample 3 as "Not Reactive" with the Enzignost assay and one laboratory reported the reactive sample 3 as "Not Reactive" with the Architect assay. The root-cause analysis of the non-satisfactory B-PTS results was performed. The single observed non-conformity was that the S/Co (1.22) of the positive control for the Architect HBsAg assay was out of rang (1.65-4.96) for the corresponding reagent lot.

Conclusion. The participation in a B-PTS study provides an objective and independent evaluation of the overall performance of the laboratory. The management of the non-satisfactory PTS results should be documented and performed in a controlled manner. Appropriate corrective and preventive measures should be taken in order non-conformities not to repeat.

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MASS SPECTROMETRY: THE NEAR FUTURE

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Diagnostic era such as clinical biochemistry, clinical microbiology, pathology and radiology, keep pace with the technology in a faster way than other medical areas. With the help of evolving technology accurate diagnosis and treatment of patients progress very quickly. Since the 1990s clinical laboratories use electrophoresis, turbidimetric and nephelometric systems in addition to traditional spectrometry and immunoassays which enable them to analyze specific molecules accurately. These systems are recently more improved and high-volume laboratories can produce serial results using a single carrier line connected to an automation system. In addition to all these improvements, in the last 15 years, with the electrospray ionization (ESI) method in sample presentation to mass spectrometers (MS), especially for relatively large molecules, mass spectrometry finds place in routine laboratories. Gas chromatography (GC), liquid chromatography (LC) can be coupled to MS systems which enable us to measure non-polar and polar small molecules in correct quantities. Trace elements and toxic heavy metals can be measured simultenously with Ion-coupled plasma (ICP)-MS in a single run.

However, despite the progress in technology all analizing methods have three common stages: Isolating the particular analyte from a complex matrix, determining the concentration and reporting the result in proper units. Mass spectrometers determine analyte concentrations more accurately than the other systems. Especially therapeutic drug concentrations, biologic amins, thyroid and steroid hormon measurements are more sensitive in MS measurements. Recent diagnostic algorithms in endocrinology quidelines are aligned particulary with LC-MS/MS results. With these features, in recent years MS systems not only found place in reference laboratories but also in clinical laboratories reporting routine patient results. However, there are several disadvantages that need to be overcome in time: Systems should be purchased by the laboratory which constitutes a serious cost. Isolating the analyte from the complex biological matrix and derivatizing requires more than one chemical preanalytic processes. They have longer throughput time than automated analyzers. In-house method development require one to two years experience.

Despite all these limitations, manufacturers work hard to produce automatic pre-processing and multiplex systems and they create databases (cook-books) for new methods which will accelarate the routine usage of MS systems. Today mass spectrometers are located in the central and specific laboratories however, all laboratory physicians need to follow the cost-benefit calculations for MS systems for their own laboratories.

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DETERMINATION OF SERUM HOMOARGININE IN PREGNANCY WITH LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY

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Aim: L-homoarginine is formed from lysine by arginine glycine amidinotransferase (AGAT) and is mainly produced in the kidney. It has been shown to increase nitric oxide (NO) production by inhibiting either arginase or protein arginine methyltransferases (PRMTs). Thus, increased L-homoarginine concentrations might exert a positive effect on endothelial function.The aim of this study was to determine the levels of homoarginine levels in the serum of pregnant participants who were subjected to binary-quad test.

Methods: A total of 200 pregnant were enrolled. These individuals were divided into four groups: control group with quadruple test (n=50) (Group 1), high-risk group with quadruple test (n=50) (Group 2), control group with binary test (n=50) (Group 3), and high-risk group with binary test (n=50) (Group 4). Participants with known systemic diseases, including cardiovascular disease, renal disease, gastrointestinal disease, pulmonary disease, acute infection, chronic inflammation were excluded. Serum homoarginine levels were analyzed with API 3200 ABSCIEX LC-MS/MS system.

Results: Serum homoarginine levels were significantly higher in group 1 [2.25 (0.47- 7.07)] compared to group 2 [1.47 (0.24- 4.22)] ($p<0.001$) and group 3 [1.34 (0.44- 4.76)] vs group 4 [0.91 (0.45- 2.71)] ($p<0.001$), respectively.

Conclusions: Normal pregnancy is associated with profound hemodynamic changes, including NO-mediated endothelium-dependent vasodilation. The difference of homoarginine concentrations may play a role in pregnancy-associated disorders.

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OXIDATIVE STRESS AND MAGNESIUM DEFICIENCY

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Magnesium deficiency (MgD) has been shown to impact numerous biological processes at the cellular and molecular levels. MgD is accompanied by increased levels of OS markers such as lipid, protein and DNA oxidative modification products. A relationship was detected between MgD and a weakened antioxidant defence. Different mechanisms associated with MgD are involved in the development and maintenance of OS. These mechanisms include systemic reactions such as inflammation and endothelial dysfunction, as well as changes at the cellular level, such as mitochondrial dysfunction and excessive fatty acid production.

It was demonstrated that the lipoprotein fractions (VLDL and LDL) were more susceptible to oxidative damage in MgD. MgD was accompanied by a two-fold decrease in glutathione (GSH) concentration in RBCs. In other types of cells, the overexpression of glutathione transferase has been suggested to be the cause of GSH depletion. After six weeks, the MgD diet led to a significant decrease of both plasma and RBC Mg levels, followed by a marked increase in plasma malondialdehyde and a corresponding decrease in the total number of radical-trapping antioxidant markers. High levels of thiobarbituric acid-reactive substances in the aorta of rats fed with Mg deficient diet correlated with a significant reduction in the activity of superoxide dismutase and catalase. MgD promoted apoptosis in rat hepatocyte primary culture, accompanied by an accumulation of malondialdehyde and a decreased GSH concentration. Low Mg levels result in an accumulation of calcium in the cytosol that contributes to the uncoupling of oxidative phosphorylation as well as the stimulation of other peroxidation pathways. An overproduction of peroxynitrite that also results from MgD further exacerbates mitochondrial dysfunction MgD promotes hypertriglyceridemia and activates lipolysis in fat tissue. In cellular membranes, an increased ratio of Ca to Mg stimulates phospholipase A2 activity, which is responsible for the mobilization of unsaturated fatty acids (UFA) from phospholipids. Free UFA as well as those bound to triglycerides and phospholipids can be easily oxidized by ROS to form lipid hydroperoxides. These hydroperoxides can decompose to form new radicals, thus initiating branching chain reactions that lead to a self-sustaining peroxidation process.

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SEASON VARIABILITY OF SERUM 25-HYDROXY-VITAMIN D LEVELS IN BILECIK PROVINCE: FOLLOW-UP STUDY FROM TURKEY

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Objective: Vitamin D is one of the major hormones involved in phosphorus metabolism in the secosteoid structure. Due to the low number of nutrients containing vitamin D, 80-90% of serum vitamin D is synthesized in the skin with the effect of UVB rays compared to 10-20% dietary source. In clinical guidelines, serum vitamin D levels were found to be deficient according to data related to foreign populations apart from Turkey. The aim of this study was to investigate the seasonal variability of serum 25-hydroxy vitamin D levels according to age and gender in Bilecik province,Turkey.

Materials and Methods: The medical records of patients admitted to hospital between January 2016 and December 2017 were retrospectively screened and patient medications were evaluated. Serum vitamin D levels of 22205 patients were evaluated according to age and gender. Serum levels of vitamin D were determined by the chemiluminescence method in Siemens Advia Centaur XP(Siemens Healthcare Diagnostics, Tarrytown, NY, USA) via commercial immunoassay kit.

Results: Serum vitamin D were analyzed from the sera of 17070 females (76.9%) and 5135 males (23.1%). The median value of serum vitamin D levels of the participiants were 17.2 (4.2-137.9) in females and 22.9 (4.3-144.0) in males.

Conclusion: According to seasonal classification, there was a lack of serum 25-OH vitamin D in all seasons in males while the females were found to be more deficient, especially in spring.

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ANALYSIS OF HEMOGLOBIN ELECTROPHORESIS DATA OF THALASSEMIA CARRIERS

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Background: Various studies in the world have shown that hemoglobinopathies are one of the most frequent disorders and affect about 7% of the world population. Since Albania is in the area affected by thalassemia, doctors in all cases of anemia recommend hemoglobin electrophoresis.

Aim of the study: The aim of our study was to evaluate the blood parameters of a carrier and possible hemoglobinopathies.

Method: Results were obtained from patient data at the Genius Laboratory after being subjected to hemoglobin electrophoresis analysis in the period September 2017 - February 2018. The study included 1146 patients, of which 147 patients had hemoglobinopathy. The average age of the patients was 29 (± 13.1) years and 66.7% were females.

Results: Data related to hemoglobinopathy classification showed that 85.7% of patients were affected by B-thalassemia minor, of which 57% were female and 28.5% were males. The rest of the patients had sickle cell disease. 12.9% of patients were heterozygous with sickle cell and 0.68% of patients with homozygous sickle cell, also known as thalassemia major. About 2.04% of patients were affected by minor β-thalassemia and heterozygous sickle cell disease.

Regarding the distribution of patients with hemoglobinopathy, it has been noted that in the Fieri area there was the largest number of individuals with thalassemia (20.2%). The rest belonged to Tirana (18.6%), as a result of multiple migrations to the capital. The area that had the highest number of sickle cell disease patients in Albania belonged to Kavaja (47.3%).

Every day the number of newborns with thalassemia increases. Hemoglobin analysis should be recommended by a gynecologist. Thus, we will have a reduction in the number of newborns affected by this disease, and consequently the reduction of cases with thalassemia major.

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OBESITY-RELATED BONE METABOLISM ALTERATIONS

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Obesity has traditionally been known as a positive regulator of bone strength, but recent studies have shown that obesity is an important risk factor for osteoporosis. Although low fat mass and low bone mineral density (BMD) are associated with an increased risk of fracture, conversely, overweight and obese patients also have an increased risk of fracture despite their greater BMD. Patients with diabetes also have a higher BMD and increased risk of osteoporosis and fractures due to the changes in bone microarchitecture, properties of bone-forming material and deterioration of bone quality. Bone fragility increases with inadequate glucose control, diabetes duration, microvascular complications and insulin need are increasing in direct proportion. Some proinflammatory cytokines such as tumor necrosis factor-alpha and interleukin-6 have negative effects on bone formation through lipid metabolism. Low bioavailability of vitamin D stored

in adipose tissue is also observed. The four components of metabolic syndrome affect bone metabolism via calcium homeostasis, regulating the differentiation of osteoblast and bone resorption by stimulation of osteoclast differentiation. Visceral abdominal fat, which is the most metabolically active tissue, may also be associated with poorer quality of bone tissue properties, as suggested in diabetes. The molecular mechanisms related to fat, glucose, and bone metabolism appear increasingly complex. They involve various transcription factors. Obesity primarily regulates the osteoclast osteocyte, osteoblast and bone microcirculation; which is associated with apoptosis of osteocytes, induces the MSCs to generate more adipocytes rather than osteoblasts, and thereby increase bone marrow cavities followed by increases in bone fragility and decreased bone microcirculation. Thus, it is of great importance to evaluate the potential cellular mechanisms how obesity may facilitate osteoporosis and bone fractures.

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RISK MANAGEMENT IN BIOCHEMICAL ANALYSES LABORATORY

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Introduction: Risk analysis methods are part of a quality assurance (QA) program and risk management attempts to answer four questions:

1. What can go wrong?

2. How bad is it?

3. How often?

4. What should be done?

Failure Modes and Effects Analysis (FMEA) involves identification of potential failure modes, determining the consequences of each failure, and reviewing the control measures implemented to prevent or detect the failure.

Aim of the study: Assessment of analytical process in Biochemical Analyses Laboratory.

Material and methods: We used FMEA, including technical risks as well as risks related to human failure in assessment of analytical procedures. The analytical method was broken down into process steps and we identified possible failure modes for each step.

Results: Each failure mode was ranked on estimated frequency of occurrence (O), probability that the failure would remain undetected later in the process (D) and severity (S), each on a scale of 1–10. Human errors turned out to be the most common cause of failure modes. Failure risks were calculated by Risk Priority Numbers (RPNs) = O × D × S. Failure modes with the highest RPN scores were subjected to corrective actions and the FMEA was repeated, showing reductions in RPN scores and resulting in improvement indices up to 5.0.

Conclusions: We recommend risk analysis as an addition to the usual analytical validation, as the FMEA enabled us to detect previously unidentified risks.

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FOOD INTOLERANCE (SPECIFIC TOTAL IgG vs. FOOD ANTIGENS) – WHAT WE KNOW AND WHAT WE DON'T KNOW

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Aim: Having a delayed immune response to an antigen triggers is a well-known fact in medicine, but imposing that usual food consumption is a trigger for various diseases still remains more or less controversial. The purpose of the study was to analyze, summarize and conclude what we already know, to emphasize what is still unknown, and how the present knowledge can be used/upgraded and further implemented in clinical practice.

Materials: Different studies were analyzed to summarize the etiology, configure the most frequent mechanism in pathogenesis, and evaluate the clinical effects. Also, the study that was previously made for local population, by the team in our laboratory, was used to complement with the prior. All of the data were summarized, and then a protocol was proposed for further evaluation and implementation of the findings.

Results: The most frequent mechanisms for inducing the immune reaction are: local intestinal mucosal changes as a result of deteriorated cell connections and inflammation, type III hypersensitivity (CIC deposits, by specific IgG toward food Ag, in various tissues) and TNF-α triggered insulin resistance. The clinical symptoms derive predominantly locally from gut mucose; by the organ affected by the CIC deposits; and as a result of lower energy status triggered by insulin resistance. What stays unanswered is why some healthy people exhibit measurable specific total IgG levels as well. The aim of the proposed protocol is to establish changes in reference values, depending on concomitant diseases, local cuisine (IgG4 interference) and population age.

Conclusion: Clinical implementation of the test is undoubtedly useful in determining the etiology of the already present clinical findings (gut disorders, migraine, obesity etc.), but it needs further upgrade so it can be used for screening and implementing as a primary diagnostic test for food intolerance.

POSTER PRESENTATIONS

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TOPIC ENDOCRINOLOGY

RELATIONSHIP BETWEEN SERUM MELATONIN AND SOME METABOLIC PARAMETERS IN PATIENTS WITH METABOLIC SYNDROME

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Aim: Insulin resistance plays a key role in the pathogenesis of metabolic syndrome (MetS). Recent studies have shown that melatonin may influence insulin secretion and glucose homeostasis. Melatonin is mainly secreted at night by the pineal gland. The aim of the study was to assess the relationship between serum melatonin in 3:00 a.m. and 8:00 a.m. and some components of the metabolic syndrome.

Materials and methods: The study included 40 patients with metabolic syndrome and 40 healthy controls. For melatonin determination blood samples were taken at 3:00 and 8:00 a.m. Serum melatonin concentration was calculated in "Sirio S microplate reader" (SEAC, Italy) using ELISA kit (IBL-Hamburg, Germany). The fasting glucose, triglycerides, total cholesterol and HDL-cholesterol were analyzed using commercially tests on clinical chemistry analyzer Konelab 60i (Finland). Immunoreactive insulin was measured using AxsymTM system (Abbott, USA).

Results: We analyzed the correlation between melatonin at 3:00 a.m. and 8:00 a.m. and metabolic parameters using variation and correlation analysis (p0.05).

Conclusion: Our data showed association between serum melatonin at 3:00 a.m. and some metabolic parameters in healthy controls, which were not established in MetS patients. This results are consistent with the possible role of melatonin in multifactorial pathogenesis of MetS.

The research was financially supported by the MU-Plovdiv, project NO-7/2006.

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SERUM MALONDIALDEHYDE IN WOMEN WITH METABOLIC SYNDROME

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Aim: Serum malondialdehyde (MDA) is one of the most known secondary products of lipid peroxidation in the human body. It has cytotoxic, mutagenous and cancerogenous characteristics and also inhibits the enzymes responsible for the cell defence against oxidative stress. Oxidative stress occurs when there is imbalance between antioxidant systems and reactive oxygen species. This imbalance leads to oxidative damage and the processes that occur in the body contribute to the development of a number of interrelated risk factors as dysglycemia, dyslipidemia, hyperinsulinemia, insulin resistance and metabolic syndrome. It is believed that serum MDA can be used as a quantitative marker of oxidative stress. The aim of our study is to evaluate changes in serum concentrations of MDA in women with metabolic syndrome.

Methods: The study includes 46 women, divided into two groups: 20 women with metabolic syndrome of age 29,16 ± 4,92 yrs. and 26 clinically healthy women of age 30.34 ± 5.76 yrs. Serum MDA is determined with an ELISA test kit (MyBioSource, USA). MDA concentrations are measured with a multiparameter photometer "Sirio S microplate reader", SEAC, Italy.

Results: Serum concentrations of MDA were significantly increased in women with metabolic syndrome compared with healthy controls (124,75 ± 46,88 vs 45.93 ± 25.10, t = 2.265, P < 0.05).

Conclusions: The MDA data we have received suggests the presence of oxidative stress in affected women and is useful in understanding the place and role of oxidative stress in metabolic syndrome.

This work is supported by the MU-Plovdiv, project NO-01/2015.

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INCIDENCE OF CONGENITAL HYPOTHYROIDISM IN DIFFERENT REGIONS OF MACEDONIA - SIXTEEN YEARS NEWBORN THYROID SCREENING

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Aim: Neonatal thyroid screening program allows early effective diagnosis and treatment of congenital hypothyroidism (CH), the most common preventable cause for intellectual disability in children. Despite similarity in the risk factors for CH in different countries the currently reported CH incidence varies widely worldwide. The aim of this study was to evaluate the incidence of CH in different regions of the country.

Methods: Newborn thyroid screening (n=295,909) has been performed in all eight regions of Macedonia, by measuring thyroid-stimulating hormone (TSH) from blood spots on filter paper (Whatman 903), sampled 48 hours after birth, using DELFIA method, between 2002 and 2017.

Results: We detected overall incidence of congenital hypothyroidism of 1/1934 in the country with different regional distribution. The incidences of CH by regions were following: Eastern Region 1/4987, Northeastern Region 1/1449, Pelagonia Region 1/1354, Polog 1/1553, Skopje Region 1/2313, Southwestern Region 1/3260, Southeastern Region 1/1937 and Vardar Region 1/1063. Interestingly, in the Vardar Region with the highest incidence of CH we found 4.75% newborns with TSH concentration above 5 mU/L, as an indicator for the iodine status in the population, compared to the Eastern Region with the lowest incidence of CH and 1.54% newborns with TSH>5 mU/L.

Conclusions: The incidence of CH significantly varies among the regions of the country. The higher CH incidence in some of the regions may be due to increasing exposure to environmental toxic agents and/or deficient iodine intake. Further research into the potential environmental determinants of increased CH risk is warranted.

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VARIATIONS IN INCIDENCE OF CONGENITAL HYPOTHYROIDISM IN ASSOCIATION WITH CHANGES OF CUT-OFF VALUE

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Aim: Congenital hypothyroidism (CH) is the most common congenital endocrine disorder with incidence of 1/3000 newborns. In many countries, lower cut-off levels in screening programs have led to an increase in the proportion of detected cases with transient hypothyroidism, leading to increase of the overall incidence of primary CH.

Methods: A total of 295,909 newborns were screened for thyroid-stimulating hormone (TSH) in dried blood spots sampled 48 hours after birth, using fluoroimmunometric assay (DELFIA), during the period 2002-2017. A TSH value of 15mIU/L was used as the cut-off point up to 2010 and 10 mIU/L thereafter.

Results: Primary CH was detected in 153 newborns with overall incidence of 1/1934; of them 116 had permanent (1/2550) and 37 had transient form (1/7997) of CH. In the period with cut-off value of 15mIU/L the incidences of 1/2489 for primary CH, 1/45625 for transient CH and 1/2632 for permanent CH were observed. On the other side, the incidences of 1/1616 for primary CH, 1/4657 for transient and 1/2474 for permanent CH were detected for the period with the lower TSH cut-off level.

Conclusions: Our results show that the lower TSH cut-off value had impact on increasing incidence of primary CH with accent on transient CH. Moreover, the observed incidence of the transient CH was almost ten times higher for the period with the lower cut-off value. Further analysis is necessary to identify the other factors associated with increasing incidence of permanent as well as transient CH in Macedonia.

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RESISTIN MARKER OF FUTURE

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Introduction: Obesity is defined as chronic, multifactorial disease, characterized by a disorder of secretory activity of the fat tissue. Resistin is a proinflammatory adipokine synthesized by macrophages of fat tissue, associated with this process.

Aim: The aim of our study was comparison of resistin concentration in serum of well-nourished and obese individuals as well as resistin correlation with a marker of low-grade inflammation- hsCRP in obesity.

Methods: Testing included 82 respondents, over the age of eighteen. The following anthropometric parameters were measured in all respondents: body height, body weight, waist circumference and BMI were also circulated. On the basis of anthropometric parameters, respondents were divided into two groups: group of normally nourished (N=22) and group of obese respondents (N=60).

Results: In the group of obese respondents, there was a significantly higher concentration of resistin in plasma (12.9±1.2 versus 6.9±1.7 ng/ml; p<0.001) compared to a group of respondents normally fed. Analyzing the concentration of hsCRP in the blood of respondents, there was significantly higher concentrations in the group of obese respondents compared to normal ones (p <0.001). We established a positive correlation between the concentration of resistin and the concentration of hsCRP in the respondents who participated in the study (p <0.001).

Conclusion: Our results point to the association of obesity with the chronic inflammation of low affinity. Resistin as a marker of chronic inflammation in the future could be used for estimation of cardiovascular risk in obesity.

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PARTICIPATION OF ADINOPEKTIN IN LOW AFFINITY INFLAMMATION IN OBESE PEOPLE

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Introduction: Adiponectin is a protein composed of 244 amino acids with molecule mass of 30 kDa, and it is synthesized only in adipocytes. Although adipocytes are the most important and only source of adiponectin, levels of this hormone in serum are not increased in obesity as it is the case with levels of leptin. Positive correlation of adiponectin levels with the amount of subcutaneous fat tissue has been confirmed as well as its inverse connection with the amount of visceral fat tissue.

Aim: The aim of our investigation is the comparison of adiponectin levels in serum in people with normal weight and in obese people as well as the correlation between adiponectin and marker of low level inflammation- hsCRP.

Methods: This study included 82 examinees of both sexes, smokers and non-smokers, and all of them were older than 18 years old. The concentration of adiponectin was measured in the serum by ELISA technique with ready-made kits (Human adiponectin ELISA Kitts), manufactured by Bio Vendor Medicine Czech Republic. Measuring of hsCRP was carried out on the same day by spectrophotometric method on biochemical analyzer model Alcyon manufactured by Abbott with commercial reagents of the abovenamed company. Samples for examinations were kept at -20°C.

Results: In the investigation negative correlation of the presence of adiponectin concentration in the examinees of the control group and the group of obese people was found. In the investigation statistically significant connection of hsCRP with adiponectin in the obese group (p=0,053) was not found.

Conclusion: In the serum of obese persons we did not have negative correlation of adiponectin concentration of highly sensitive CRP;

In the serum of obese persons we noticed that there is a reduction in adiponectin concentration. Further investigations about the connection of adipocytokine isoforms and their correlation with inflammation markers are necessary.

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OXIDATIVE STRESS BIOMARKERS IN SERUM OF PATIENTS WITH SUBCLINICAL HYPOTHYROIDISM

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Background. Oxidative stress results from either overproduction of free radicals or decreased efficiency of scavenger antioxidant system. Oxidative stress has been implicated in a number of diseases. However, in hypothyroidism the presence of oxidative stress is controversial.

The aim of our study was to investigate the oxidative stress biomarkers in patients with subclinical hypothyroidism (sHT) (n=28) and health controls (n=30). Their serum thyroid and lipid profile, malondialdehyde (MDA) and blood antioxidant enzyme levels were estimated.

Methods. The diagnosis of sHT was based on the finding of high thyroid-stimulating hormone (TSH) level associated with normal free triiodothyronine (fT3) and free thyroxine (fT4) levels and high serum levels of autoantibodies (anti-thyroglobulin antibody and anti-thyroid peroxidase antibody). Total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, MDA and arylesterase were analyzed. MDA levels in the serum were evaluated by the spectrophotometric method based on the reaction between malondialdehyde and thiobarbituric acid.

Results. Patients with sHT showed significantly high MDA, TC, LDL-C and TG levels ($p<0.001$, $p<0.01$, respectively), and significantly low HDL-C levels compared to controls ($p<0.05$). MDA levels were inversely correlated with HDL-C levels in patients with sHT (r -0.471, $p<0.001$). Arylesterase activity also was significantly lower in the group with sHT, compared to the control group ($p<0.05$).

Conclusion. These results suggest an increased oxidative stress in subclinical hypothyroidism, which can be explained by both the insufficient increase in the antioxidant status and the altered lipid metabolism in these cases.

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AUTOIMUNE ANTIBODIES IN THYROID DISEASES

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Background: Irrespective of the recommendations to use the measurement of serum TSH as cornerstone of thyroid function testing, the laboratory diagnosis and monitoring of thyroid diseases are based on the thyroid panel including TSH, FT4, TT4, TT3, FT3, anti–TPO and anti-TG. Autoimmune thyroid diseases include Graves' disease, Hashimoto thyroiditis and these types of disorders are caused by immune system malfunction. In other words, instead of protecting the body's healthy tissues, malfunctioning immune cells actually attack them.

Methods: Morning serum concentrations of anti-TPO and anti-TG were assessed in a prospective study in 50 subjects with Graves' disease, 50 subjects with Hashimoto thyroiditis and 40 healthy subjects as control

group. Serum concentration of anti–TPO and anti-TG were determined by chemiluminescence immunoassay using Immulite 2000 analyzer.

Results: The following results were obtained: serum concentration of anti-TPO in the control group was 3.7 IU/mL ± 0.46, in Graves' disease 195 IU/mL ± 0.70 and in Hashimoto thyroiditis 238.5 IU/mL± 0.95. Serum concentration of anti-TG in Hashimoto thyroiditis was highest (333.3 IU/mL ± 0.55). Patients with Graves' disease and Hashimoto thyroiditis showed significantly higher concentrations of anti-TPO and anti-TG compared to healthy individuals (P<0.001).

Conclusion: Serum concentrations of anti-TPO and anti-TG organ specific autoantibodies respectively are very precious parameters - markers for reliable diagnosis of autoimune thyroid diseases.

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INVESTIGATION OF SERUM DICKOPF-1 LEVELS IN CHILDREN AND ADOLESCENTS WITH TYPE-1 DIABETES MELLITUS

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Aim: Interaction between diabetes mellitus (DM) and osteoporosis is a complex issue and needs more evaluation. Recently, the Wnt/beta-catenin signaling pathway and its one of inhibitors dickkopf-1 (Dkk-1) was found to be involved in the control of bone mass. The aim of the present study was to measure serum Dkk-1 protein levels in children and adolescents with type-1 DM.

Methods: This study was performed on 40 children and adolescents with type-I DM (type-1 DM group, 19M, 21F) aged between 7-17 years and 40 healthy children and adolescents (control group, 18M, 22F) aged between 6-17 years.

Results: Fasting blood glucose (p<0.001), hemoglobin A1c (p<0.001) and Dkk-1 (p<0.05) levels of the children and adolescents with type-1 DM were significantly higher, osteocalcin (p<0.05) levels were significantly lower than those of the controls.

Conclusions: Higher Dkk-1 levels and lower osteocalcin levels of type-1 DM group shows that osteoblastic activity was decreased. Because, Dkk-1 inhibits osteoblastic activity and osteocalcin levels shows osteoblastic activity. In conclusion, both bone remodelling and it is compensatory mechanism bone loss is lower in children and adolescents with type-1 DM compared to those of the controls. Also, higher levels of Dkk-1 plays a role in decreased bone turnover in these patients.

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LEVELS OF CREATINE KINASE IN HYPOTHYROID DISEASE

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Aim: The aim of this study was to determine serum levels of creatine kinase (CK) in overt and subclinical hypothyroidism. It was our aim to investigate the change in CK levels with treatment and to evaluate the relationship between free triiodsothyronine (FT3), free thyroxin (FT4), and thyrotropin (TSH) levels and the degree of skeletal muscle involvement, as determined by serum CK levels. Patients with other causes of CK elevation were excluded.

Methods: We included 26 patients (24 women and 2 men, age 40.65 ± 12.55 years) with overt hypothyroidism, 36 patients (35 women, 1 man, age 41.55 ± 10.45 years) with subclinical hypothyroidism, and 30 age- and gender-matched controls (27 women, 3 men, age 40.81 ± 11.20 years) in the study. Serum levels of TSH, FT4, FT3, and CK were measured in all subjects.

Results: Creatine kinase elevation was found in 17 patients (58%) with overt hypothyroidism and in 4 patients (10%) with subclinical hypothyroidism. Although a statistically significant elevation of CK levels was found in patients with overt hypothyroidism when compared to patients with subclinical hypothyroidism and controls (p=0.0001, p=0.01, respectively), no difference was found between the subclinical hypothyroidism and control groups (p = 0.14). In hypothyroid (overt and subclinical) patients, a positive correlation was found between CK and TSH (r = 0.422; p = 0.04), and a negative correlation between CK and FT3 (r = 0.526; p = 0.002) and between CK and FT4 (r =0.437; p = 0.04).

Conclusions: Creatine kinase levels decreased to normal levels after thyroid function normalized with treatment. In conclusion, skeletal muscle is affected by hypothyroidism more profoundly in cases of overt hypothyroidism, and less in subclinical hypothyroidism.

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INVESTIGATION OF THE EFFECT OF ARONIA MELANOCARPA FRESH FRUIT JUICE INTAKE ON CHANGES OF LABORATORY PARAMETERS FOR OXIDATIVE STRESS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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The authors investigated the effects of Aronia melanocarpa juice intake on oxidative stress and anti-oxidant plasma barrier in 48 type 2 diabetes mellitus patients of various age groups. All subjects took 70 ml of juice three times daily over a period of 60 days. Changes in Carratelli panel were monitored, including SHp test, OXY- adsorbent test, LP CHOLOX test, anti-ROMs test, d-ROMs test and BAP test to assess the oxidative stress metabolites and the total anti-oxidant plasma capacity. The results obtained showed: a considerable decrease in reactive oxygen substances; a considerable decrease in lipid peroxidation; moderate elevation of plasma barrier with aspect to the thiol radicals action; a significant positive effect on quickly-acting anti-oxidants and a moderate effect on slow-acting antioxidants; a somewhat weaker effect on the anti-oxidant barrier against hypochlorousacid radicals; a pronounced increase in biological anti-oxidant potency of plasma barrier.

A daily supplement of aronia juice to one's routine diet regulates the quantity of oxidative active radicals – free radicals (ROS). Alongside, the anti-oxidant capacity of blood plasma is improved. We recommend daily intake of Aronia melanocarpa fruit juice as a vital functional food for patients with type 2 diabetes mellitus.

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INVESTIGATION OF COPPER AND ADIPONECTIN LEVELS IN BLOOD OF OBESE SUBJECTS

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Objectives: Obesity is one of the most serious public health problems encountered in developed and even developing countries today. Adiponectin (AN) is expected to be a new therapeutic tool for diabetes and metabolic syndrome. Copper ions can play the role of catalyst in the emergence of free radical damage. Since redox is an activating metal, it has an effect on oxidative stress.

Material and methods: This study was performed in 70 (22M, 55F) obese people, aged 18-70 years, and 50 (11M, 39F) control subjects, aged 18-70 years. Body mass index (BMI) was used as an obesity criteria. The obese group was selected from persons with BMI>30 kg/m2 and the control group was selected from persons with 18.5-24.9 kg/m2 of BMI. Quantitative determination of serum AN concentrations was measured by competitive ELISA. In addition, copper levels were measured by an atomic absorption spectrophotometer. Statistical analysis was performed with SPSS v16.

Results: AN levels in obese subjects were significantly lower ($p<0.001$) whereas copper levels were significantly higher ($p<0.001$) than those in control subjects.

Conclusions: As a result, in our paper, AN has proved to play an important role in the etiopathogenesis of obesity. AN support will be useful in the treatment of obesity, for AN levels in obese persons are lower than in controls. Moreover, copper restriction may be important in obesity treatment since copper level in obesity is higher than in controls.

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IS TYPE 2 DIABETES A CARBOHYDRATE OVERLOAD DISEASE THAT CAN BE REVERSED BY A SIMPLE DIET?

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It is estimated that in the next few years, Type 2 Diabetes (D2T) is threatening to bankrupt most western health care system budgets. With more than 100 million US adults living with diabetes or prediabetes today, and a 2017 cost of more than $327 billion to the US economy, these great concerns and prognoses are looking more real than ever. Although billions of dollars are spent on research of this disease, few new drugs or breakthroughs have been made thus far. On the other hand, there have been several reports that a simple, low carbohydrate diet, if instituted for a few weeks under physician supervision, reverses most if not all of diabetes markers, including normalization of blood glucose and eliminates the need of anti-diabetic drugs. Two physician associations, one from Canada and one from the UK have even voiced their opinion of the need to classify D2T as a reversible disease, and that most of its chronic effects can be easily prevented by a simple diet. We present the seminal studies of the last decade that investigate the metabolic pathology of D2T and the spectacular results of the last few dietary studies which have indisputably shown that just a simple diet may be all that is needed to reverse D2T and prevent its many serious complications.

TOPIC P4 MEDICINE & CLINICAL EFECTIVNES IN LABORATORY MEDICINE

PHARMACOGENETIC TESTING IN OPTIMIZATION OF TREATMENT WITH STATINS

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Statins are a class of drugs that have been widely prescribed nowadays for treating hypercholesterolemia and thus prevent the risk of atherosclerotic cardiovascular events and consecutive mortality. Unfortunately, the patient's compliance with treatment is frequently compromised by the high incidence of adverse effects including hepatotoxicity, myotoxicity, increased risk for diabetes mellitus etc. The expansion of the precision medicine concept in pharmacology has introduced pharmacogenetic testing as a potential predictive strategy in statins pharmacotherapy.

A thorough literature survey was performed using the PubMed database on the published data in English language in the period 2000-2017, regarding genotype-phenotype associations in statin-induced toxicity, identifying a growing body of evidence supporting the need for pharmacogenetic approach in treatment with statins. Polymorphisms in the genes coding for the CYP450 enzymes: CYP2D6, DYP2D9, CYP3A4 and drug transporter genes like ABCB1, ABCG2 and SLCO1B1 appear to be responsible for the variable response and toxicity of statins. But, many studies highlight the importance of drug interactions and epigenetics in modifying the response towards this class of drugs metabolized via pathways shared by the majority of pharmaceutical agents.

With the rapid development of molecular techniques accompanied by a dramatic cost reduction in genetic testing, it can be easily anticipated that pharmacogenetic patient profiling will soon become standard of care in designing the optimal statin treatment either as a monotherapy or in combination with other pharmaceuticals.

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INTERFERENCE TESTING OF OMNIPAQUE (IOHEXOL) ON BETA-HCG, HCG AND AFP ASSAYS ON TOSOH AIA 360

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Aim: Interference in immunoassays is a serious, but underestimated problem. The purpose of our study was to test whether there is an interference between contrast agent Omnipaque (iohexol) and beta-HCG, HCG and AFP assays on the TOSOH AIA 360.

Methods: Protocol for the survey was prepared by the manufacturer TOSOH. All tests were carried out on TOSOH AIA 360, Automated Enzyme Immunoassay Analyzer, with assay methodology – one-step sandwich and competitive FEIA. Concentrations of beta-HCG, HCG and AFP in sera were measured twice and the median value was taken into account. First Omnipaque was measured only with the reagents. After that, Omnipaque was added in the sera by dilution 1:10 and the concentrations of tested parameters were measured again. This was repeated after 30 min, 60 min and 120 min of incubation at 37°C.

Results: A total of 15 samples were examined. The concentrations of the tested parameters ranged from immeasurably low to very high The results were statistically processed with ANOVA test. The ANOVA table decomposes the variance of the data into two components: between-group component and within-group component. Since the P-value of the F-test was greater than or equal to 0.05, there was no statistically significant difference between the means of the variables at the 95.0% confidence level.

Conclusion: From the results obtained, it was obvious that Omnipaque contrast agent does not interfere with the assays of beta HCG, HCG and AFP on TOSOH AIA 360, either with the reagents or with the analyzes examined.

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MEASLES OUTBREAK IN ALBANIA: OUR ESTIMATION OF THE IMMUNIZATION STATUS AND THE NEED FOR REVACCINATION

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Background and aim: Measles has rebounded in the WHO European region, and also in Albania. The first measles case in our country was confirmed on 10 January 2018, and by 13 February 115 cases were confirmed. We aimed to determine the level of immunization of 221 patients, by measuring their measles IGG antibodies, to understand the needs for revaccination.

Method: We divided the patients into three age groups - Group A: 15 patients aged 6-18, group B: 60 patients aged 19-29 and group C: 145 patients aged 30-40. Patients were tested for measles IGG antibodies, using EIA method.

Results: We found 11 positive, 3 negative and 1 gray zone results in group A; 49 positive, 8 negative, 3 gray zone results in B; 109 positive, 27 negative, 9 gray zone results in C. Adding gray zone results to the negative ones, we found that 26.7% of patients in group A, 18.3% in group B and 24.8% in group C needed revaccination.

Conclusions: In year 2000, the Public Health Institute updated the vaccination calendar adding a second measles vaccination at 5 years. The same year all children ≤ 14 years and women 15-45 years were revaccinated. Despite this, we found a high percentage (26.7%) of negative immunization in patients 6-18 years who received both vaccination doses. Another peak was at group age 30-40, where 24.8 % needed revaccination. We believe that testing for the level of immunization is a reliable tool that can be used to expose the contingent that has not developed immunity and needs revaccination.

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INVESTİGATİON OF SOME İMPORTANT CLİNİCAL BLOOD PARAMETERS İN SHEEP WİTH TRAUMATİC MYİASİS

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Aim: Traumatic myiasis, the parasitic infestation by fly larvae in traumatic lesions of the tissues of living vertebrates, is a serious medical condition in humans and a welfare and economic issue in domestic animals. The present study was aimed to determine the effect of traumatic myiasis infestation on some important blood parameters in sheep.

Methods: Myiasis larvae were collected from the infested body areas of 10 sheep with traumatic myiasis. Microscopic examination revealed that these larvae were Wohlfahrtia magnifica and Lucilia sericata. Blood samples were collected from 10 traumatic myiasis and 6 clinically healthy sheep. The obtained serum samples were analyzed for blood parameters.

Results: pH and oxygen saturation increased significantly in the infected group, while tHb decreased ($p \leq 0.05$). No statistically significant differences were found in other parameters (pCO2, pO2, HCO3, TCO2, Beb, BEECf). In the infected group, creatine level ($p \leq 0.05$) and AST ($p \leq 0.05$), ALP ($p \leq 0.01$) activities decreased significantly while total protein was higher ($p \leq 0.01$). There was no significant change in glucose, urea, albumin, uric acid, triglyceride, cholesterol, ALT, GGT, CK, amylase and globulin levels. There was no significant change in sodium, chlorine, phosphorus, Na, K, Ca parameters, while potassium level decreased significantly in the infected group ($p \leq 0.05$), and there was no significant change in inflammatory parameters (ASO, CRP) and blood hematologic parameters (Hct, WBC, RBC).

Conclusions: As a result, it was determined that some blood parameters (pH, oxygen saturation, tHb, creatine, AST, ALP, total protein, potassium) were affected statistically significantly in sheep with traumatic myasis. It was concluded that these parameters could be important in the veterinary laboratory diagnosis.

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TOPIC PREANALYTICAL PHASE OF LABORATORY TESTING & QUALITY MENAGMENT IN LABORATORY MEDICINE & POCT- PRACTICAL IMPLICATIONS, QUALITY CONTROL

INTERNAL VS. EXTERNAL QC - WHAT WHEN DISCREPANCIES HAPPENED?! (EXPERIENCE FROM SMALL LABORATORY)

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Background: The study refers on solving the problem when discrepancies happen in results between internal and external QC measurements i.e. what when excellent internal QC has bad results on EQAS?

Materials and Method: The measurements were made on Glucose and Triglycerides by using Bio-Rad (C-310-5) chemistry control and Bio-Rad EQAS (Clinical Chemistry (Monthly) Program - Cycle 16) on Kroma Linear analyzer whit reagent from linear program. The obtained results from internal QC were analyzed for imprecision and inaccuracy, and TAE was calculated for a period of 1 month (by using internal QC software of the analyzer and Microsoft excel). EQAS results were analyzed per peer group, method and mode. Prior testing all pre-analytical factors were excluded (temperature, dissolving, etc.)

Results: Pre-analytical factors and imprecision study showed no deviations. On EQAS results, since the peer group was too small, method and mode comparison were taken into consideration, and showed that EQAS had more accuracy than internal QC .Subsequently, portions of the monthly EQA materials were separated, frozen and furtherly used as daily routine control (by establishing our own QC ranges), and accordingly the analyzes were calibrated and correlated to. The following EQAS results were excellent.

Conclusion: After all research, we came to the conclusion that the provided internal QC range by the manufacturer did not correlated with acceptable bias. Subsequently new QC material (using EQA materials as it) with our own ranges was established, and bias was solved. But even so, the problem with small peer groups and small analyzers stays as a moment - for resolving by the manufacturer.

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IDENTIFICATION OF PRE-ANALYTICAL ERRORS IN THE HOSPITAL LABORATORY

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Aim: Pre- and post-analytical errors are estimated to constitute 93% of errors in the biomedical laboratory. Errors at any stage of the collection, testing and reporting process can potentially lead to a serious patient misdiagnosis. Errors during the collection process are not inevitable but can be prevented with a diligent application of quality control, continuing education and effective collection systems.

Methods: A perspective analysis of the results obtained from the biomedical laboratory of Clinical center of Nis, Serbia for errors of the preanalytical phase has been carried out to summarize data. Laboratory personal were asked to register rejections, and causes for rejection of the wards.

Results: Out of the 48328 blood collection tubes screened over a period of 8 months, pre-analytical errors were observed in approximately 4.9% of the total number of samples received. The distribution of the different types of errors was then calculated. The majority of the rejected samples were hemolyzed, which accounts for 1.1% of the total number of samples received during this period. The amount of blood was insufficient for complete analysis in 0.08%. A total of 0.4% samples in the wards were accompanied by inappropriate requisition slips.

Conclusions: The human role in sample collection makes complete elimination of errors associated with laboratory testing unrealistic. However, good practise and compliance with the new strategies for error prevention can lead to a substantial reduction in pre-analytical errors. A practice of keeping a record of the errors at all stages of analysis and then divising corrective strategies for their prevention can gradually free a laboratory from such errors.

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IDENTIFICATION OF TYPES AND FREQUENCIES OF PRE-ANALYTICAL ERRORS IN THE CLINICAL BIOCHEMISTRY LABORATORY- EMERGENCY DEPARTMENT

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Background: Owing to remarkable advances and modern innovations, laboratory diagnostics has been transformed from manual and labor-intensive service to fully automated process. Despite this, there are a number of pre-analytical errors that might lead to erroneous patient diagnosis and treatment that follows.

Aim: The aim of this study was to describe quality indicators for the pre-analytical process, grouping errors according to patient risk as critical or major, and assess their evaluation over one-year period. This is a retrospective study performed to investigate the major causes of pre-analytical errors that led to sample rejection at emergency department in the Laboratory of the Surgery clinics, PHO UC Clinical biochemistry in Skopje.

Results: The results of this study showed visible hemolysis after centrifugation was the most common cause accounting for 39% of total rejections of samples. This study also reported a number of different reasons for sample rejection including: clotted samples (17.5%), mismatching patient information on the tube and request (4.6%), incomplete patient data (4.6). Therefore, this study suggests keeping a record of the errors at all stages of the pre-analytical process and then devising corrective strategies for prevention of such laboratory errors.

Conclusions: Grading laboratory errors on the basis of their seriousness should help identify the priorities for quality improvement and encourage actions on corrective and preventive actions.

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TOPIC BIOMARKERS IN KIDNEY DISEASE

URINARY INFECTIONS IN PATIENTS WITH DIABETES MELLITUS

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Introduction: Urinary infections are very common and dangerous in patients with diabetes mellitus due to kidney failure from diabetes, and these injuries are related to the disease and age of the patients. Different disorders and changes of the immune system, impaired metabolism, incomplete emptying of the urinary bladder due to neuropathic damage contribute to the increased risk of developing urinary infections.

Aim: Knowing or recognition of microscopic examinations of urinary sediment as a routine examination and evaluation of indicators such as proteinuria, leukocytouria, hematuria, etc.

Method and material: In this study a total of 119 patients were included, of which 69 (57.9%) patients were diagnosed with diabetes mellitus and 50 (42.01 %) patients were healthy and were included in the control group. Clinical overview showed a frequent urination accompanied by hematuria. All patients underwent sugar blood analyses HbA1c, urine analyses with test track (strips) and microscopy of urine sediment.

Results: The results obtained showed that from the 69 diabetic patients 37 (53.6%) had proteinuria, whereas in 32 (46.3%) patients proteins in urine were not found. Diagnosed patients with proteinuria were associated with leukocyturia in a total number of 22 (31.8%), and 15 (21.7%) of patients with proteinuria and leukocyturia were associated with hematuria.

Conclusion: Urinary infections are more frequent in diabetic patients associated with proteinuria than in non-diabetic patients. People with diabetes are more vulnerable to urinary infections for several reasons. First, their immune systems tend to be weaker, second high blood sugar can spill into the urine and encourage the growth of bacteria. Also nerve damaged related to diabetes can prevent the bladder from fully emptying. People with diabetes should talk with their doctors as the first sign of urinary infections.

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DYSLIPIDEMIA IN THE FIRST YEAR AFTER KIDNEY TRANSPLANTATION AND CORRELATION WITH CYCLOSPORINE TROUGH LEVEL

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Aim: Post-transplant dyslipidemia is multifactorial complication. However, several classes of immunosuppressive agents appear to play a role. The objective of this study was to evaluate the most prominent lipid disorders in the first year after allogeneic kidney transplantation and to assess the correlation between cyclosporine (CsA) trough levels and lipid disorders.

Methods: A total of 32 kidney transplant recipients divided in two groups with different CsA trough levels were enrolled in this study. All patients were on equal doses of other immunosuppressive agents and had stable graft function. CsA blood levels, plasma total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc) were measured after 12-14 fasting three months after transplantation. Pearson's test and t-test were used for data analyses.

Results: The most prominent lipid disorder was elevated TC, LDLc and TG. Statistical analysis showed that CsA was positively correlated with TC ($r=0.369$, $p<0.05$) and LDLc ($r=0.372$, $p<0.05$). In the first group (15 pts.) with CsA trough level above 200 ng/ml, the mean value of the TC was 7.29 ±1.19 mmol/l and of LDLc 4.83± 0.81 mmol/l. In the second group (17 pts.) with CsA trough level less than 200 mg/l, the average value of TC was 6.07 ± 1.02 mmol/l and of LDLc 3.81±1.19 mmol/l, which was significantly lower ($p<0.01$, for both) than in the first group.

Conclusion: Higher CsA trough levels adversely affects plasma lipoprotein levels by increasing total cholesterol levels, primarily due to an increase in low-density lipoprotein cholesterol level.

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RELATIONSHIP BETWEEN SERUM MYELOPEROXIDASE AND KIDNEY DAMAGE IN T2DM

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Aim: Myeloperoxidase (MPO) is considered to be both a biomarker and a mediator of microvascular complications in type 2 diabetes mellitus (T2DM), including diabetic nephropathy (DN). Since there are conflicting data regarding its relationship with the severity of kidney damage, this study investigated serum MPO activity along different stages of DN.

Methods: A total of 90 patients with T2DM and 30 age- and sex-matched healthy control subjects were enrolled in the study. Routine laboratory blood tests were performed. Serum chlorinating MPO activity was measured kinetically. The stage of DN was determined according to MDRD formula, and patients were assigned to CKD1 (n=20), CKD2 (n=37), CKD3 (n=18), CKD4 (n=5) and CKD5 (n=10) groups. Relationships between groups were analyzed using parametric and non-parametric tests.

Results: Compared to controls, serum MPO activity was higher in T2DM group (66.7 ± 21.0 U/L vs. 92.2 ± 38.7 U/L, in controls vs. T2DM; $p< .001$). In T2DM group, serum MPO activity was poorly correlated to the blood HbA1c levels ($rho = –0.141$; $p = 0.183$), as well as to WBC ($rho= 0.193$; $p=0.069$), and neutrophil cell count ($rho = 0.113$; $p = 0.286$). Serum MPO activity significantly declined along CKD1-5 stages ($rho = –0.664$, $p < 0.001$), resulting in lower activity in CKD5 than in controls (48.9 ± 14.9 U/L vs. 66.7 ± 21.0 U/L, in CKD5 vs. controls; $p = 0.018$).

Conclusion: Serum MPO activity steadily declines with the severity of kidney damage in T2DM.

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ASSOCIATION OF NEUTROPHIL-TO-LYMPHOCYTE RATIO IN HEMODIALYSIS PATIENTS: A RETROSPECTIVE OBSERVATIONAL STUDY

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Objective: Neutrophil-to-lymphocyte ratio (NLR) is a prognostic marker of morbidity and mortality for various diseases including cardiovascular diseases, liver diseases and general surgery. Recently, NLR was also associated with all-cause mortality in patients with hemodialysis. Hemodialysis patients with end-stage renal disease have a higher risk of mortality compared with the healthy population. NLR can be important biomarker in hemodialysis patients.

Aim: The aim of the present study was to determine the value of neutrophil to lymphocyte ratio (NLR) in predicting mortality in hemodialysis patients.

Material and method: This study was performed in 74 hemodialysis patients admitted to the Polyclinic of Nephrology at the Faculty of Medicine of the Selcuk University and analyzed by hospital automation system data. Sixty healthy adults were included as a control group. Neutrophil and lymphocyte levels were measured with a Beckman Coulter LH-780 hematology analyzer. Statistical analysis was performed with SPSS v16. Values of $p < 0.05$ were considered to indicate statistical significance.

Results: NLR values in patients with hemodialysis were significantly higher compared to control group ((3.32 (1.35-32.96)) ((1.79 (0.92-3.14)) $p<0.001$).

Conclusions: NLR is a beneficial biomarker and a potential predictor of inflammation. Our results suggest that high NLR is independently associated with all-cause mortality in hemodialysis patients. Hemodialysis patients with high NLR levels have increased risk of mortality.

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SERUM LEVELS OF ANTI-PHOSPHOLIPASE A2 RECEPTOR ANTIBODIES IN PATIENTS WITH MEMBRANOUS NEPHROPATHY

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Introduction. Membranous nephropathy (MN) is the most common cause of nephrotic syndrome in adults. Two forms of MN have been described – the primary form (PMN) and the secondary form (SMN), which represent 70% and 30% of cases, respectively. Current clinical studies indicate the significance of circulating autoantibodies against the M-type phospholipase A2 receptor (aPLA2R-ab) in the pathogenesis of PMN.

Aim.The aim of this study was to compare the level of aPLA2R antibodies between patients with PMN, SMN and healthy controls.

Methods: The study included 33 patients with PMN (mean age 53.36±14.10 years), 10 patients with SMN (mean age 55.40±17.54 years) and 35 healthy controls (mean age 45.71±13.07 years). Serum PLA2R antibodies levels were measured with ELISA kit (Anti-PLA2R ELISA, IgG, EUROIMMUN, Lübeck, Germany). The data was analyzed using SPSS, version 24. All data was expressed as mean ±SD. Significance was considered at p≤0.5.

Results: The PMN patients had significantly higher mean level of aPLA2-Ab compared to SMN patients (309.18±678.70 RU/ml vs. 2.99±2.00 RU/ml).

Conclusions: In PMN patients the higher levels of aPLA2-Ab might be regarded as a new opportunity to more accurately define the etiology of MN and might be used as an indication for close monitoring of such patients.

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THROMBOSPONDIN TYPE -1 DOMAIN-CONTAINING 7A IN SERUM – METHODICAL RESOLUTIONS

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Idiopathic membranous nephropathy is an autoimmune disease. In approximately 70% of patients with active disease, it is associated with autoantibodies against phospholipase A2 receptor 1 (anti-PLA2R). The remaining patients that are anti-PLA2R negative have antibodies against thrombospondin type-1 domain-containing 7A (THSD7A).

The aim of this study was to present contemporary methods for determining autoantibodies against THSD7A in biological material.

Methods.The search was made in the Medline and Pubmed systems by keywords "membranous nephropathy", "autoantibodies against thrombospondin type -1 domain-containing 7A", "methods for determination" for the period 2009-2018. For determination of anti-THSD7A-ab were considered Western bloot analysis, immunoprecipitation and indirect immunofluorescence method. A rabbit polyclonal antibody at a 1:1000 dilution was used in the detection of THSD7A-ab by Western bloot assay. For qualitative and semi-quantitative determination of human autoantibodies (Ig G) against THSD7A indirect immunofluorescence method was used. In this method antibodies against thrombospondin type-1 domain-containing protein 7A react with transfected cells of the test substrat, producing a fine-granular cytoplasmic fluorescence with accentuated cell membrane.

Conclusion. Immunofluorescent test is reliable for detection of THSD7A-ab. This test combines opportunity for serial work. There is no need for special and expensive instrumentation.

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L - THEANINE INHIBITS DOXORUBICIN-INDUCED ACUTE NEPHROTOXICITY IN RATS

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Objective.The beverage of the tea plant, which is a member of Theaceae family, has been a worldwide popular beverage for centuries in terms of both of its production and consumption. L-theanine is a nonprotein derivative amino acid, comprising 50% of the free amino acids present in Camellia sinensis tea species and it has such protective effects such as relaxing, antioxidant, antiinflammatory and hepatoprotective etc.

Aim.The aim of this study was to investigate whether theanine has a protective effect on Doxorubicin (DOX)-induced nephrotoxicity in rats.

Material and methods.For this purpose, 32 male Sprague Dawley rats weighing 300-400 g were used and randomly assigned into 4 groups: 1st group (control, n=8) which was intraperitoneally given saline; 2nd group (Theanine, n=8) 200 mg/kg/day theanine for 5 days; 3rd group (DOX, n=8) single dose 20 mg/kg DOX; 4th group (DOX+Theanine, n=8) which was given 20 mg/kg DOX at first day and 200 mg/kg/day theanine for 5 days.

Blood urea nitrogen (BUN) and creatinine levels were measured in serum samples by enzymatic colorimetric method with auto analyzer. Caspase-3 levels as apoptotic marker and nuclear factor kappa B (NF-κB) as inflammatory marker were determined with ELISA method in both plasma and kidney tissue. Histopathological examination was performed in kidney tissues.

Results.The serum levels of BUN and creatinine were higher in the DOX group according to DOX+theanine group ($P<0.05$). Plasma and tissue levels of caspase3 and NF-κB were found high in the DOX group according to DOX+theanine group ($P<0.05$).

Conclusion. According to these findings, which were also supported by histopathological analyses, L-theanine may have protective effects against DOX-induced nephrotoxicity in rats.

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BIOMARKER FOR THE EARLY DETECTION OF ACUTE KIDNEY INJURY

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Aim: Dehydration, which may be associated with electrolyte disturbance and metabolic acidosis caused by acute rotavirus gastroenteritis is a frequent finding ininfants and young children, and it is the dangerous complication. The most important treatment modality in these patients is recognising and treating dehydration, electrolyte imbalance and acute kidney injury. The aim of this study was to investigate the urine NGAL concentrations as an early biomarker of prerenal acute kidney injury ininfants and young children with acute rotavirus gastroenteritis.

Methods: 75 Patiens with Dg Acute rotavirus gastroenteritis.were enrolled in the study at University Children Hospital Skopje since2016 years till 2018 years. We have two groups , investigategroup 45 patiens was age <5-years;moderate and severe dehydrationsymptoms include vomiting, diarrhea, fever, decreased oral intake, inability to keep up with ongoing losses, decreased urine output, ,control group was 30 patiens was age <5 years; healthy controlsMean age weight and genderwere 3 ± 2,1 years, 12kg ± 1.5k g, respectively. Chronic hepatic, intestinal, renal, neurologic, metabolic and immunologic diseases for any disease were considered as criteria for exclusion. Clinical and laboratory parameters analyzed .Concentrations of NGAL in urine samples were determined by a quantitative kit on an Architect i1000SR analyzer (Abbott Diagnostics),using Chemiluminescent microparticle immunoassay technology.

Results: Urine NGAL levels of the two groups were compared.The mean of serum creatinine concentrationscollected in the first hour is normal in the two groups.The mean urine NGAL levels collected in the first hour of the investigate group were significantly higher than controls. In investigate group infants and young children with severe dehydration had significantly higher urinary NGAL concentrations than moderate dehydrated ones.NGAL levels predict acute renal injury earlier than serum creatinine levels.

Conclusion: The urine NGAL concentrations as an early biomarker that predicts development of prerenal acute kidney injury ininfants and young children with acute rotavirus gastroenteritiswith unknown timing of kidney injury.

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TOPIC LABORATORY MEDICINE IN DIAGNOSIS AND TREATMENT OF CANCER

LIPID PROFILES OF HUMAN CANCER CELL MEMBRANES. EFFECTS OF DIFFERENT AGENTS

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Polyunsaturated fatty acids are major components of phospholipids, the principal structural unit of biological membranes. Unsaturated fatty acids have one or more double-bonds in a cis or trans configuration. Trans isomers are able to perturb both cell membrane arrangement and lipid enzymatic cascades. Endogenous trans fatty acid isomers are formed by the isomerization of fatty acids in cell membranes due to an endogenous free radical process. Reactive oxygen species (ROS) lead to the oxidative degradation of lipids in cell membranes, resulting in cell damage. Cell membranes, which are structurally made up of large amounts of PUFA, are highly susceptible to oxidative attack and, consequent changes result in altered membrane fluidity, permeability, and cellular metabolic dysfunction. Some chemotherapeutic agents and all radiation therapy induce oxidative stress by generation of ROS, which might be an alternative mechanism for their cytotoxic effect via inducing cell death. In this study we aimed to compare the fatty acid profile of human cancer cell membranes during normal culturing and treatment with different agents. The membrane fatty acid profile analysis in control and other samples was performed using gas chromatographical (GC) analysis with external reference standards. Lipid extraction and transesterification were performed to obtain the fatty acid residues as the corresponding methyl esters. Incubation of the cells with different agents caused significant changes in membrane lipid profiles including trans lipid concentration.

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INVESTIGATION OF THE EFFECTS OF TREATMENT OF SERUM METHODS IN BLADDER CANCER DISEASES

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Bladder cancer is one of the commonest cancers. Intravesical chemo-immunotherapies are used to reduce the risk of progression in at-risk patients. Immunotherapy by BCG is the best adjuvant therapy found. Tumor angiogenesis plays a very important role in the formation and metastasis of tumors. Change in the vascularization system contributes to changes in the expression of angiogenic factors for the development of angiogenic regulatory pathways and vascularization around the tumor. Nitric oxide is a key enzyme in angiogenesis. It increases endothelial cell proliferation and migration and the breakdown of extracellular matrix. In addition to angiogenesis, NO plays a role in the cycle progression, metastasis and life of cells.

Asymmetric dimethylarginine (ADMA) is an endogenous inhibitor of endothelial nitric oxide synthetase, which inhibits NO from being free of arginine. DDAH1 has been reported to be formed in increase in tumor vascularization and in cerebral tumor growth. Overexpression of DDAH1 in glioma cell lines plays a leading role in increasing NO synthesis and increasing the production of VEGF, which increases angiogenesis. The aim of the present study was to determine whether there was any change in the levels of arginine, citrulline, ornithine, SDMA, L-NMMA or ADMA in the serum of blood samples of bladder cancer patients, and to explain the correlation between methylarginine before and after treatment.

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PLEURAL FLUİD PROGRANULİN, EPİTHELİAL CELL SPECİFİC MOLECULE, CLUSTERİN, HUMAN EPİDİDYMİS - 4 LEVELS IN DİAGNOSİS OF PLEURAL EFFUSİON

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Aim: Pleural fluids such as malignant effusion (MPE), tuberculosis effusion (TPE) or parapneumonic effusion (PPe) are the most common causes of exudat fluids in the pleura. It is important to perform a malignant-non-malignant differentiation quickly and accurately. The aim of this study is to be able to detect markers to distinguish malign pleura from other etiologic pleurases in pleura fluids.

Methods: The study population consisted of 90 patients over the age of 18 with pleural effusion. Pleura fluids progranulin (PGRN), epithelial cell specific molecule (ECSM), clusterin (CLU) human epididymis-4 (HE-4) levels were measured by ELISA method.

Results: Of the 90 patients (54 males, 36 females; median age 65 ± 16), 23 (25%) were of transudative nature and 67 (74%) were exudative. Twenty-seven of the exudates were PP (40%), 19 were TPE (28%) and 21 were MPE (29%). Levels of CLU, HE-4, PRGN was higher in malign fluid than non malign group ($p<0.05$). There was no difference between malign and nonmalign fluid levels in ECSM ($p=0.454$). CLU, HE-4 and PGRN levels were significantly higher in malignant fluid than those of tuberculous fluids ($p < 0.001$). There was no statistically significant difference in ECSM levels ($p=0.768$).

Conclusions: Pleura fluids CLU, HE-4, PRGN levels was thought to be a potential diagnostic markers for differentiating from non-malignant effusions; for distinguishing malign effusions from tuberculous potential diagnostic marker was CLU, HE-4, PRGN. In addition, we believe that these findings may provide a basis for future research.

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CLINICAL SIGNIFICANCE OF THE COMBINATION OF CEA AND CA 19-9 TUMOR MARKERS IN MALIGNANT AND BENIGN TUMORS OF VARIOUS ORIGINS

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Aim: The present study aimed to assess the diagnostic and prognostic value of clinical tumor markers carcinoembryonic antigen (CEA) and carbohydrate antigen-19.9 (CA-19.9), used in combination as helpful diagnostic method for malignant and benign tumors from different origin. Smoking habit of patients was considered as a factor for evaluation of the risk of malignancy development.

Method: The electro-chemiluminescence immunomethod was performed with automated analyzer to detect the levels of the two tumor markers in 71 patients, part of whom had malignant or benign tumor and the other part were without tumor. The statistical program StatsDirect was used for statistical analyses.

Results: Combined use of two tumor markers CEA and CA 19-9 can allow mistakes in diagnosing malignant and benign diseases because these tumor markers do not have 100% sensitivity and specificity. Combined specificity for malignant tumors was 92.45% and for benign tumors 82.26%. Combined sensitivity for malignant tumors was 44.44% and for benign tumors 11.11%. Smoking as a risk factor for malignant disease was calculated in 1.4.

Conclusion: 7.55% of patients would have been diagnosed with malignant diagnosis incorrectly, while 55.56% of patients with such a disease would remain undetected. 17.74% of patients would have been diagnosed with a benign illness diagnosis, while 88.89% would remain undetected. The prevalence of malignant disease was 25.35% while of benign disease 12.68%. Smokers were 1.4 times more likely to have malignant neoplasm than non-smokers, while smoking was insignificant factor for development of benign neoplasm.

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EVALUATION OF SERUM INHIBIN B CONCENTRATIONS ASSAY PERFORMED BY ELISA METHOD

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Aim: Inhibin B is a dimeric hormone that is composed of alpha and beta B subunits. The free alpha subunits usually do not have any physiological effect, and only dimeric forms of inhibins are biologically active. Inhibins are protein hormones secreted by granulose cells of the ovary in the female and Sertoli cells of the testicles in males. Inhibin B enzyme- linked immunosorbent assay (ELISE) kit provides materials for the quantitative measurement in human serum and other biological fluids. The aim of this study was to evaluate the ELISA method for determination of inhibin B.

Materials and methods: Measurements of inhibin B were performed by ELISA method (DRG Instruments GmbH, Germany). The inhibin B ELISA is a quantitative three-step sandwich type immunoassay. Imprecision of the inhibin B assay was determined using two kit controls. Inhibin B levels were measured in serums obtained from 20 healthy subjects and 38 patients with histologically confirmed adult-type granulose cell tumors (AGCTs). Median age of the women with AGCTs was 29 year (range 21-39 years).

Results: The inter-assay coefficient of variation (CV) for ELISA assay was 3.9% and 4.4% at 68 pg/ml and 121.5 pg/ml and the intra-assay CV was 5.5% and 5.0% at 99.3 pg/ml and 308.1 pg/ml, respectively. Median values for inhibin B levels were significantly higher in patients with AGCT compared to the control group (34.3 vs. 81.2 pg/ml, $p<0.0001$). Serum levels of inhibin B were elevated in 74% (23/31) of AGCTs patients.

Conclusions: The presented results performed by ELISA method for determination of human inhibin B in serum showed an acceptable precision. Serum inhibin B levels were specifically elevated in AGCTs patients.

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DETECTION OF FUSION ABL-BCR GENE IN PEDIATRIC PATIENTS WITH LEUKEMIA

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Aim: The Philadelphia chromosome or Philadelphia translocation is an acquired abnormality of chromosome 22 which is most commonly associated with chronic myelogeneous leukemia (CML). It is the product of a reciprocal translocation between chromosome 9 and chromosome 22 [t(9;22)(q34;q11)] and this gives rise to a fusion gene bcr-abl, that juxtaposes the Abl1 gene on chromosome 9 (region q34) to a part of the BCR ("breakpoint cluster region") gene on chromosome 22 (region q11). The presence of this translocation is found in 95% of people with CML. The presence of the Philadelphia (Ph) chromosome is not sufficiently specific to diagnose CML, since it is also found in acute lymphoblastic leukemia (ALL, 25–30% in adult and 2–10% in pediatric patients) and occasionally in acute myelogenous leukemia (AML).

Methods: Pediatric patients with acute and chronic lymphoblastic and myelogeneous leukemia were tested for the presence of the fusion bcr-abl gene. RNA isolation from leukocytes from fresh bone marrow and peripheral blood samples was performed by Trizol extraction per manufacturer's protocol. The principle of RT-PCR is reverse transcription of mRNA from complementary DNA (cDNA) with subsequent amplification. The final result is bcr-abl fused gene detected on the 1% agarose gel as a 450bp band.

Results: During the ten year period (2002-2015) 266 pediatric patients with various forms of leukemia were tested for presence of fusion gene bcr-abl gene. It was found in 7 patients (2.6%). Six patients had CML while the seventh patient with microBCR had rare Ph+ chronic neutrophilic leukemia.

Conclusion: RT-PCR method is useful for detection of fusion bcr-abl gene. This is an accurate investigation, relatively cheap and the result is issued within two days.

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TOPIC MASS SPECTROMETRY: THE NEAR FUTURE

COMPARISON OF COLORIMETRIC, ENZYMATIC ASSAY AND MASS SPECTROMETRIC SERUM CREATININE METHODS

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Aim: Enzymatic and Jaffe methods are commonly used in clinical settings. However, notable differences exist among these methods for absence of adequate specificity. Additionally, these methods are more vulnerable to interference from hemolysis, lipemia , bilirubin, proteins, and ketones. The aim of this study was to compare Jaffe, enzymatic assays and mass spectrometric serum creatinine methods.

Methods: A total of 90 serum samples were analyzed as 30 sample below reference intervals, 30 within reference intervals and 30 above reference intervals. For the measurement of serum creatinine, 40 microliters of internal standard (d3-creatinine) in acetonitrile and 460 microliters of acetonitrile were added to 40 microliters of serum or standard. The reaction tube was centrifuged for protein removal at 2300 rpm for 10 minutes. The supernatant was collected and 20 microliters were injected into a high performance liquid chromatography device for chromatography.

Results: According to Deming regression analysis, the LC-MS/MS and enzymatic comparison r value was found to be 0.9942. In the LC-MS / MS and Jaffe comparison study, the r value was found to be 0.9959. Enzymatic and Jaffe comparison r value was found to be 0.9981. The Bland Altman evaluation demonstrated a partial mean bias of 14.4% between the Jaffe and mass spectrometric methods, but demonstrated a partial mean bias of 14.02% between enzymatic assays and mass spectrometric methods.

Conclusions: The comparison has shown that the measurement of creatinine by the chromatographic method gives more accurate results.

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LEVELS OF ZINC, ARSENIC, CADMIUM, LEAD IN PATIENTS WITH ASBESTOSIS AND MESOTHELIOMA

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Aim: Asbestos-related lung diseases are a common clinical problem and a major health concern worldwide. We aimed to identify some biochemical important pathways in asbestosis and mesothelioma which occur following to exposure to asbestos, and commonly seen in Yozgat, and called as environmental diseases as well as occupational diseases.

Methods: The study was carried out in Bozok University Faculty of Medicine with the patients admitted to policlinics of Chest Diseases and Thoracic Surgery.

• Group 1 (healthy control group, n=27) - consisting of healthy individuals without any chronic disease and regular use of drugs.

• Group 2 (patients group, n=34) - after clinical, pathological and radiological evaluation of the patients as mesothelioma and/or pleural plaques and asbestosis.

Analysis of blood samples were performed in Selcuk University Faculty of Medicine in Medical Biochemistry Department of the Central Research Laboratories. Zinc, arsenic, cadmium, lead levels were analyzed in ICP-MS and determined as x±SE (µg/l).

Results: Arsenic (3.4±0.63; 5.4±0.77), cadmium (19.45±1.32; 23.28±6.41) and lead (22.9±2.28; 24.5±1.34) levels were statistically lower in control group than in patients group ($p \leq 0.05$) whereas the differences between the groups according to zinc levels ($p=0.49$) were not significant.

Conclusion: Evaluating the changes in blood levels of trace elements especially As, Cd and Pb in this pathway will create a basic data for further studies in therapeutic applications. In addition, analyzing the levels of these elements may be important in contributing to diagnosis in these patients.

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TOPIC LABORATORY DIAGNOSIS OF PATHOLOGICAL CONDITIONS IN PREGNANCY

MATERNAL HAMP RS10421768 VARIANT IS NOT LINKED TO PREGNANCY LOSS IN BOSNIAN WOMEN

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Background: Hepcidin is an antimicrobial peptide encoded by the HAMP. It is synthesized in hepatocytes and plays a crucial role in regulation of iron metabolism. One of the effects of mutations in the HAMP gene may be iron deficiency. During pregnancy, iron is essential to support placental and fetal growth, to increase in maternal red blood cell mass as well as compensate for blood losses during delivery. Currently, the data on the role of hepcidin variants in pregnancy complications are scarce. Aim: Therefore, the aim of the study was to investigate the prevalence of rs10421768 (-582A>G) and to determine the variant correlation with the risk of pregnancy loss (PL). Material and methods: We prospectively recruited 154 women with PL, mean age 33 (±5.4) y. The min. week of miscarriage was 6, while max. 28. As a control group, equal number of mothers with at least one live-born child was included. All women were of Bosnians origin. Genotypes were determined by real-time PCR using LightCycler® 96 (Roche Diagnostics, Warsaw, Poland) and TaqMan SNP Genotyping Assays (Life technologies, Assay ID: C_2604942_10). Results: In women with and without PL, the distribution of AA, AG and GG genotypes was: 61.7%, 35.1%, 3.2% and 64.3%, 30.5%, 5.2%, respectively. Our results, did not confirm association of rs10421768 with PL in Bosnian women (P-value = 0.5429). Conclusions: Further research will enable to understand the correlation between hepcidin variants and pregnancy complications, and detect new methods of treating iron deficiency.

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FIRST BOSNIAN STUDY OF RELATIONSHIP BETWEEN VDR RS731236 AND RS1544410 VARIANTS AND PREGNANCY LOSS

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Background: The vitamin D receptor is expressed in different uteroplacental parts. It influences hormone secretion, modulates the immune system of the placenta, regulates implantation of the embryo. It is suggested that the immunomodulatory effects might have a protecting role in pregnancy loss (PL). Aim: The aim of the study was to investigate the prevalence of rs731236 (TaqI, T/t) and rs1544410 (BsmI, B/b) and to determine the haplotype correlation with the risk of PL. Material and methods: Group of 154 women with PL, mean age 33 (±5.4) y, were enrolled in the study. As a control group, 154 mothers mean age 31.4 (±6.7) y with at least one live-born child were included. All women were of Bosnians origin. Genotypes were determined by real-time PCR using StepOneTM Real-Time PCR System, Applied Biosystems and TaqMan SNP Genotyping Assays (Life technologies, Assay ID: C_2404008_10 and C_8716062_10 for rs731236 and rs1544410, respectively). Results: The prevalence of haplotypes: Tt/Bb, TT/BB, tt/bb, Tt/bb, TT/Bb in women with and without PL was: 71(46.2%), 57(37.0%), 23(15.0%), 1 (0.6%), 1(0.6%), and 72 (46.8%), 50 (32.6%), 25 (16.2%), 2 (1.3%), 1(0.6%), respectively. The Tt/BB (2 (1.3%)), tt/BB and TT/bb genotypes (each 1(0.6%)) were found only in the control group, while the tt/Bb (1 (0.6%)) in women with PL. Our results, did not confirm association of rs731236 and rs1544410 with PL in Bosnian women (P-value = 0.7532, OR: 1.1399). Conclusions: We suggest to conduct a large-scale epidemiological studies to fully-understand the contribution of VDR polymorphisms to pregnancy loss.

HYPERTENSIVE DISORDERS IN PREGNANCY

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Introduction: Hypertension is the most common medical problem encountered during pregnancy, complicating 5-10% of pregnancies. It's defined by a systolic blood pressure ≥ 140mm Hg, and a diastolic blood pressure ≥ 90 mm Hg or by a rise in blood pressure of systolic ≥ 30 mm Hg and diastolic ≥ 15 mm Hg. Preeclampsia and superimposed preeclampsia are pregnancy-induced multi-organic diseases, endangering both the mother and the fetus.

The aim of the investigation was to determine biochemical parameters associated with hypertension in pregnancy.

Material and methods: We examined 78 pregnant women in 20-32 g.w. with high blood pressure more than 140/90 mm Hg and determined urea, creatinine, uric acid, AST, ALT, LDH, total protein, albumin and plates in blood, and urine dipstick protein. The control group consisted of 40 pregnant women without hypertension. We used usual biochemical methods for determination of all these parameters.

Results: Our results were: urea-3.4 mmol/l±0.8, creatinine 48.4 μmol/l ±12.6, uric acid 282.9 μmol/l ± 64.4, ALT 36.3 U/l ±11.7, AST 37.2 U/l ± 10.6, LDH 388,1 U/l ±94.4, total protein 68.9 g/l ± 13.3, albumin 42.3 g/l ± 9.2, Plt 207x 109/l ± 65 and 27 positive urine protein (+1 to +3).There was no statistical difference in all parameters in both groups of pregnant women ($p>0.05$), except that urine proteins (34.6%) were positive in pregnant women with hypertension.

Conclusion: There were no biochemical parameters for laboratory diagnostics considering hypertension in pregnant women. Positive urine protein is the first indicator according to clinical indications for hypertension.

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SECOND-TRIMESTER MATERNAL SERUM LEVELS ANALYSIS AND TRISOMY 13/18/21

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Aim: The aim of our study was to select patients with high risk of trisomy using Prisca method which includes biochemical and echosonography methods.

Methods: The study included 144 pregnant women with previous trisomy 21 pregnancies unknown. With standardized echosonography methods, different parameters such as crown rump length in mm, nuchal translucency MoM, nasal bone and meridians were measured in order to construct the corr.mom and curve between corr. MoM and biochemical parameters.

Results: Two patients were with neural tube defects and high risk for trisomy 21, with corr.mom AFP 3.43 and 2.53 respectively and corr.mom HCG 2.69 in both cases. In all patients the values for uE3 were 0.70 that was within the risk.

Conclusion: The AFP and HCG values depend on each other, but are not affected by uE3 values. We also conclude that with increasing age of the mother and the fetus the level of the curve is also raising, which means an increasing risk. The calculated risk for trisomy 13/18/ (with nuchal translucency) was <1:10000, which was a low risk for all of the patients included in study.

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TOPIC PAEDIATRIC AND ELDERLY LABORATORY TESTING

PROCALCITONIN VS C-REACTIVE PROTEIN AS MARKERS FOR EARLY-ONSET NEONATAL INFECTION AT SHGO "MOTHER THERESA"

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Aim: As early-onset neonatal infection presents with non-specific symptoms, it is suspected in newborns where risk factors combined with clinical signs are present. The most used diagnostic biomarkers for suspected infections in neonatal care units (NCU) are procalcitonin (PCT) and C-reactive protein (CRP). The aim was to compare both of them as indicators of inflammation and infection in neonates. The sensitivity, specificity and early detection potential of each inflammation marker are very important, especially in NCUs.

Methods: A retrospective study of 220 newborn neonatal histories at the Department of Neonatology at SHGO "Mother Theresa" was done. Blood for detecting biomarkers was taken when there was a risk factor from the mother's side and/or there was clinical suspicion of infection. PCT and initial CRP were measured as soon as possible in the first 24 hours and control CRP was done after 24 or 48 hours depending on clinical symptoms.

Results: Of the 220 samples taken from newborns, 96 (43.64%) showed to be positive for elevated PCT and/or CRP. PCT, first CRP and control CRP presented as follows: in 28 results or 29.17% results PCT, CRP1, CRP2 were positive, positive, positive; followed by 26 or 27.08% of results with negative, positive, positive; 16 or 16.62% of results negative, negative, positive; 14 or 14.58% results positive, negative, negative (probably false positive) and 12 or 12.5% results were positive, negative, positive, respectively.

Conclusion: The results obtained showed that CRP was more specific than PCT, as PCT high levels were detected in 41.67% (excl. false positives), and CRP1 elevated levels were detected in 56.25% of samples.

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NEUTROPHILIC GELATINOUS ASSOCIATED LIPOCALIN AS AN EARLY BIOMARKER OF ACUTE KIDNEY INJURY IN NEONATES

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Aim: Acute kidney injury (AKI) is a common clinical problem in newborns in the neonatal intensive care unit (NICU). Predisposing factors associated with neonatal kidney injury are: certain clinical conditions, therapeutic interventions and nephrotoxic drugs. The aim of the study was to determine the incidence, risk factors and efficiency of the biomarker urinary neutrophilic gelatinous associated lipocalin (NGAL) in early diagnosis of neonatal AKI.

Subjects and Methods: The study included 100 newborns hospitalized in NICU of University Children's Hospital (50 with AKI and 50 without AKI). Medical data records of admitted neonates with AKI were analyzed. NGAL was analyzed in urine samples collected with urinary sachet or urinary catheter using ELISA method (Bioporto).

Results: The estimated prevalence of AKI in neonates was 6.4%, according to the standard definition. There was a significant difference between the values of urinary NGAL of newborns with AKI compared to the control group ($p<0.001$). NGAL's monitoring on the day of hospitalization and three days later showed a slight upward trend. There was a significant difference between the values of urinary NGAL in newborns with AKI and lethal outcome and newborns without lethal outcome ($p<0.001$).

Conclusion: Urinary NGAL is an early predictive biomarker of AKI in critically ill newborns that provides better outcome and prognosis of the disease. The results have shown that NGAL allows early diagnosis of AKI in the first hours of its onset, when the disease is clinically manifested, and degradation products are within normal range.

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TOPIC BIOMARKERS OF INFLAMMATION AND VASCULAR DAMAGE

OXIDATIVE STRESS AND RESPONSE MECHANISMS

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Introduction. Ischemia due to atherosclerotic changes often results in AMI and fatal outcome. In aim to find most efficient model in fast detecting of such changes, we investigate parameters involved in oxygen supply or detecting its deficit.Myoglobin as oxygen depot and transporter is earliest but not most specific cardiac marker, while heart muscle constituent proteins Troponins (TnT, I, C), are considered as specific marker for ischemic event and signal for affected heart muscle integrity and function. According to literature data, we investigate activation of Hsp70 antibody as stress marker due to impaired tissue stability in case of oxygen deficit. This marker, also, has been proved as good inflammatory marker, so it was used along with measurement of CRP and Le count.

Material and methods. Study involved 200 patients admitted to EU with symptoms for AMI. After evaluation of first results, patients were divided in 4 groups. AMI, AP/NSAP, Cardiomiopathy and pulmonary edema. Blood donors were used as a control group (CG). All samples were submitted to testing for Le count, CRP, Myoglobin, Troponin and Hsp 70.

Photometric, ECLIA and ELISA principle of determination was used for all parameters. The results were processed with ANOVA statistical model.

Results. Results shows significant increase of myoglobin concentration (5 fold vs CG), TnT (196- fold) and TnI (186 -fold), indicating high oxygen deficit or demand especially at patients with AMI and AP/NSAP. Elevation of Hsp 70 antibody level was most significant at the patients with AMI (26-fold vs CG) and at patients with pulmonary edema(63-fold).

Conclusions. Our result supports some previous standing that beside others tests, changes in Hsp 70 has its role as signal for cell stability and function in case of ischemia. This position came from the fact that Hsp 70 engages system of process that prevents additional protein denaturation as result of cell membrane damage in case of AMI. Furthermore, Hsp 70 can be use as a predictive marker at patients in follow up for future eventual events, since it has been shown it has prolonged, but limited activity.

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PRELIMINARY STUDY OF THE RATIO OF TRIGLYCERIDES TO HDL IN TYPE 2 DIABETES PATIENTS AS A POTENTIALLY BETTER MARKER FOR VASCULAR DISEASE RISK ASSESSMENT THAN LDL CHOLESTEROL

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In the last decade it has been established that cholesterol, and particularly LDL cholesterol do not have the central pathogenic role in cardiovascular disease as once postulated. It has become clear that only small dense LDL particles, whose defective molecules are prone to biochemical modifications and thus modified might be deposited in the subendothelium are the fraction mostly pathogenically involved, but also that triglyceride rich lipoproteins may also have an important atherogenic role, especially in suppressing the atheroprotective and anti-inflammatory effects of HDL by blocking sterol efflux from monocytes and macrophages. For this reason, it has been proposed that the Triglyceride-to-HDL Ratio (TtHR) may be a better marker of vascular disease progression, especially in type 2 diabetes, where hypertriglyceridemia is more prevalent.

In this preliminary study, we measured HbA1c, glucose, triglycerides, total and HDL cholesterol in 16 control patients and in 44 patients with type 2 diabetes. Correlation of HbA1c levels and TtHR (0.41) was second only to glucose (0.76) and much higher than LDL cholesterol, which had a correlation coefficient of -0.11 in the patient group.

We conclude that the TtHR has good potential for use in assessing risk as a screening marker and that further studies are needed which will investigate it's correlation with other laboratory and clinical markers of vascular disease.

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EVALUATION OF PAIN AND OXIDATIVE STRESS IN CUPPING THERAPY

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[3]Konya Education and Research Hospital, Department of Biochemistry, Konya, Turkey Abstract

Aim: In this study, it was aimed to investigate the relationship between ischemia modified albumin (IMA) and malondialdehyde (MDA) levels and visual analogue scale (VAS) pain scores in the cupping blood of the interscapular region in women with head, waist, and back pain.

Methods: This study was performed on 96 women between the ages of 18-55. Participants were divided into three groups according to complaints of back (30 women, group 1), waist (31 women, group 2) and head (35 women, group 3) pain. IMA and MDA levels were measured spectrophotometrically in the cupping blood of the interscapular region.

Results: There was no significant difference between IMA and MDA levels in the cupping blood of the interscapular region of groups. There was a statistically significant positive correlation between MDA levels and VAS values of group 1, group 2 and group 3 ($p < 0.01$). In addition, statistically significant positive correlation was found between IMA levels and VAS values of group 3 ($p < 0.01$).

Conclusion: Our study was the first study in the literature investigating the MDA and IMA levels in the cupping blood in the differential diagnosis of different region pain types. The levels of these parameters were not found to be different in distinguishing different region etiologies of pain in the obtained findings. However, according to our VAS scores, there was a decrease the pain of the patients after cupping therapy and the relationship between these values and oxidative parameters was also determined.

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COMPARATIVE STUDY OF ENZYMATIC MARKERS IN MEN SEMINAL FLUID BETWEEN NORMOSPERMIA AND AZOOSPERMIA

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AIM According to WHO, infertility is defined as the absence of conception after two years of exposure to the risk of pregnancy. In about half of cases, the man is responsible, because the degradation of sperm quality is increasingly observed. Azoospermia is one of the causes of infertility. The aim of this study was to assess the enzymatic activity in the seminal fluid of patients with normospermia and azoospermia.

METHODS Sixty-four men samples were collected by masturbation after four days of sexual abstinence and with either azoospermia or a normospermia were selected. 43 normospermia and 43 azoospermia were found. After cytological analysis, samples of all patients were centrifuged and lactate dehydrogenase (LDH), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and creatine kinase (CK) in seminal plasma using commercial tests.

RESULTS There was no significant difference ($p<0.001$) in ALP and CK levels between normospermia and azoospermia patient s group. There was significant difference in LDH levels in normospermia samples (4796.15±1982.77) and azoospermia group (3314.53±1797.46) ($p<0.001$). Also, AST levels were significantly higher in normospermia group (454.10±446.58) compared with azoospermia group (328.81±536.11) ($p<0.001$). The same trend was found in ALT levels: ALT in azoospermia were significantly higher compared with normospermia 133.81±375.00 vs. 97.61±295.31.

CONCLUSIONS Our results show that biochemical analysis of the seminal fluid could be important for better undestanding of the functioning of the glands.The evaluation of LDH, AST and ALT activities in seminal plasma could be helpful for diagnosis normospermia and azoospermia.

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HOMOCYSTEINEMIA AND POLYMORPHYSM OF THE GENE FOR METHYLENTETRAHYDROFOLATE REDUCTASE (C677T) IN PATIENTS WITH CORONARY ARTERY DISEASE

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Purpose: The aim of this study was to determine the concentration of total homocysteine (tHcy) in healthy subjects, and in patients with coronary artery disease (CAD), as well as to determine the prevalence of C677T mutation of the enzyme methylentetrahydrofolate reductase (MTHFR).

Material and Methods: The study included 204 participants divided into two main groups: 123 healthy individuals and 81 patients with CAD. The concentration of plasma tHcy was determined by cyclical enzymatic method, and mutation of MTHFR gene C677T by polymerase chain reaction by Schneider.

Results: The concentration of plasma tHcy in patients was significantly higher than in healthy subjects ($p<0.001$). The highest frequency in healthy subjects and patients for mutations in the MTHFR gene had C677T heterozygous genotype CT (46% vs 50%), of homozygous wild genotype CC (44% vs 33%), and the lowest frequency had the genotype TT (10% vs 17%).

Conclusion: There is a significant association of tHcy with CAD development; hence tHcy is not a marker but a risk factor for occurrence and development of CAD. Mutations in the gene MTHFR C677T are not risk factors for CAD.

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INVESTIGATION OF SERUM ISCHEMIA MODIFIED ALBUMIN AND MALONDIALDEHYDE LEVELS IN PROFESSIONAL ATHLETES AND SEDENTARY WOMEN

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Aim: Sedentary lifestyle is a risk factor for the development of numerous disease. Along with this, physical activity has emerged as an important lifestyle factor for primary prevention of numerous diseases. In this study, it was aimed to investigate the ischemia modified albumin (IMA) and malondialdehyde (MDA) levels in serum of professional athletes and sedentary women.

Methods: Totally 60 women were included in the study, 30 of whom are sedentary (Group 1), and 30 of whom are professional athlete (Group 2). Serum IMA and MDA levels were measured spectrophotometrically.

Results: Serum IMA levels were significantly higher in group 2 compared with group 1 ($p<0.05$). There was no significant difference between serum MDA levels of groups. There was a statistically significant positive correlation between MDA and IMA levels of group 1 ($p<0.05$).

Conclusion: We conclude that increase in production of free radicals with intense physical exercise can exceed the capacity of the antioxidant defense systems in the body and induce oxidative condition. There is clearly much more to be learned about this exciting field.

Keywords: Exercise, sedanter life, ischemia modified albumin, malondialdehyde.

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THE RELATIONSHIP BETWEEN ANTIOXIDATIVE ENZYMES AND LIPID PEROXIDATION IN NEUTROPHILS OF PATIENTS WITH UNSTABLE ANGINA PECTORIS

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Aim. The aim of this study was to research the relationship between antioxidative enzymes and the conjugated dienes (CD) and malondialdehyde (MDA) as a marker of lipid peroxidation, in neutrophils during acute myocardial ischemia in patients with unstable angina pectoris.

Methods: The activities of superoxide dismutase (SOD), glutathione peroxidase-1 (GPx-1), catalase (CAT) and the concentrations of conjugated dienes (CD) and malondialdehyde (MDA) in neutrophils lysate, were determined in 47 patients with unstable angina pectoris and compared with 33 healthy subjects. Simultaneously, ratio SOD/(GPx-1 + CAT) was calculated, representing ratio of enzymes that produce and consume hydrogen peroxide.

Results: The activity of the neutrophil SOD ($p<0.05$) and the concentration of CD ($p=0.0001$) was found significantly increased in unstable angina, and SOD was positively correlated with the CD ($\rho= 0.717$, $p<0.0001$). The ratio of the activities of antioxidative enzymes SOD/(GPx-1 + CAT) was significantly increased ($p<0.05$) and positively correlated with the CD ($\rho = 0.55$, $p=0.0001$) in neutrophils in unstable angina. There were no other significant differences in the activity of glutathione peroxidase-1 (GPx-1) and catalase (CAT), and the concentrations of malondialdehyde (MDA) in neutrophils lysate between groups.

Conclusion: Early lipid peroxidation in neutrophils in unstable angina, presented by CD increase, is the result of the increased production and accumulation of hydrogen peroxide.

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TOPIC VITAMINS AND NUTRITION

EVALUATION OF VITAMIN D (25 OH) MEASUREMENTS IN 2017, CONCLUSIONS AND CURRENT GUIDELINES

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Introduction: Vitamin D is no longer important solely for prevention and cure of rickets and musculoskeletal health. It is related with extra-skeletal diseases such as cancer, cardiovascular diseases and infections. Low Vitamin D level is an indicator of poor health status. Evaluation of low prevalence of vitamin D levels is important for public health perspective; hence, we evaluated our results from 2017. We also present Synlab Academy guidelines for optimal daily dosage.

Methods: A total of 380 serum samples were measured for vitamin D total using ECLIA/ROCHE cobas e 411. Samples were collected from Skopje, Tetovo and Bitola. Results were analyzed regarding reference values, location and gender of the patients.

Results: 41.06% of patients had results of <20 μg/L (deficiency); 26.95% had 20-30 μg/L (insufficiency); 31% of patients were between 30-100 μg/L (therapeutic levels) and 0.94% had intoxication >150 μg/L.

In patients from Tetovo higher level of deficiency (59.25%) was found, in patients from Skopje 37% and from Bitola 28.55%. Therapeutic levels (30-100 μg/L) were found in 36% of patients from Skopje and Bitola; 16.6% from Tetovo. 68.2% of patients were females and deficiency was found in 62% of them.

Conclusion: Our results show that in our country deficiency of vitamin D is present with high percentage, alarming for the population in Tetovo (59.25%) and for females. It can be a result of cultural behavior and non-exposure to daylight. Part of the population in Skopje takes preventive nutritional, behavioral and supplemental measures.

Recommendation: 400-800 IU Vit D per day (modern guidelines for optimal dosage of vitamin D) for all patients with deficiency should be included in all lab reports signed by medical lab specialists.

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5-HYDROXY VITAMIN D IN WOMEN AT DIFFERENT AGES

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Aim: Vitamin D is important for bone health and its deficiency is associated with osteoporosis in adults. The major circulating form of vitamin D is 25-hydroxy vitamin D and its concentration is the best indicator of vitamin D status. The aim of the study was to measure serum 25(OH) vitamin D in women at different ages in order to determine their vitamin D status.

Methods: A total of 261 women aged 30-79 years were included in this study. They were divided in five age groups (30-39; 40-49; 50-59; 60-69; 70-79). Serum 25(OH) vitamin D concentrations were measured on automatic analyzer using chemiluminescence microparticle immunoassay. Levels of serum 25(OH) vitamin D (collected during summer) were interpreted as follows:

- <20 ng/ml : Vitamin D deficiency
- 20-29 ng/ml: Vitamin D insufficiency
- 30-80 ng/ml: Vitamin D sufficiency

Results: 59.8% of all women had 25(OH)vitamin D serum values less than 20 ng/ml, with half of them having severe vitamin D deficiency (<10ng/ml). 29.1% of the women had vitamin D insufficiency and 11.1% had vitamin D sufficiency. By groups, the rates of vitamin D deficiency and insufficiency for the four age groups (40-79 yrs) were similar to the aforementioned results, however in the first age group (30-39 yrs), only 28.6% were deficient, while 35.7% were insufficient. The results indicated that vitamin D deficiency increased with advancing age while vitamin D sufficiency declined.

Conclusion: The results confirmed a high prevalence of vitamin D deficiency in women and its age dependence including factors such as inadequate dietary vitamin D intake, limited sun exposure and postmenopause.

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INVESTIGATION OF THE RELATIONSHIP BETWEEN VISUAL ANALOGUE SCALE PAIN SCORES AND VITAMINE D3 LEVELS IN CHRONIC PAIN SYNDROME

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Aim: Standing apart from the various other essential nutrients, vitamin D3 was spotlighted recently as having special therapeutic potential. This has important implications for the management of chronic pain syndrome. In this study, it was aimed to investigate the relationship between visual analogue scale pain scores and vitamine D3 levels in women with chronic pain syndrome.

Methods: We have evaluated vitamine D3 levels (25-OH-Vitamin D3) of 55 women aged 18-65 years. The all patients who were diagnosed in Traditional and Complementary Medical Center of Meram Medical School were recruited into the study. Vitamin D3 levels were measured by routine chemiluminessans method. For this review, vitamin D3 deficiency is defined as serum 25-hydroxyvitamin (25-OH-Vitamin D3)<30 ng/ml.

Results: Serum vitamine D3 levels of the women were found as 22.4 ± 2.7 ng/ml. There were significantly negative correlations between serum vitamine D3 levels and visual analogue scale values of the women (r=-0.285, p=0.035).

Conclusion: Possible mechanisms for vitamin D3 in pain management are the anti-inflammatory effects mediated by reduced cytokine and prostaglandin release and effects on T-cell responses. However, the underlying mechanism of the negative correlation between serum vitamine D3 levels and visual analogue scale values is not known and needs to be more investigated.

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THE LEVEL OF VITAMIN D IN PATIENTS WITH POSMENOPAUSAL OSTEOPOROSIS

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Introduction: Determination of vitamin D levels in patients with postmenopausal osteoporosis (PMOP) is significant for two reasons. First, vitamin D deficiency reduces calcium absorption from the gastrointestinal tract, and second, vitamin D deficiency increases the risk of fracture.

Aim: To show the level of vitamin D in patients with PMOP according to age.

Material and methods: The research involved 90 patients who were diagnosed and treated at the Institute for Physical Medicine and Rehabilitation in Skopje. The level of D vitamin was determined by measuring 1.25 (OH) D vitamin in serum with electrochemiluminescence. The value of ≥30 ng/ml is normal, the value between 10 and 30 ng/ml is insufficient and the value ≤10 ng/ml is very low.

Results: Patients were at an average age of 60.64 ± 6.7 years. The largest number were patients aged from 60 to 69 years - 53 (57.61%). The mean serum vitamin D level in the age group 40-49 was 22.47 ± 9.9, in the age group 50-59 was 13.61 ± 6.5, in 60-69 was 20.37 ± 8.7, and in the age group 70-75 it was 16.31 ± 7.2. Vitamin D values were lowest in the group of patients aged 50 to 59 years, compared to other age categories (13.61 ± 6.5 μg) (p = 0.16). The level of vitamin D in serum was low, regardless in which age group patients with PMOS belonged.

Conclusion: The mean values of vitamin D in the serum did not differ significantly among the age groups of patients with PMOS. Vitamin D should be recommended in all patients with PMOP regardless in which age group they belong to.

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EFFECTS OF PLANTAGO MAJOR EXTRACT ON SOME SERUM VITAMINS AND MINERALS IN BROILER

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Aim: The aim of this study was to determine the effects of Plantago major (P. major) water extract added into broiler diets at different levels on serum antioxidant vitamin and mineral concentrations of broiler.

Methods: A total of 112 Ross 308 broiler chicks were used in the study. The experiment included control and 3 treatment groups with 28 chicks in each group. Each experimental group was divided into four subgroups consisting of 4 chicks. A basal (control) diet was prepared and three experimental diets were established by addition of P. major into basal diet; P. major 1 (5 g/kg feed), P. major 2 (10 g/kg feed), P. major 3 (15 g/kg feed). Broiler chicks were fed with these diets for 42 days ad libitum. The serum micronutrients (retinol, α-tocopherol, vitamin D, calcium, magnesium, iron, manganese, and zinc) levels were determined.

Results: Zn levels decreased in PM1 and PM2, but, other vitamins and minerals levels were not affected. Vitamin D decreased in PM2. While vitamin D levels decreased in PM2, there was no alteration in PM1 group.

Conclusion: The supplementation of P. major has affected the serum vitamin D and Zn levels in this study, and should be analyzed for the alterations on the metabolism in subsequent studies.

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RELATIONSHIP BETWEEN LEUKOCYTE VOLUMES AND VITAMIN D LEVELS

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Aim: Vitamin D plays a major role in the regulation of calcium homeostasis, but also in the modulation of the immune response. Vitamin D receptors besides kidney tissue are available in many organs and tissues such as T lymphocytes, brain, pancreas, etc. The aim of this study was to investigate the relationship between vitamin D levels and leukocyte subgroup volumes.

Material and Methods: 25(OH) Vitamin D (Vit D) and leukocyte volume results of 1324 individuals were screened retrospectively from the hospital information system. Vit D (ng/mL) levels were grouped as <20 (Vit D Deficiency, Group I), 20-30 (Vit D Insufficiency, Group II) and >30 (Vit D Sufficiency, Group III). Correlation of Vit D levels with leukocyte volumes and differences between in each leukocyte subgroup volume were investigated.

Results: There was no correlation between Vit D levels and neutrophil, lymphocyte, eosinophil, monocyte subgroup volumes ($p>0.05$). When the difference between the groups was examined, there was a significant difference only between Group I and II (mean lymphocyte volume 87.1 and 87.9, respectively) ($p<0.05$).

Conclusions: Vitamin D has a proapoptotic, antiinflammatory and immunomodulatory effect as well as regulating calcium homeostasis. There was no correlation between Vit D and any leukocyte subgroup volume. There was a statistically significant difference in the lymphocyte volumes between groups of Vit D deficiency and Vit D insufficiency. We believe that further investigation of the possible link between Vit D levels and leukocyte volumes in more specific diagnosed groups associated with Vit D may be appropriate.

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EFFECTS OF SUBSTITUTING PROTEIN COMING FROM SOYBEAN MEAL WITH PEA IN DIET ON SERUM ANTIOXIDANT VITAMIN AND MINERAL LEVELS OF BROILER TURKEY

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Aim: The aim of this study was to determine the effects of substituting protein coming from soybean meal with pea at different levels in broiler diets on serum antıoxıdant vitamin and mineral levels.

Methods: A basal (control) diet was prepared and three experimental diets were established by substituting protein coming from soybean meal with pea in basal diet; 20% (20% Pea) and 40% (40% Pea) of crude protein coming from soybean meal in the basal diet (control) was substituted with protein coming from pea to obtain treatment groups. Chicks were fed these diets as group of 5 chicks within each subgroup (a total of 16 chicks for each treatment group) and experiment lasted 42 days. The blood samples were collected from 12 chicks in each group. Serum Ca, Fe, Mg, Mn, Zn retinol, tocopherol and vitamins D were determined. The serum concentrations of Ca, Fe, Mg, Mn and Zn were determined by means of a UNICAM Atomic Absorption Spectrometer using standard laboratory procedures. The levels of retinol, tocopherol and vitamins D were determined using HPLC (Agilent-1100, Germany).

Results: Serum α-tocopherol, Fe, Mn and Mg levels did not change, but retinol and vitamin D levels increased in P20 and P40 groups. Ca levels significantly increased, while Zn levels decreased in the P20 group.

Conclusions: It can be concluded that levels of pea in soybean meal based diet may affect serum mineral and vitamin levels in a different ways.

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DETERMINATION OF NUTRITIONAL VALUES OF SOME WILD PLANTS CONSUMED IN EASTERN ANATOLIA, TURKEY

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In this study, the usage and nutrient contents of wild plants consumed as food by people in and around Van, eastern Anatolia, Turkey were investigated. It is found that in this region there are wild plants belonging to 10 families which consist of 19 taxa such as Urtica dioica L., Eremurus spectabilis BİEB., Nasturtium officinale R.Br., Tragopogon reticulatus Boiss. & Huet, Rumex tuberosus L. subsp. horizontalis KOCH RECH., Allium akaka S.G.Gmel. ex Schult. & Schult.f, Chaerophyllum macropodum Boiss, Thymus fallax Fisch. & C.A.Mey, Malva neglecta Wallr., Allium shatakiense Rech. f., Ornithogalum oligophyllum E. D. CLARKE, Ferula rigidula Fisch. ex DC., Heracleum persicum Desf, Gundelia tournefortii L., Rheum ribes L., Prangos ferulacea (L.) Lindl, Mentha longifolia (L.) HUDSON subsp. longifolia (L) HUDSON, Plantago major L. subsp. intermedia (Gilib.) Lange, Eryngium billardieri F. Delaroche. In the study, the wild plants were analyzed for their macro- and microelement concentrations (N, P, K, Mg, Ca, Fe, Zn and Mn). Additionally, some food quality aspects (dry matter, moisture contents, total ash contents and protein contents) were also evaluated in the plant samples. It can be concluded that analyzed wild plants had great diversity of mineral compositions and other food quality properties and had a richer content than some leaf consumed culture species.

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TOPIC VARIA

SERUM LEVELS OF MALONDIALDEHYDE IN PATIENTS WITH CHRONIC LIVER DISEASE

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Aim: Oxidative stress is described as an impaired balance between the oxidant and antioxidant systems in the cells. More important oxidants are cytochrome p450 and malondialdehyde (MDA). MDA is a typical aldehydic product of lipid peroxidation of polyunsaturated fatty acids. The aim of the present study is to evaluate serum levels of MDA in patients with liver cirrhosis, chronic hepatitis, and healthy controls.

Methods: This cross-sectional study included 84 participants, categorized into three groups: 30 patients with liver cirrhosis, mean age 63.53 ± 11.59 years; 25 patients with chronic hepatitis, mean age 49.96 ± 15.74 years; and 29 healthy controls, mean age 35.62 ± 13.05 years. Data analysis was carried out with the Statistical Package for the Social Sciences (SPSS), Version 24. Differences of $P<0.05$ were considered statistically significant.

Results: The post hoc analysis with Dunnett's T3 procedure showed that cirrhosis patients had a significantly higher mean MDA value (192.16 ± 62.43 nmol/ml) than the healthy controls (65.84±17.31 nmol/ml), $p < 0.001$. The hepatitis patients also had a significantly higher MDA mean level (158.34±53.59 nmol/ml) as compared to the healthy controls, $p < 0.001$. Of the two patient groups, the cirrhosis group had a higher MDA level than the hepatitis patients (mean difference = 33.81 nmol/ml), but the difference was not statistically significant, $p = 0.101$.

Conclusions: Both patients' groups show significantly higher MDA levels than the control. This result suggest that oxidative stress could play role in chronic liver disease.

The work was supported by the MU-Plovdiv, project NO-4/2017.

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CORRELATION BETWEEN PLATELET COUNT AS A NONINVASIVE MARKER AND LIVER TESTS

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Liver blood tests are one of the most frequently screening blood tests as routine analysis, suspected liver disease or its monitoring. Focusing on noninvasive system has become a common interest, so knowledge of how to correctly analyse liver enzymes is very essential. Thrombopoietin (TPO) is a glycoprotein hormone produced by the liver and kidneys which regulates the production of platelets (PLT). TPO production

in humans is dependent on functional liver cell mass and it is reduced when liver cell mass is severely damaged. The aim of this study is to establish the correlation between platelet count (PLT) as parameter from a differential blood test with liver enzymes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), lactate dehydrogenase (LDH) from biochemical blood test.

The case-control study was conducted on 242 patients with suspected liver disease, during a period of one year. The patient with high ALT and AST were taken under observation. The PLT count was compared with these parameters.

According to the Pearson correlation coefficient (r), there is significant correlation ($p>0.05$) between activity of ALT, AST, GGT and PLT. There is no correlation between LDH, ALP and PLT. In terms of results interpretation in clinical biochemistry, such correlation indicates that the increase of ALT, AST and GGT leads to decrease of the PLT value.

In conclusion, hematological changes in complete blood count (decreased PLT) can be an early noninvasive diagnostic marker for liver disease. With simply routine analyses it is possible to see the health status of the liver.

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EOSINOPHILS IN NASAL MUCOSA AND DIFFERENTIAL DIAGNOSIS OF UPPER RESPIRATORY SYMPTOMS

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Objective. Upper respiratory symptoms such as sneezing, cough, nasal secretion, and nasal congestion are a common pathology in everyday medical practice, especially in urban areas. Proper differentiation of the etiology of these symptoms, which may be of an infective, allergic or vasomotor nature, is crucial for the therapeutic approach in their treatment.

Aim: To determine the value of laboratory finding of eosinophils in the nasal mucosa by differentiating the etiology of upper respiratory symptoms.

Material and methods: A total of 2220 patients with upper respiratory symptoms were examined. Swabs were taken from patients' nasal epithelium and a preparation on microscopic glass was made. The procedures were colored according to the Pappenheim method.

Results: In 735 patients or 33.10% of the examinees, eosinophils were found in the nasal mucous membrane, which clearly defines allergic etiology in almost one- third of the patients with upper respiratory symptoms.

Conclusion: Finding eosinophils in the nasal epithelium is a simple, fast, non-invasive, and cheap laboratory method that distinguishes allergic from non-allergic etiologies of upper respiratory symptoms and therefore it traces a proper therapeutic approach.

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CLINICAL SIGNIFICANCE OF ELEVATED HBF IN ADULT PATIENTS HOSPITALIZED IN UNIVERSITY HOSPITAL CENTRE "MOTHER TERESA"

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Background/Aim. Fetal hemoglobin (HbF α2γ2) synthesis declines during the third trimester and is gradually replaced to adult hemoglobin (HbA α2β2) resulting in less than 1% HbF in normal adults. Our aim was to create a profile of acquired or inherited disorders in adult patients with elevated HbF values.

Methods. Whole K2-EDTA blood samples were analysed by Alkaline Gel Electrophoresis, Sebia Hydrasis. Data from patients hospitalized in the University Hospital Centre "Mother Theresa" from January 2015 to January 2018 were analyzed and adult patients with abnormal HbF values were selected as our subjects.

Results and Discussion. A total of 124 patients presented with elevated HbF in hemoglobin electrophoresis performed in our laboratory. Sixty-nine (55.6%) 69 patients had HbF above 10% and 44.4% (55 patients) had HbF less than 10%. In HbF>10% category, 7 patients (10%) had thalassemia major, 47 patients (68%) had drepanocytosis (68% with normal HbA2, 32% with HbA2>3.5%). Fifteen patients (22%) showed HbF values 10-20% with possible diagnosis HPFH, (δ-β-)-thalassemia carriers or sardinian (δ-β) thalassemia heterozygotes. In HbF<10% category, 29 patients (53%) had thalassemia minor, 2 patients (4%) had borderline HbA2, which diagnosis should be determined between carriers of β-thalassemia silent mutations, α-gene triple locus or δ-β-thalassemia heterozygotes and 24 patients (43%) had HbA2<3.2%. Such values might be due to iron-deficiency anemia, δ-globin anomaly coexistence, aplastic anemia, acute/chronic myeloid leukemia, myelodysplasia, HbH-β+thalassemia trait, etc.

Conclusion. HbF is an important diagnostic parameter in various hematological disorders that should be known by clinicians. Elevated HbF with HbA2<3.2% requires further investigation.

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THE MOST FREQUENT TYPES OF FOOD THAT CAUSE FOOD INTOLERANCE IN OUR POPULATION

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Introduction: The intestinal wall can be damaged and become permeable as a result of stress, infection or medication and large quantities of undigested foods can make their way into the bloodstream. The immune system falsely considers these as harmful substances, and produces IgG antibodies. IgG fix to the food proteins (antigens) forming circulating immune complexes. The complement system then initiates the destruction of the CIC, followed by a low-grade inflammatory reaction. A regular intake of the concerned food then causes a chronic inflammation (with unspecific and specific symptoms). It is very difficult to pinpoint which food causes problems because of the delayed appearance.

Aim: This is a retrospective study of the most frequent types of food with IgG immune response detected in our population.

Material and methods: We analyzed 160 sera from randomized patients aged 18 to 65 years in a 18-month-period. Food-screen detection of total IgG antibodies was performed with standard ELISA method with RIDASCREEN Spec IgG, r-Biopharm, Germany. IgG titre was quantified in several groups (negative, low, increased and high).

Results: The percentage for the commonest type of food was: cow's milk (increased-i 10.6%, high-h 44.4%), cow sour milk (i-11.9%, h-41.9%), goat cheese (i-16.3%, h-23.1%), sheep cheese (i-15.0%, h-25.6%), eggs (i-18.1%, h- 45.5%), wheat (i-26.3%, h-36.3%), gluten (i-22.5%, h-48,8%), almond (i-15.0%, h-21.9%), black pepper (i-37.5%, h-29.4%) and vanilla (i-11.3%, h-32.5%).

Conclusion: Out of the total of 90 types of foods, our patients most frequently showed intolerance towards: milk and milk products, nuts, eggs, gluten and spices. Gluten (71.3% increased and high titer of antibodies) is one of the most common causes of food intolerance.

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CASE REPORT OF IgG FOOD INTOLERANCE

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Violeta Soleva, Pecko Desoski

PHU Avicena laboratory

IgG food intolerance (type III food allergy) is when the immune system produces specific IgG antibodies after consumption of a trigger food. These IgG antibodies can lead to inflammatory processes causing specific (e. g. migraine, irritable bowel syndrome, psoriasis, eczema) or unspecific (e.g. fatigue, retention of water, variation of body weight) symptoms. An IgG foodscreen test helps to limit the suspecting food. After this, testing the recommendation is to avoid foods with elevated IgG titre 10-12 weeks. A 9-year-old twin child was complaining on hair loss and discomfort in the abdomen. He has been regularly vaccinated. He was in a good general condition without any illness or allergy. Dermatologically, there were no scalp parasites or microspores. He was examined for all biochemical parameters for autoimmune diseases (ANA, ANCA, anti dsDNA, RF...), enzymes (AST, ALT) and total IgE. The results were negative. Next, the pediatrician suggested him for IgG food intolerance testing. The IgG foodscreen plate contained 90 foods. The IgG titre was very high for hazelnuts, wheat and gluten; high for cow's milk, cow's sour milk, sheep's cheese, eggs and peanuts, and incresed IgG titre for cow's cheese, goat's cheese, sunflower seeds, pepper, vanilla and orange. After obtaining these results the child's mother said that the patient had consumed products that contained hazelnuts (chocolates with hazelnuts) for a long period, and at the same time it coincided with a more intense hair loss. We gave him recommendations for avoiding foods with high IgG titre for 3 months and including foods with increased IgG values in a 4-day rotating cycle. After 6 months, the child came to a control visit. Anamnestic data, given by his mother, was that the child had complied with the recommendations and there were visible changes in the scalp and hair growth. After 6 months, the IgG titre of foods with high and elevated IgG values were significantly decreased. In accordance with the obtained control results, a visible clinical changes were observed.

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PREVALENCE OF VIRAL HEPATITIS B IN HEALTH PERSONNEL IN TIRANA OCTOBER 2017 - APRIL 2018

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Introduction: Sexually transmitted infections (STI) are one of the biggest health problems throughout the world. Viral hepatitis makes up a large percentage of STI. Our country is among the endemic places where the expressed form of the infection is hepatitis B virus.

Aim: To determine the specific percentage of viral hepatitis in health personnel in Tirana.

Material and Method: This paper includes all health personnel that have come to the laboratory of VCT (Voluntary Counselling and Testing) to undergo testing from October 2017 – April 2018. The immune chromatography method was used in the membrane for qualitative detection of superficial antigen of hepatitis B virus. ELISA method was used to confirm positive cases.

Results: The examinations showed that 3.9% of the serums taken from the health personnel were positive for HBsAg. From the examined individuals 5.1% were positive for HBsAg.

Conclusions: Prevalence of hepatitis in Tirana is at high level among the population and among the health personnel. Viral hepatitis is still a concern for the public health. Ages between 25 and 45 are the most affected.

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EVALUATION OF TWO NEW 5 DIFFERENTIAL HEMATOLOGY ANALYZERS – YUMIZEN H500 AND YUMIZEN H550 (HORIBA MEDICAL)

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The aim of the study is to evaluate the analytical performance of two new hematology analyzers – Yumizen H500 and Yumizen H550 (Horiba Medical). In the study we compared both Yumizen analysers with Pentra DX120 (Horiba Medical). Furthermore we performed testing of theire accuracy. Samples and Methods: The method verification procedure (confirmation of manufacturer's data) is in accordance with the CLSI Protocol EP 15 A2 (Clinical and Laboratory Standards Institute). For the comparison study venous obtained K2EDTA samples (normal and pathological) were analysed, using three hematological analysers - Yumizen H500, Yumizen H550 and Pentra DX120. As statistical methods we used correlation and regression analysis to assess the performance of the new analysers in comparision to our reference analyzer Pentra DX120.

We compared the WBC count, RBC count, PLT count, HGB measurement and the 5-diff leukocyte count. To assess the whitin-run precision we used 3 patients samples, normal and pathological. The between-run precision we evaluated using the three quality materials - low, normal and high, which we analyzed daily as a part of the internal quality assurance in the laboratory.

Results: All CV% , that we obtained as a results of the precision studies were a little lower than those, declared by the manufacture for Yumizen H500 and Yumizen H550. The correlation coefficients were between 0.9982 for WBC and 0.967 for EOS#.

Conclusions: According to the results we find the performance characteristics of Yumizen H500 and Yumizen H550 highly acceptable. Both analysers use the same set of three reagents. They report 27 parameters, using 20 µl sample. Yumizen H550 has the advantage of an automatic rack mixing system.

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ASSESSMENT OF HIT-AB WITH PLATELET FACTOR 4 (HIT-AB-PF4-H)IN PATIENTS WITH CARDIOPULMONARY SURGERY

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Introduction: Postoperative cardiac patience may develope heparin/PF4 antibodies in high percent, but the incidence of isolated HIT remains low. In this study we assess the role of HIT-Ab-PF4-H in the clinical decision of HIT.

Method: We used a fully automated latex enhanced immunoassay for quantitative detection of HIT-Ab-PF4-H on the ACL TOP 500 analyzer. According to protocol, cut- off value for HIT-Ab-PF4-H was 1.0 U/m.

Results. Three patients who received a conventional heparin therapy were evaluated in the study: A 71-years old male, CABGx1 (LAD-LIMA), 4Ts score, 7 points;heparin exposition for 7 days; platelet count decrease to 56x10^9/l, HIT-Ab-PF4-H score 7.3 U/ml. A 72-years old male, CABGx2 (LAD-LIMA), 4Ts score, 7 points; heparin exposition for 6 days; platelet count decrease to 86x10^9/l, HIT-Ab-PF4-H score 2.3 U/ml. A 20-years old female, Marfan syndrome, scoliosis, anemic syndrome, mitral insuficiency high grade, without previous history of heparine therapy, MVR (carbomedics31), 4S score, 1 points; heparin exposition for 14 days; without platelet count decrease, HIT-Ab-PF4-H score 1.3 U/ml

Conclusions: The method for detection of HIT-Ab-PF4-H is a rapid, on-demand laboratory assay that retain high diagnostic sensitivity. However, a positive result may not correlate with clinically significant antibodies or incrised risk of thrombosis; the appointment of the test should be after scoring system to determine the probability of HIT (4Ts) and note the need of functional assay (SRA) that may provide greater specifity.

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USING SERUM PROTEIN ELECTROPHORESIS IN VETERINARY CLINICAL LABORATORY MEDICINE

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Blood serum proteins perform many important physiological functions in the organism. They are present in varying amounts in serum under different physiological and pathological conditions. Serum proteins vary quantitatively and qualitatively depending on physiological (age, temperature, pregnancy, nutrition, sex, environment, etc.), genetic and disease factors.

Electrophoresis is a suitable separation technique for monitoring changes in serum protein fractions. Albumin and globulins (α1, α2, β1, β2, γ) are the main fractions in normal serum electrophoresis. The electrophoretic profile of serum proteins can be affected by various conditions. Detection of abnormal serum protein profiles can be used to diagnose various diseases such as infectious diseases, liver diseases, acute inflammatory and proliferative cases, tissue damages and many other physiological disorders.

Albumin, which plays a role in the transport of various lipophilic compounds and cations, can be thought of as an endogenous amino acid storage and is markedly reduced in different diseases and at different times.

The levels of α-globulin (α1, α2, macroglobulin, haptoglobin, etc.) increase more in trauma. Changes in lipoprotein metabolism cause changes in the β-globulin fraction. Immune system proteins are in the γ-globulin region. Total serum protein values and changes in fractional distribution and A/G ratio might be the first indication of protein abnormality.

Electrophoretic analysis of serum proteins has been performed in clinical laboratories for many years in human laboratory medicine. This presentation will discuss the utility of electrophoretic separation of serum proteins in the diagnosis of animal health disorders and their application in veterinary laboratory medicine.

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THE PRESENCE AND PREVALENCE OF ENTEROCOCCUS FAECALIS AND ENTEROCOCCUS FAECIUM STRAINS IN URINE AND STOOL SAMPLES

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[2] Mersin University, Technical Sciences Vocational School, Mersin, Turkey

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In this study, it was aimed to investigate the presence and the prevalence of Enterococcus faecalis and Enterococcus faecium strains isolated from the urine and stool samples. A total of 500 routine urine and feces samples were used for testing as the study materials, and a total of 349 Enterococcus spp. were collected for investigation. For the isolation, blood agar and bile esculin agar were used. DNA isolations of the 24-hour growth cultures of possible enterococci were carried out using a DNA isolation kit. Out of 350 routine urine and 150 stool samples taken with the approval of the patients, 235 (67.1%) and 114 (76%) Enterococcus spp. were isolated respectively. Using the multiplex PCR method with species specific primers, 136 (57.8%) of urine and 22 (19.2%) of stool originated enterococcal strains were identified as Enterococcus faecalis; on the other hand, 17 (7.2%) of urine and 61 (53.5%) of stool originated enterococci were identified as Enterococcus faecium. As a result of the study in Van, Turkey, the isolation rate of Enterococcus faecalis and Enterococcus faecium strains were found to be lower than other regions.

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ORGANIZATION OF WORK IN LABORATORIES IN THE REPUBLIC OF MACEDONIA

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Within the framework of the organization of the laboratories and the work that takes place in them, as a basic rule, it is stated that each laboratory should have sufficient space, equipment and staff as well as possibilities for performing the required work with optimal capacity, efficiency, quality and safety.

The main goal of the abstract is the problem of organizing the work of laboratories as health systems that serve to provide health services, but also for achieving health goals.

Initially, we put the accent on the space, the equipment, and especially the expertise of the staff who performed the laboratory work.

For this purpose, we selected the comparative analysis as a method of researching this problem, in order to compare the organization and the way the laboratories operate in Macedonia compared to the way they work in laboratories in other countries, namely Turkey and Slovenia.

As a result of the comparative analysis as a method of research we can determine all similarities and differences in terms of organization and work in the laboratories.

Regarding the organization and the way of work in the laboratories, we would like to conclude that certain measures should be taken by the state in relation to the recruitment of professional staff. An annual plan should be drawn up with which a plan for laboratory staff to attend trainings more often in order to increase their expertise (necessary for the job).

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Estradiol
Testosterone
free Testosterone
DHEA-S
Progesterone
free Estriol
17-OH Progesterone
AMH
SHBG
Androstenedione
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TORCH
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Toxo IgM
Rubella IgG
Rubella IgM
CMV IgG
CMV IgM
HSV-1/2 IgG
HSV-1/2 IgM
HSV-2 IgG
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***HSV-1 IgG**
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Tumor Markers
Ferritin
AFP
CEA
Total PSA
f-PSA
CA 125
CA 15-3
CA 19-9
HCG/β-HCG
Tg(Thyroglobulin)
PAP
CA 50
CYFRA 21-1
CA 242
CA 72-4
NSE
S-100
SCCA
TPA-snibe
Pepsinogen I
Pepsinogen II
Gastrin-17
H.pylori IgG
β_2-MG
Calcitonin
Proinsulin
H.pylori IgG
H.pylori IgA
H.pylori IgM
ProGRP
HE4
HER-2
***AFP-L3**
***PIVKA-II**

Bone Metabolism
Calcitonin
Osteocalcin
25-OH Vitamin D
Intact PTH
***β-CTX**
***PINP**

Autoimmune
TGA(Anti-Tg)
Anti-TPO
TRAb
TMA
ICA
IAA(Anti Insulin)
GAD 65
Anti-IA2
Anti-dsDNA IgG
ANA Screen
ENA Screen
Anti-Sm IgG
Anti-Rib-P IgG
Anti-Scl-70 IgG
Anti-Centromeres IgG
Anti-Jo-1 IgG
Anti-M2-3E IgG
Anti-Histone IgG
Anti-nRNP/Sm IgG
Anti-SS-B IgG
Anti-SS-A IgG
***Anti-CCP**

Infectious Disease
HBsAg
Anti-HBs
HBeAg
Anti-HBe
Anti-HBc
Anti-HCV
Syphilis
Anti-HAV
HAV IgM
HIV p24 Ag
HIV Ab/Ag combi
Chagas
HTLV I+II
H.pylori IgG
H.pylori IgA
H.pylori IgM
***Anti-HBc IgM**

Cardiac
CK-MB
Troponin I
Myoglobin
NT-proBNP
Aldosterone
Angiotensin I
Angiotensin II
D-Dimer
LP-PLA2
hs-cTnI
hs-CRP
Direct Renin
H-FABP
***BNP**

Hepatic Fibrosis
HA
PIIIP N-P
C IV
Laminin
Cholyglycine

Drug Monitoring
Digoxin
CSA (Cyclosporine A)
FK 506 (Tacrolimus)

EBV
EBV EA IgG
EBV EA IgA
EBV VCA IgG
EBV VCA IgM
EBV VCA IgA
EBV NA IgG
EBV NA IgA

Prenatal Screening
AFP (Prenatal Screening)
Free β–HCG
PAPP-A
HCG/β–HCG
free Estriol

Anemia
Vitamin B12
Ferritin
Folate (FA)

Glyco Metabolism
C-Peptide
Insulin
ICA
IAA(Anti Insulin)
Proinsulin
GAD 65
Anti-IA2

Inflammation Monitoring
hs-CRP
PCT(Procalcitonin)
IL- 6

Immunoglobulin
IgM
IgA
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